The effect of Lewis acids on the intramolecular Diels–Alder reaction of the furan diene

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A general method is described for effecting the intramolecular Diels–Alder reaction of the furan diene in which the side arm connecting the diene to the dienophile contains four carbon atoms. The use of 1.1 equivalents of methylaluminum dichloride at −78°C for 2–8 h shifts the Diels–Alder equilibrium towards the products and provides the oxatricyclo adducts in good to excellent yield. Catalytic quantities of methylaluminum dichloride (10 mol%) provided a higher quantity of adduct than excess Lewis acid when the enone was substituted with alkyl groups. The scope was extended to include a precursor containing a five carbon atom side arm, and two examples containing acetylenic dienophiles that were activated by a carbonyl moiety on the side arm. Precursors having a four carbon atom side arm provided only oxatricyclo adducts having the side arm *syn* to the oxygen bridge. The assignment of the stereochemistry of the oxatricyclo adducts is discussed in detail.

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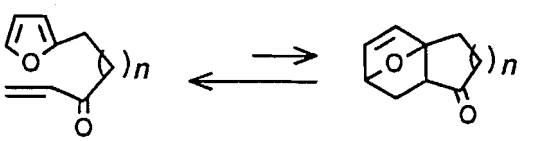
On décrit une méthode générale d'effectuer une réaction intramoléculaire de Diels–Alder avec des dièmes furaniques portant une chaîne latérale de quatre atomes de carbone qui relie le dième au diénophile. L'utilisation de 1,1 équivalent de dichlorure de méthylaluminium, à −78°C, pendant 2–8 h, déplace l'equilibre de Diels–Alder vers les produits et les adduits oxatricyclo avec des rendements allant de bons à excellents. Lorsqu'on substitue l'énone avec des groupes alkyles, les quantités d'adduit formées lorsqu'on utilise des quantités catalytiques de dichlorure de méthylaluminium (10 mol%) sont plus grandes que celles obtenues avec un excès d'acide de Lewis. On a étendu le champ d'application à un précurseur contenant une chaîne latérale de cinq atomes de carbone et à deux exemples contenant des diénophiles acétyléniques activés par une portion carbonyle sur la chaîne latérale. Les précurseurs portant une chaîne latérale contenant quatre atomes de carbone ne fournissent que les adduits oxatricyclo dans lesquels la chaîne latérale est *syn* par rapport au pont oxygène. On discute en détail de l'attribution de la stéréochimie des adduits oxatricyclo.

[Traduit par la rédaction]

The intramolecular Diels–Alder (IMDA) reaction is a widely utilized synthetic strategy for the simultaneous formation of two rings with high stereo- and regio-control (1). The use of a furan moiety as the diene component in the IMDA reaction leads to the creation of an oxygenated cyclohexane ring in a rigid cycloadduct that has potential application for the synthesis of natural products. The intramolecular Diels–Alder reaction of the furan diene (IMDAF) has been studied extensively both when the tether connecting the diene and dienophile consists of three carbon atoms (1, 2), and when the tether contains a heteroatom and is either three (n = 1) or four (n = 2) atoms in length (eq. 1) (1, 3). The IMDAF reaction of precursors that have a side arm containing four (n = 2) (1, 4) or five (n = 3) (1, 5) carbon atoms have been studied to a lesser extent, and are generally reported to have equilibria that lie toward starting material. Methods employed to overcome the unfavourable equilibrium have included heat (4*a*), β-cyclodextrin (6), aqueous solutions (4*h*, 7), substituted side arms (3*g*, 3*h*, 4*k*, 4*m*, 4*n*, 5*b*, 8) and high pressure (4*b*, 4*c*, 4*j*). The success of these methods has been variable. The first four methods have produced increased starting material:adduct (SM:A) ratios for precursors with unsubstituted dienophiles but usually required long reaction times (2–14 days). High pressure (1.0–1.2 GPa) has been successful in overcoming the unfavourable equilibrium with both unsubstituted and substituted dienophiles; however, the isolated yields of the adducts have been poor, the reaction scale is limited, and access to specialized equipment is necessary. We therefore sought a generally applicable method for performing the IMDAF reaction that would overcome these limitations.

[1] 

***n*=1 (a CH_2 may be substituted by an S, O, or N atom)**
***n*=2 (a CH_2 may be substituted by an O or N atom)**

Lewis acids have been used extensively in the *intermolecular* Diels–Alder reaction of the furan diene (9) to increase both the regioselectivity and the rate of reaction. Lewis acids have also been used to accelerate the rate of the *intramolecular* Diels–Alder reaction (10); however, their successful use in the IMDAF reaction (4*i*, 5*a*, 11) has been limited to only two reports: one employing an internally coordinated magnesium salt (12), and the second an application of zinc iodide (13). The paucity of examples of Lewis acid-mediated IMDAF reactions may be due to competing side reactions such as: (*a*) the polymerization of the furan ring or the dienophile (14), (*b*) the susceptibility of the furan ring to Friedel–Crafts-type reactions (14), and (*c*) the aromatization of the oxatricyclo adducts (15). We recently reported that the IMDAF reaction, in which the side arm contained four or five carbon atoms, is accelerated by the Lewis acid methylaluminum dichloride at low temperatures to provide the oxatricyclo adducts in good to excellent yield (16). We herein provide a full account of this work.

Preparation of IMDAF precursors ***1–17***

Precursors **1–8** were prepared as outlined in Scheme 1. Lithiation of either furan **18** or 2-methylfuran **19** under

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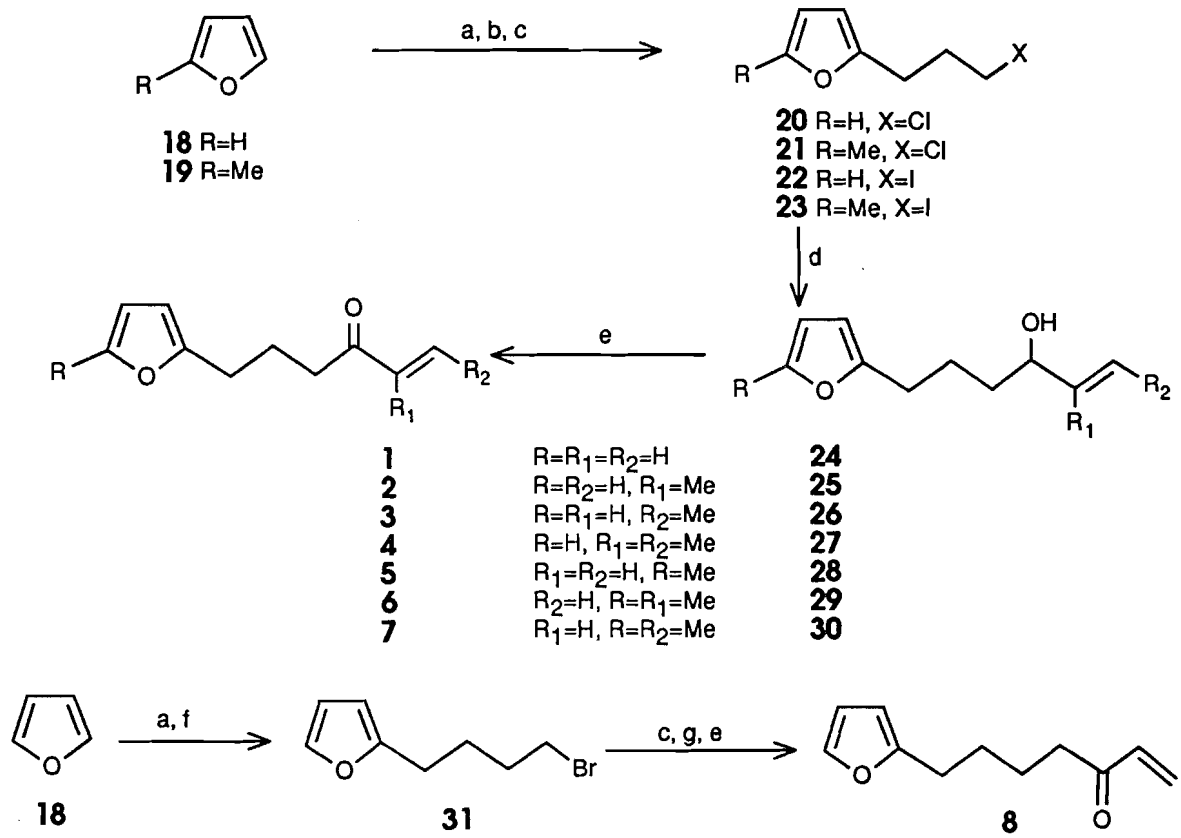


Reagents: (a) 1.2 equiv. n-BuLi, THF, 0°C, 1.5h; (b) 1-bromo-3-chloropropane; (c) NaI, acetone, reflux; (d) 2.2 equiv. t-BuLi, Et_2O, -78°C; then, acrolein, methacrolein, crotonaldehyde or tiglic aldehyde; (e) Swern [O]; (f) 1,4-dibromobutane; (g) 2.2 equiv. t-BuLi, Et_2O, -78°C; then acrolein

SCHEME 1

standard conditions (17) followed by trapping of the resultant anion with 1-bromo-3-chloropropane, afforded alkylated furans **20** (63%) and **21** (95%), respectively. Conversion of the chlorides **20** and **21** into the iodides **22** and **23** was accomplished in excellent yield under Finkelstein conditions (18). Halogen–metal exchange of the iodides **22** and **23** with *tert*-butyllithium (19) followed by quenching of the resulting carbanion with acrolein, methacrolein, crotonaldehyde, or tiglic aldehyde provided allylic alcohols **24–30**. Swern oxidation (20) of the allylic alcohols **24–30** yielded the IMDAF precursors **1–7** respectively. Furan **8** was prepared by reaction of the anion of furan **18** with 1,4-dibromobutane to provide bromide **31**, which was converted to furan **8** by the identical sequence described above (Scheme 1).

The synthesis of IMDAF precursors **9–15** is summarized in Scheme 2. Ismail and Hoffman (21) have reported that Friedel–Crafts alkylation of either furan **18** or 2-methylfuran **19** with 4-methyl-2-oxo-3-pentenenitrile **32** (22) in the presence of aluminum trichloride in benzene provided esters **33** and **34**, respectively, in reasonable yield after the reaction mixture was quenched with methanol. Our attempts to repeat this reaction provided esters **33** and **34** in poor yield (<20%) due to the competing Friedel–Crafts alkylation of the solvent benzene. Changing the solvent to carbon disulfide provided esters **33** and **34** in 30 and 66% yield, respectively. The yield of ester **33** was diminished due the formation of the 2,5-dialkylated product **35**. Attempts to prevent formation of **35** by blocking one α-site of furan with a *tert*-butyldimethylsilyl moiety were unsuccessful; the silylated furan did not undergo Friedel–Crafts reactions when subjected to a variety of Friedel–Crafts conditions.

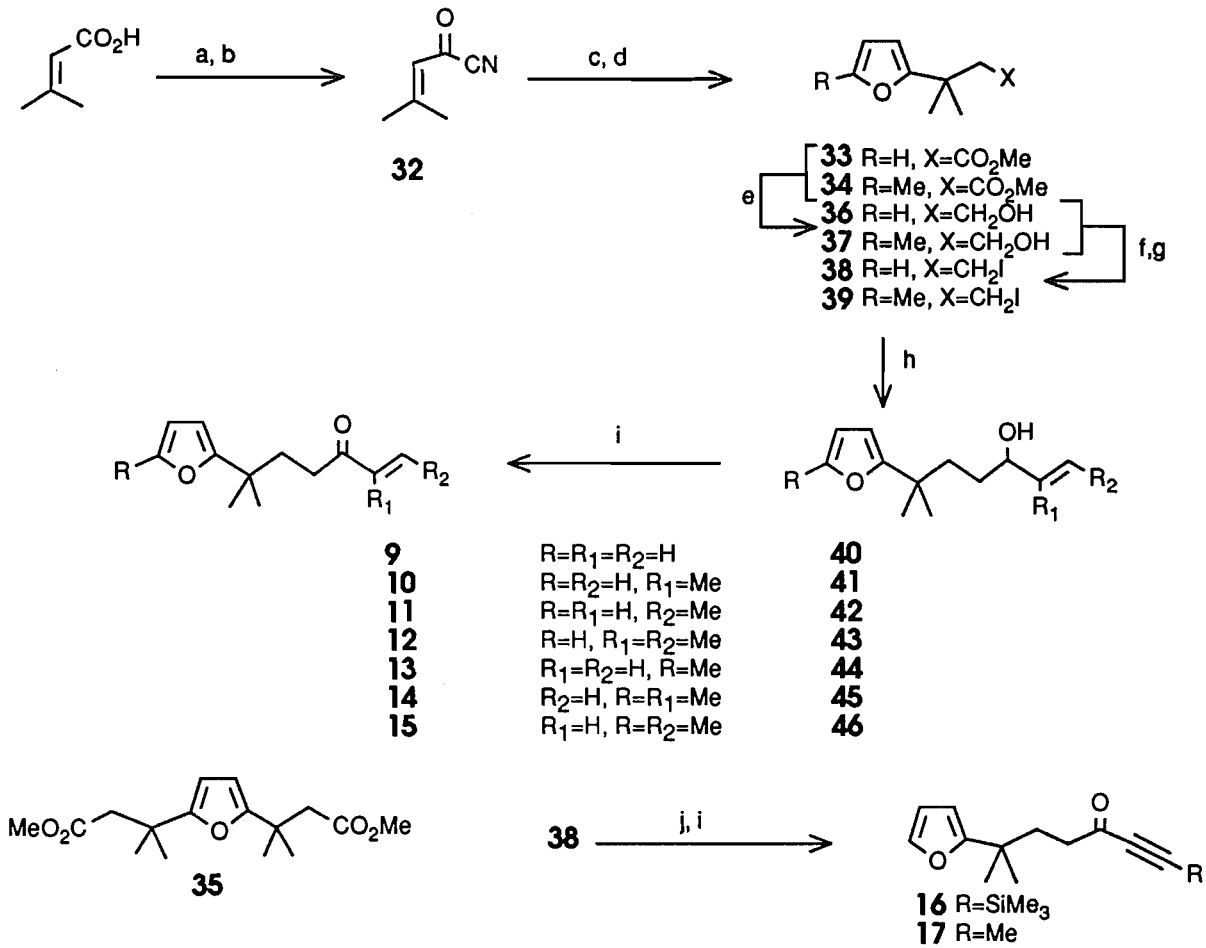
Although Lipshutz and co-workers (23*a*) reported successful 1,4 additions of the higher-order cyanocuprate of 2-lithiofuran to α,β-unsaturated ketones, we were unsuccessful in effecting the same reaction on 3-methyl-2-butenal, methyl 3-methyl-2-butenoate, or dimethyl isopropylidenemalonate. The failure of these reactions may be due to both the low reactivity of the cuprate reagent (23*b*), and to the hindered nature of the position to be attacked.

Reduction of esters **33** and **34** with lithium aluminum hydride provided alcohols **36** and **37**, respectively, which were converted to the corresponding iodides **38** and **39** via the tosylates (18). The iodides **38** and **39** were then converted to precursors **9–12** and **13–15** via: (*a*) halogen–metal exchange, (*b*) quenching the anion with an α,β-unsaturated aldehyde to give allylic alcohols **40–46**, and (*c*) Swern oxidation.

The acetylenic precursors were prepared by treating the anion formed by halogen–metal exchange of iodide **38** with either 3-(trimethylsilyl)propynal **47** (24) or 2-butynal **48** (Scheme 2) (25). Swern oxidation provided compounds **16** and **17** in good yield.

Results and discussion

Compound **2** was treated with a number of Lewis acids (26) that had been reported to accelerate both inter- (9*c*, 27)



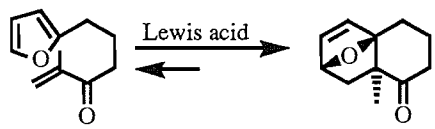
Reagents: (a) oxalyl choride, hexane; (b) CuCN, MeCN; (c) 0.25 equiv. $AlCl_3$, CS_2, furan **18** or 2-methylfuran **19**; (d) MeOH; (e) $LiAlH_4$, Et_2O; (f) TsCl, DMAP, CH_2Cl_2; (g) NaI, acetone, reflux; (h) 2.2 equiv. t-BuLi, Et_2O, -78°C; then acrolein, methacrolein, crotonaldehyde, or tiglic aldehyde; (i) Swern [O]; (j) 2.2 equiv.t-BuLi, Et_2O, -78°C; then TMSC≡CCHO (**47**) or MeC≡CCHO (**48**).

SCHEME 2

and intra-molecular (10*m*, 13, 28) Diels–Alder reactions (Table 1). Compound **2** was chosen for this model study since it had previously shown reluctance to undergo the IMDAF reaction when treated with Florisil either in methylene chloride or aqueous 2.0 M $CaCl_2$ solutions (entries 9 and 10) (4*h*). In each example, 1.1 equivalents of Lewis acid was added to a dilute solution (0.02–0.03 M) of compound **2** in methylene chloride at −78°C. Aliquots were removed from the reaction mixture and their ^{1}H NMR spectra were measured. The reaction was stirred at a particular temperature until there was no further change in the starting material to adduct (SM:A) ratio by ^{1}H NMR. The reaction was then warmed another 10 or 15°C, and the process repeated until a temperature was reached at which decomposition was detected. The aliquots removed from the reaction mixture were quenched with cold 10% sodium bicarbonate to prevent re-equilibration and to neutralize acidic by-products. The SM:A ratios were measured by integration of the ^{1}H NMR spectrum of the crude reaction mixture, in particular by comparison of the integral of the vinyl protons of the adduct **50** (δ 6.48 and 6.14) and that due to the β-furan protons of the starting material **2** (δ 6.28 and 6.00).

The results are summarized in Table 1. Zinc iodide (entry 1) was the least effective Lewis acid examined, which was surprising in light of its proven synthetic utility for accelerating both the intermolecular Diels–Alder reaction of the furan diene (9*c*) and an IMDAF reaction in which the side arm contained three carbon atoms (13). Although some adduct was produced within 3 h at room temperature, the equilibrium still favoured starting material. The ratio of SM:A did not change significantly after 39 h and decomposition products were detected by ^{1}H NMR. These findings are attributed to the unfavourable heterogeneous nature of the reaction mixture when zinc iodide is used. Tin(IV) chloride (entry 2) provided a favourable SM:A ratio of 24:76 within 1 h at −78°C; however, extensive decomposition was also observed (by ^{1}H NMR). The remaining Lewis acids (entries 3–8) provided SM:A ratios favouring adduct after only 2 h at either −78 or −50°C; decomposition was evident at temperatures above −50°C for all Lewis acids examined. The yields of the adduct were in excess of 95% (based on recovered starting material) after flash chromatography (29), indicating that decomposition below −50°C was insignificant. For ease of handling and reaction work-up, methylaluminum dichloride was chosen as the Lewis acid to continue the study.

TABLE 1. Effect of various Lewis acids on the IMDAF reaction of compound **2**



2 **50**

	Lewis acid	Conditions	2:50 Ratio
1	ZnI_2	1 h, −78°C	100:0
		3 h, r.t.	69:31
		39 h, r.t.	65:35[a]
2	$SnCl_4$	1 h, −78°C	24:76[b]
3	$BF_3 \cdot Et_2O$	2.5 h, −78°C	28:72
		3.5 h, −50°C	28:72[c]
4	$TiCl_4$:$Ti(O^iPr)_4$	4.5 h, −78°C	32.68
		2.5 h, −50°C	32.68[d]
5	$EtAlCl_2$	2.5 h, −78°C	35:65
		2.5 h, −50°C	35:65[d]
6	$MeAlCl_2$	2.5 h, −78°C	35:65
		2.5 h, −50°C	35:65[d]
7	Et_2AlCl	2.5 h, −50°C	35:65
8	Me_2AlCl	2.5 h, −50°C	32:68
9	Florisil/CH_2Cl_2	14 days, r.t. or 40°C	100:0
10	2.0 M $CaCl_2$	4 days, r.t.	50:50

[a]Some decomposition after 64 h (by ^{1}H NMR).
[b]Extensive decomposition (by ^{1}H NMR).
[c]Some decomposition after 3.5 h (by ^{1}H NMR).
[d]Decomposition occurred above −50°C.

The effect of solvent on the Lewis acid-mediated IMDAF reaction was also examined. Treatment of compound **2** in hexane with methylaluminum dichloride resulted in the formation of a gummy precipitate. Both ^{1}H NMR and TLC indicated that no IMDAF reaction had occurred. Toluene was also unsuitable as a solvent because many unidentified products formed even at −78°C. All subsequent reactions were therefore performed in methylene chloride.

The results from treating precursors **1**–**7** and **9**–**15** with methylaluminum dichloride at −78°C are summarized in Tables 2 and 3 respectively. Previous results from our lab (*4h*) using Florisil are also included for comparison purposes. Several observations are noteworthy. The use of 1.1 equivalents of methylaluminum dichloride with precursors **1**, **2**, **5**, and **6** provided their corresponding oxatricyclo adducts in excellent yields. Both compounds **1** and **5**, which have unsubstituted dienophiles, provided adducts **49** and **53** in 99% yield after only 1 h at −78°C. Compounds **2** and **6**, which were unreactive with Florisil, gave adducts **50** and **54** in 63 and 80% yields, respectively. In contrast, precursors **3**, **4**, and **7**, which have substitution at the terminus of the dienophile, had SM:A ratios in favour of starting material. The unreactive nature of these dienophiles in the IMDAF reaction is well precedented in the literature (*4i*), and may be a result of both increased steric interactions in the transition state as well as increased electron density of the carbon–carbon double bond.

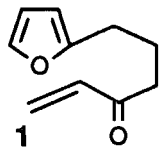
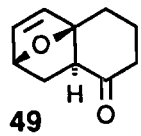
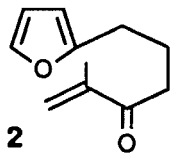
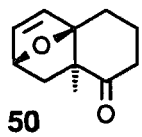
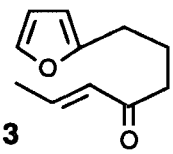
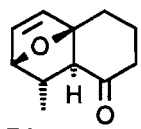
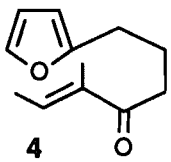
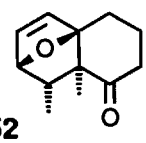
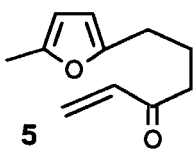
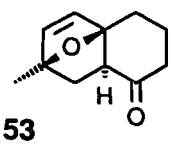
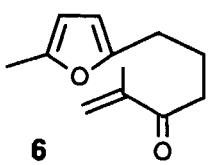
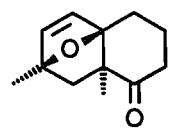
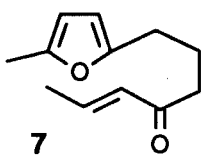
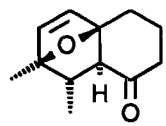
The geminally substituted precursors **9** and **13** (Table 3) provided adducts **56** and **60** in 88% yield, respectively, upon treatment with Florisil alone after only 1 day at room temperature, and therefore were not treated with methylaluminum dichloride. Compounds **10**, **11**, **14**, and **15** provided varying SM:A ratios when Florisil was employed; however, in all cases adduct was detected and isolated. This finding is in contrast to the results from the corresponding unsubstituted precursors **2**, **3**, **6**, and **7** (Table 1) in which no adduct was detected after 6 days. The increased reactivity of the substituted precursors may be due to the *gem*-dialkyl effect (*3g*, *3h*, *4m*, 8, 30).

Treatment of compounds **10**, **11**, **14**, and **15** with 1.1 equivalents of methylaluminum dichloride provided SM:A ratios in favour of starting material; increased quantities of adduct were formed relative to the results from using Florisil, except for compound **14**. The lower SM:A ratios for compounds **10** and **14** (Table 3) when compared to the SM:A ratios for compounds **2** and **6** (Table 2) can be explained by unfavourable 1,3-diaxial methyl interactions present in adducts **57** and **61**, which are absent in adducts **50** and **54**. Thus the 1,3-diaxial interactions may be promoting the retro Diels–Alder reaction. Compound **12** provided no adduct with 1.1 equivalents of methylaluminum dichloride.

We then sought a means of overcoming the unfavourable equilibrium for precursors containing more hindered dienophiles. A survey of the literature revealed very few examples in which catalytic quantities of Lewis acids had been employed to accelerate IMDA reactions (*10h*, *10j*, *10k*, *28c*, 31) and no examples involving the IMDAF reaction. Dramatic improvements in the SM:A ratios were observed when compounds **3**, **6**, **7** (Table 2), **10**, **11**, and **14** (Table 3) were exposed to 0.1 equivalents of methylaluminum dichloride at −78°C. In all cases the SM:A ratios favoured the adducts (SM:A ratios ranged from 40:60 to 0:100) and provided the oxatricyclo adducts in good to excellent yield. The SM:A ratios of compound **4** and **15** improved only slightly when compared to the results from the use of 1.1 equivalents of Lewis acid, and the tiglic precursor **12** did not react at all. These findings therefore represent the first examples of Lewis acid-catalyzed IMDAF reactions. In addition, these are also the first examples of Lewis acid-catalyzed IMDA reactions involving systems containing an internally activated dienophile.

The greatly improved SM:A ratios obtained when 0.1 equivalents of methylaluminum dichloride was employed, when compared with 1.1 equivalents, were rationalized by considering the effect that the amount of Lewis acid present has on the reaction equilibria. Our IMDAF reactions were shown to be under thermodynamic control: the reaction of pure adduct **50** with 1.1 equivalents of methylaluminum dichloride at −78°C for 2.5 h provided the same ratio of compounds **2**:**50** (35:65) that was obtained when pure precursor **2** was treated under the identical conditions (Scheme 3). The proposed equilibria are illustrated in Scheme 4. In the presence of 1.1 equivalents of Lewis acid the starting material and adduct are essentially complexed with Lewis acid and therefore both the forward and reverse Diels–Alder reactions are accelerated, leading to a thermodynamic ratio of Lewis acid complexed starting material **A*** and adduct **B***. Treatment of the reaction mixture with a bicarbonate quench at −78°C destroys the Lewis acid and provides, in the case of compound **3**, a SM:A ratio of 78:22 (Table 2). This ratio

TABLE 2. Effect of methylaluminum dichloride on IMDAF reactions

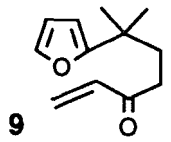
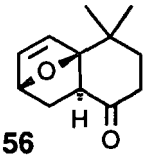
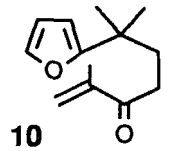
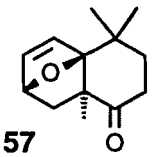
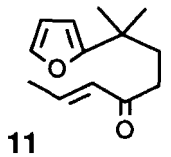
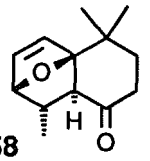
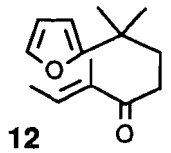
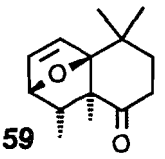
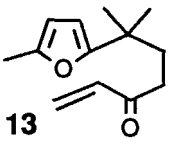
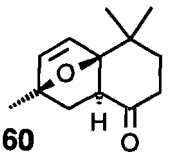
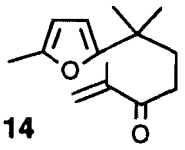
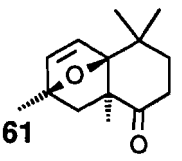
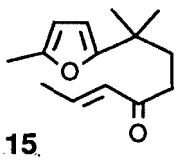
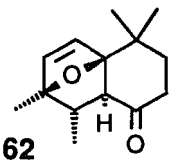
Starting Material	Conditions	Time (h)	SM:Adduct Ratio	Yield[a] (%)	Adduct
 1	Florisil	144	10:90	71 (79)	 49
	1.1 eq. $MeAlCl_2$	1	0:100	99	
 2	Florisil	144	100:0	0	 50
	1.1 eq. $MeAlCl_2$	2.5	35:65	63 (96)	
 3	Florisil	144	100:0	0	 51
	1.1 eq. $MeAlCl_2$	8	78:22	11 (65)	
	0.1 eq. $MeAlCl_2$	2	31:69	69	
 4	1.1 eq. $MeAlCl_2$	2	100:0	0	 52
	0.1 eq. $MeAlCl_2$	2	95:5	4	
 5	Florisil	336	12:88	65 (72)	 53
	1.1 eq. $MeAlCl_2$	1	0:100	99	
 6	Florisil	144	100:0	0	 54
	1.1 eq. $MeAlCl_2$	8	19:81	80 (97)	
	0.1 eq. $MeAlCl_2$	2	0:100	99	
 7	Florisil	144	100:0	0	 55
	1.1 eq. $MeAlCl_2$	8	82:18	18 (97)	
	0.1 eq. $MeAlCl_2$	2	24:76	74	

[a]Yield in parentheses is based on recovered starting material.

is therefore indicative of the **A***:**B*** ratio in solution, since it has been shown that compound **3** and adduct **51** do not interconvert in the absence of Lewis acid or upon work-up at room temperature. When catalytic quantities of methylaluminum dichloride are employed, the Lewis acid should preferentially complex with the more basic enone in the starting material **A** (Scheme 4) rather than with the saturated ketone in the adduct **B** (32). The dissociation of the Lewis acid from the adduct **B*** and complexation with **A** thus not only slows the rate of the reverse Diels–Alder reaction but accelerates the forward reaction, leading to a shift in the equilibrium towards adduct. The SM:A ratio for compound **3**:**51** increased to 31:69 (Table 2) with 0.1 equivalents of Lewis acid. Attempts to probe the nature of the species in solution by ^1H NMR studies have been inconclusive to date. Further work is in progress to establish support for the above hypothesis.

The utility of mild Lewis acids in the IMDAF reaction was not limited to either a four carbon atom side arm or dienophiles comprising enones. Compound **8**, containing a five carbon atom side arm, provided two oxatricyclo adducts **63** and **64** in a ratio of 84:8 in favour of the *endo* isomer in addition to unreacted starting material when treated with 0.1 equivalents of methylaluminum dichloride at −78°C for 2 h (Table 4). The stereochemistry of the major isomer (**63**) was determined by comparison of the ^1H NMR spectrum of **63**

TABLE 3. Effect of $MeAlCl_2$ on the IMDAF reaction of geminally substituted precursors

Starting Material	Conditions	Time (h)	SM:Adduct Ratio	Yield[a] (%)	Adduct
 **9**	Florisil	12	0:100	88	 **56**
 **10**	Florisil	24	83:17	16 (68)	 **57**
	1.1 eq. $MeAlCl_2$	8	68:32	31 (96)	
	0.1 eq. $MeAlCl_2$	2	40:60	60	
 **11**	Florisil	192	87:13	12 (67)	 **58**
	1.1 eq. $MeAlCl_2$	8	73:27	22 (94)	
	0.1 eq. $MeAlCl_2$	2	27:73	70	
 **12**	1.1 eq. $MeAlCl_2$	2	100:0	-	 **59**
	0.1 eq. $MeAlCl_2$	2	100:0	-	
 **13**	Florisil	12	0:100	96	 **60**
 **14**	Florisil	240	77:23	19 (68)	 **61**
	1.1 eq. $MeAlCl_2$	8	78:22	22 (97)	
	0.1 eq. $MeAlCl_2$	2	23:77	75	
 **15**	Florisil	336	85:15	13 (62)	 **62**
	1.1 eq. $MeAlCl_2$	8	78:22	18 (93)	
	0.1 eq. $MeAlCl_2$	2	69:31	30	

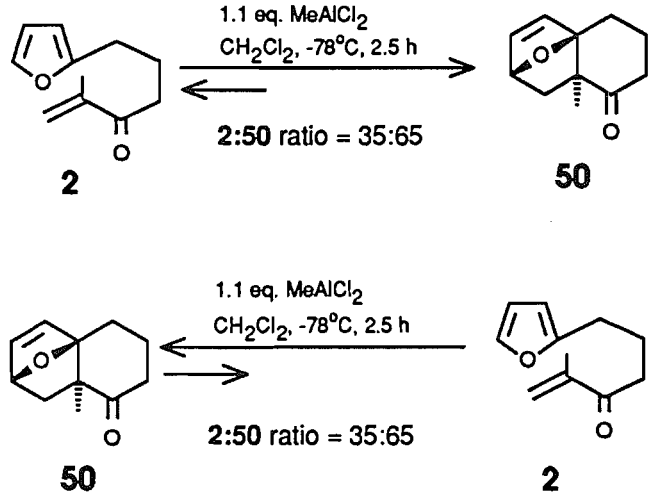
[a]Yield in parentheses is based on recovered starting material.

with that reported by Harwood and co-workers (5*a*). Interestingly, compound **8** has been previously reported to provide adducts **63** and **64** only at 1.2 GPa and in a ratio of 1:1 (5*a*).

Acetylenic precursors **16** and **17** provided the strained adducts **65** (88%) and **66** (97%), respectively, when treated with 1.1 equivalents of dimethylaluminum chloride at −50°C for 2.5 h (Scheme 5). The weaker Lewis acid dimethylaluminum chloride (26) was employed to minimize possible side reactions such as aromatization of the adducts. The use of internally activated acetylenic dienophiles in either the IMDA or IMDAF reaction is rare (1, 33), and no successful examples have been reported with the IMDAF reaction (4*l*). Usually the acetylene has been activated from the terminus by an ester moiety (1, 10). Thus, the reactions of compounds **16** and **17** are the first successful IMDA reactions involving internally activated acetylenic dienophiles. Adduct **65** was easily purified by flash chromatography, while adduct **66** was not as stable and partially isomerized to compound **67**, which contains an exocyclic double bond, upon standing.

Stereochemistry of the adducts

The stereochemistry of all the adducts formed in the Lewis acid accelerated IMDAF reactions containing a four-carbon



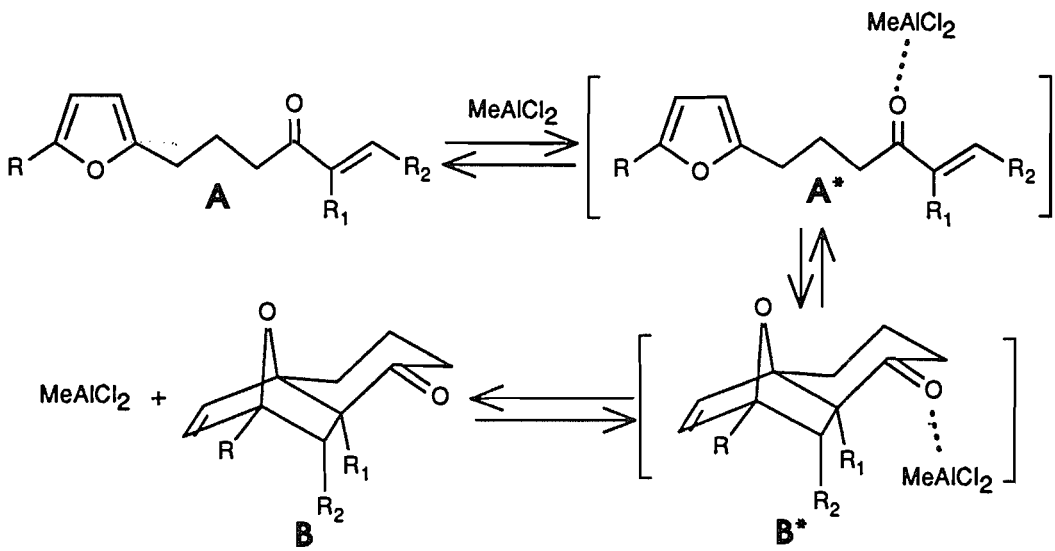
SCHEME 3

side arm had the side arm orientated *syn* with respect to the oxygen bridge resulting from an *exo* mode of attack. This is not surprising since (1) the calculated $\Delta G^0 = +12.9$ kJ/mol (PCModel 4), for the equilibration between the *exo* adduct **49** and the corresponding *endo* adduct, favours the *exo* adduct and (2) the reactions are under thermodynamic control (*vide supra*). This stereochemistry is consistent with that reported by others in the literature for tethers consisting of four carbon atoms with an internally activated dienophile (4*a*,*f*). The delineation of the stereochemistry in adducts **49–51** and **53–55** (Scheme 6) will be described in detail as representative examples. The stereochemistry of the remaining adducts arising from either acrolein-, methacrolein-, or crotonaldehyde-type dienophiles were determined in a similar manner.

The stereochemistry of adducts **49** and **53** was determined by ^{1}H NMR based on the coupling constants of protons H-6α, H-7α, and H-7β (Scheme 6). The bridge proton in adduct **49** H-8 (δ 4.91) was coupled to both H-7β (3.8 Hz) and H-9 (0.9 Hz). Coupling of H-8 to H-7α was not observed since the dihedral angle of H-8—C-8—C-7—H-7α was 90°. Proton H-7β (δ 2.49) was a multiplet with couplings of 3.0 Hz, 3.8 Hz, and 11.8 Hz to protons H-6α (δ 2.28), H-8, and H-7α (δ 1.49), respectively. The 3.0 Hz coupling constant observed between H-7β and H-6α was indicative of a 60° dihedral angle, thereby placing the side arm *syn* to the oxygen bridge. If the side arm was orientated *anti* to the oxygen bridge then the C-6 proton would have a dihedral angle of 0°C to the C-7α proton and a coupling constant of approximately 8 Hz would be expected (34). The 8.3 Hz coupling observed between H-7α and H-6α therefore confirmed our assignment of the relative stereochemistry. Since compound **53** has a methyl group at C-8, proton H-7α was identified by its upfield shift as the doublet of doublets at δ 1.61. This upfield shift was observed in compound **49** for H-7α, and was probably due to the diamagnetic anisotropy of the carbon–carbon double bond. The coupling constants of 11.8 Hz to H-7β and 8.2 Hz to H-6α again confirmed the *syn* orientation of the side arm to the oxygen bridge in compound **53**.

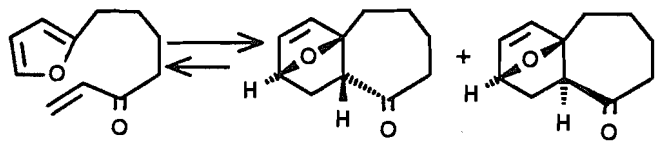
The determination of the stereochemistry of the side arm with respect to the oxygen bridge in adducts **50** and **54** could not be directly related to coupling constants since a methyl group is attached at C-6 (Scheme 6). If the adducts were formed from the mode of cyclization in which the side arm was orientated *exo*, the C-6 methyl substituent would be *anti* (i.e., *endo*) to the oxygen bridge and be shielded by the C-9—C-10 double bond. The methyl group at C-6 had an upfield chemical shift of δ 1.11 and δ 1.08 for adducts **50** and **54**, respectively, which is indicative of *endo* orientated methyl groups in oxatricyclo adducts (35). The proton H-7β was a doublet of doublets at δ 2.86 in compound **50**, due to vicinal coupling with the bridge proton H-8 (5.1 Hz) and geminal coupling to H-7α (11.8 Hz). Proton H-7α coupled only geminally to H-7β (11.8 Hz), and was highly shielded at δ 1.00 due to the anisotropy of the carbon–carbon double bond. Similarly, protons H-7α and H-7β appeared as an AB quartet (11.8 Hz) at δ 1.12 and δ 2.55, respectively, in compound **54**.

The crotonaldehyde-derived adducts **51** and **55** contain an additional stereocenter at C-7. Since IMDAF reactions catalyzed by Lewis acids have a concerted mechanism (36), the



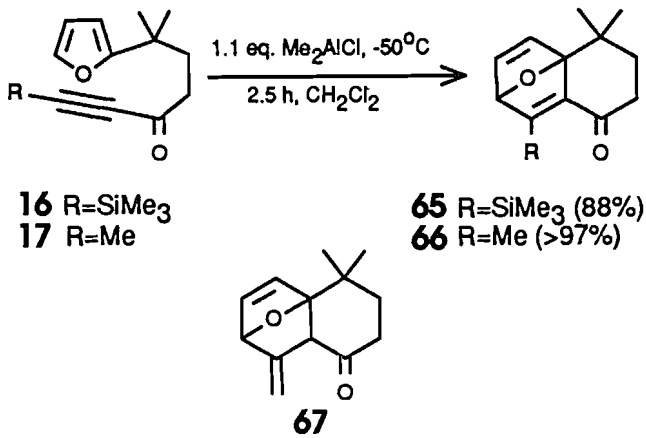
SCHEME 4

TABLE 4. IMDAF reaction of compound **8**



8 **63** *endo* **64** *exo*

	Temperature (°C)	SM : *endo* : *exo*
0.1 eq. $MeAlCl_2$	-78	8 : 84 : 8
	-65	8 : 81 : 11



16 R=$SiMe_3$
17 R=Me

65 R=$SiMe_3$ (88%)
66 R=Me (>97%)

67

SCHEME 5

methyl group at C-7 should be *anti* to the oxygen bridge (Scheme 6) if an *exo* mode of cyclization had occurred. Proton H-8 (δ 4.69) in adduct **51** was a doublet of doublets coupled to H-9 (1.6 Hz) and H-7β (4.7 Hz), indicating that the methyl group at C-7 was indeed *anti* to the oxygen bridge. If the C-7 methyl group was *syn* to the oxygen bridge, the protons H-8 and H-7 would form a 90° dihedral angle, and would therefore show no coupling (34). This stereochemical assignment was also supported by the highly shielded chemical shift of the C-7 methyl doublet (δ 0.93) due to the anisotropy of the C-9—C-10 carbon–carbon double bond. Proton H-6 was a doublet (4.0 Hz, δ 1.73) and coupled to H-7β (δ 2.79). The 4.0 Hz coupling constant was indicative of a 60° dihedral angle, thereby placing H-6 *anti*, and the side arm *syn*, with respect to the oxygen bridge. The stereochemistry of compound **55** was assigned in a similar manner. The C-7 methyl group appeared as an upfield doublet at δ 0.95, consistent with the moiety being *anti* to the oxygen bridge. Proton H-6 (δ 1.89) was a doublet with 4.2 Hz coupling to H-7, indicating the side arm was *syn* with respect to the oxygen bridge.

Conclusions

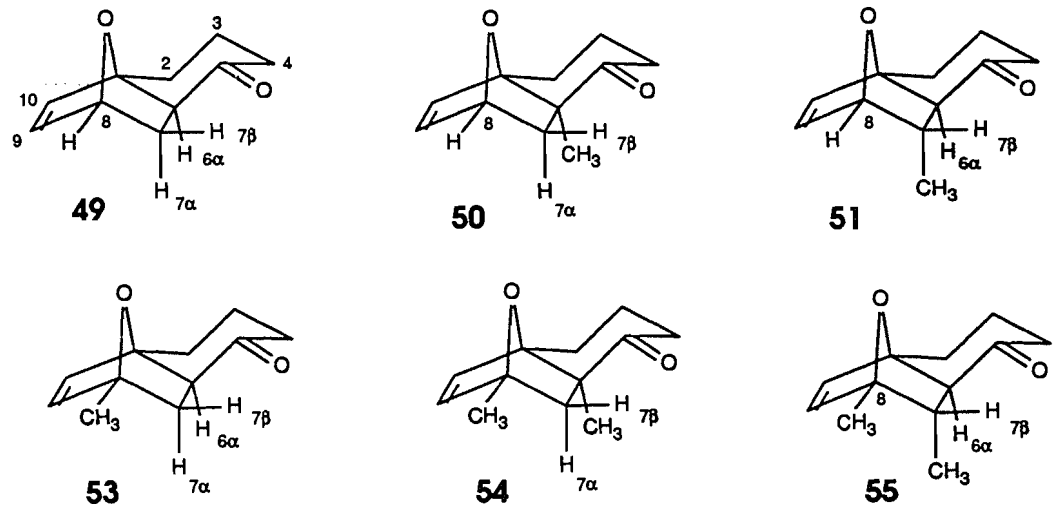
We have shown that Lewis acids are effective reagents for promoting the IMDAF reaction in which the diene and dienophile are connected by four or five carbon atoms. The reaction conditions are also applicable to acetylenic dienophiles internally activated by a carbonyl moiety. The use of methylaluminum dichloride makes the IMDAF reaction a viable synthetic transformation since: (1) the time for the reaction to reach equilibrium is reduced to a few hours from 4 to 14 days; (2) the isolated yields of adducts are very high, and (3) only one adduct is formed with up to four asymmetric centres of known relative stereochemistry. Synthetic applications of this methodology are currently in progress.

Experimental

General methods

Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. Boiling points refer to the air-bath temperature using Kugelrohr distillation apparatus, and are also uncorrected. Infrared spectra were obtained as either thin films (oils) on either NaCl or KBr plates, or as KBr pellets (solids). The infrared spectra were recorded on either a Nicolet 5-DX FT-IR spectrophotometer or a Mattson model 4030 FT-IR.

Nuclear magnetic resonance spectra were obtained on one of three instruments: Bruker AC-300 (^1H 300 MHz, ^{13}C 75 MHz), Bruker ACE-200 (^1H 200 MHz, ^{13}C 50 MHz), or a Bruker AM-400 spectrometer (^1H 400 MHz). Deuterochloroform was used both as the solvent, and the internal standard (^1H, δ 7.27; ^{13}C, δ 77.0) un-



SCHEME 6

less otherwise stated. All ^{1}H NMR spectra listed will have the following format: chemical shift (in ppm), (multiplicity, number of protons, coupling constants (Hz), assignment). The abbreviations used to describe the multiplicities are as follows: br = broadened, s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, and ABq refers to a quartet due to an AB spin system. The ^{13}C NMR spectra listed will have the following format: chemical shift (in ppm), (number of attached protons as determined by DEPT experiments).

Low-resolution mass spectra were recorded using either a Varian CH5 spectrometer, or a VG 7070 instrument. The data are listed as mass (*m/e*), (relative intensity, assignment). The spectra were obtained either by the electron-impact (EI) method or field ionization (FI), and the method will only be listed if FI was used. High-resolution mass spectra were recorded on a Kratos MS80 spectrometer. Microanalyses were performed either by Guelph Chemical Laboratories Limited, Guelph, Ontario, or by Mrs. D. Fox, Department of Chemistry, University of Calgary.

Solvents were either dried by standard methods (37), then distilled prior to use, or were purchased as anhydrous solvents in Sure-Seal® bottles from the Aldrich Chemical Company. THF was dried over sodium and benzophenone, as was diethyl ether. Methylene chloride, diisopropyl amine, and triethylamine were dried over CaH_2. Methanol was refluxed with Mg^0 metal for 12 h, then distilled. DMSO was dried over NaOH. Acetonitrile, DMF, and diethyl ether were purchased as anhydrous solvents, and HPLC-grade acetone was used.

The Lewis acids employed in this study were used as purchased, with no further purification. Boron trifluoride etherate and titanium(IV) chloride were used as neat liquids. The aluminum-containing reagents were purchased as molar solutions in hexane from Aldrich.

All glassware and syringes were dried in a 120°C oven for at least 4 h, then cooled under a stream of Ar, or in a desiccator containing Drierite. Reactions that were sensitive to moisture or atmospheric conditions were performed under an Ar atmosphere.

General procedure 1: conversion of tosylate or chloride to iodide

The tosylate or chloride (10 mmol) and NaI (25 mmol) were dissolved in HPLC-grade acetone (75 mL) and heated to reflux for 24 h under Ar. The reaction was cooled, and the solvent removed *in vacuo*. Diethyl ether (100 mL) and water (75 mL) were then added to dissolve the crude material. The aqueous layer extracted with Et_2O (3 × 100 mL) and the combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and the solvent removed *in vacuo* to provide the crude iodide. The iodide was purified either by flash chromatography, or distillation.

General procedure 2: coupling of iodide with unsaturated aldehydes

The iodide was purified by filtration through basic alumina, then distillation just prior to use. The iodide (1.0 mmol) was dissolved in anhydrous Et_2O (10 mL), and the solution was cooled to −78°C in a Dry Ice – acetone bath. *tert*-Butyllithium (2.2 mmol) was added dropwise to the cooled solution by syringe, and the reaction was stirred for 1 h at −78°C. The α,β-unsaturated aldehyde was distilled from Na_2SO_4 under Ar, and was added neat (1.5 mmol) by syringe to the reaction. The reaction was continued for a further 30 min (or until monitoring by TLC showed no starting material was present), then was quenched at low temperature with saturated NH_4Cl (10 mL). After warming to room temperature, the aqueous layer was extracted with Et_2O (3 × 25 mL) and CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent removed *in vacuo* to provide the crude coupled product, which was purified by flash chromatography, then distillation.

General procedure 3: Swern oxidation

The method of Swern (20) was used to oxidize the allylic alcohols to the enones. Oxalyl chloride (11 mmol) was dissolved in dry CH_2Cl_2 (25 mL) and cooled to −60°C (Dry Ice – chloroform) in an Ar-purged 3-neck round-bottom flask equipped with a dropping funnel. Freshly distilled alcohol (10 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and placed in the dropping funnel. DMSO (22 mmol) was added neat (by syringe) to the oxalyl chloride solution, the reaction was stirred for 2 min, and then the alcohol solution was added within 5 min. The mixture was stirred an additional 15 min, then Et_3N (50 mmol) was added and stirring was continued for another 5 min before warming the reaction to room temperature. Water (50 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (5 × 25 mL). The combined organic layers were washed with 5% HCl (15 mL), 5% Na_2CO_3 (15 mL), and water (15 mL), dried over Na_2SO_4, filtered, and the solvent removed *in vacuo* to provide the crude bad-smelling product, which was purified by flash chromatography, then distilled.

General procedure 4: IMDAF reactions in Florisil

The freshly distilled enone (1 mmol) was dissolved in dry CH_2Cl_2 (15 mL) and placed in an Ar-purged round-bottom flask. To this was added Florisil (100–200 mesh, 10 weight equivalents to the enone). The reaction was wrapped in foil and stirred at the appropriate temperature for the required length of time. The reaction was then filtered, the Florisil washed well with EtOAc (20 mL), and the solvent removed *in vacuo* without external heating to provide the crude product, which could be purified by flash chromatography.

General procedure 5: IMDAF reactions using Lewis acid

The freshly distilled enone (0.2 mmol) was dissolved in dry CH_2Cl_2 (10 mL), placed in an Ar-purged 3-necked flask, and cooled to the appropriate temperature. Methylaluminum dichloride (1.0 M in hexane) was added to the cooled enone solution, and the reaction was stirred for the appropriate length of time. The reaction was quenched with 10% $NaHCO_3$ (10 mL), and warmed until no frozen material remained. The aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL), then the organic layer was washed with H_2O (15 mL), dried over Na_2SO_4, filtered, and the solvent removed *in vacuo* without external heating to provide the crude product, which was purified by flash chromatography.

*3-(2-Furyl)-1-chloropropane (**20**)*

Furan **18** (6.0 mL, 82.5 mmol) was dissolved in dry THF (140 mL) under Ar and cooled to −78°C. Butyllithium (2.5 M in hexanes, 39.6 mmol) was added, then the solution was warmed to 0°C and stirred for 2 h. The 1-bromo-3-chloropropane (15.5 g, 98.7 mmol) was passed through basic alumina, then distilled before being added dropwise to the yellow anion solution. The reaction was stirred at room temperature overnight. The solvent was removed *in vacuo*, then ether (100 mL) and saturated NH_4Cl (100 mL) were added to the oily residue. The aqueous layer was extracted with ether (3 × 100 mL), dried over Na_2SO_4, and the solvent removed *in vacuo*. Distillation under aspirator provided compound **20** as a clear, colourless oil (9.1 g, 63.1 mmol), 76% yield; bp 60–70°C/20 Torr (1 Torr = 133.3 Pa); IR (neat) cm^{-1}: 2959–2850(C-H), 735(C-Cl); ^{1}H NMR (200 MHz): 2.12(qu, 2H, J = 7.0 Hz), 2.82(t, 2H, J = 7.0 Hz), 3.57(t, 2H, J = 7.0 Hz), 6.05(dd, 1H, J = 0.8 Hz, J = 3.0 Hz), 6.30(dd, 1H, J = 1.8 Hz, J = 3.0 Hz), 7.33(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 25.07(t), 30.86(t), 44.01(t), 105.55(d), 110.09(d), 141.13(d), 154.29(s); mass spectrum: 144(15, $M^{+\cdot}$), 81(100, M − $(CH_2)_2Cl$). Exact Mass calcd. for C_7H_9ClO: 144.0342; found: 144.0352.

*3-(2-(5-Methylfuryl))-1-chloropropane (**21**)*

2-Methylfuran **19** (7.9 mL, 80.0 mmol) was dissolved in dry THF (140 mL) under Ar and cooled to −78°C. Butyllithium (2.5 M in hexanes, 38.4 mmol) was added, then the solution was warmed to 0°C and stirred for 2 h. The 1-bromo-3-chloropropane (17.0 g, 108.2 mmol) was passed through basic alumina, then distilled before being added dropwise to the yellow anion solution. The reaction was stirred at room temperature overnight. The solvent was removed *in vacuo*, then ether (100 mL) and saturated NH_4Cl (100 mL) were added to the oily residue. The aqueous layer was

extracted with ether (3 × 100 mL), dried over Na_2SO_4, and the solvent removed *in vacuo*. Distillation under aspirator provided chloride **21** as a clear, colourless oil (12.3 g, 77.5 mmol), 97% yield, bp 75–85°C/20 Torr; IR (neat) cm^{-1}: 2956–2867(C-H), 653(C-Cl); ^1H NMR (200 MHz): 2.10(qu, 2H, J = 6.9 Hz), 2.27(s, 3H), 2.76(t, 2H, J = 7.2 Hz), 3.58(t, 2H, J = 6.5 Hz), 5.87(d, 1H, J = 3.0 Hz), 5.92(d, 1H, J = 3.0 Hz); ^{13}C NMR (50 MHz): 13.27(q), 25.02(t), 30.87(t), 43.96(t), 105.66(d), 106.02(d), 150.43(s), 152.25(s); mass spectrum: 158(11, $M^{\cdot+}$), 95(100, M − $(CH_2)_2Cl$). Exact Mass calcd. for $C_8H_{11}OCl$: 158.0498; found: 158.0501.

3-(2-Furyl)-1-iodopropane (22)

Using general procedure 1, chloride **20** (9.1 g, 63.1 mmol) was converted to iodide **22** (14.1 g, 59.7 mmol) in 95% yield after distillation; bp 20–30°C/0.04 Torr; IR (neat) cm^{-1}: 3144–3001(C-H), 2953–2843(C-H); ^1H NMR (200 MHz): 2.15(qu, 2H, J = 7.0 Hz), 2.77(t, 2H, J = 7.0 Hz), 3.20(t, 2H, J = 7.0 Hz), 6.06(dd, 1H, J = 0.8 Hz, J = 3.1 Hz), 6.29(dd, 1H, J = 1.8 Hz, J = 3.1 Hz), 7.32(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 5.79(t), 28.57(t), 31.61(t), 105.70(d), 110.09(d), 141.16(d), 153.92(s); mass spectrum: 236(51, $M^{\cdot+}$), 81(100, M − $(CH_2)_2I$). Exact Mass calcd. for C_7H_9IO: 235.9697; found: 235.9704.

3-(2-(5-Methylfuryl))-1-iodopropane (23)

Using general procedure 1, chloride **21** (3.75 g, 23.6 mmol) was converted to the iodide **23** (5.60 g, 22.4 mmol) in 95% yield after distillation; bp 100°C/20 Torr; IR (neat) cm^{-1}: 3102(C-H), 2942–2845(C-H); ^1H NMR (300 MHz): 2.13(qu, 2H, J = 6.8 Hz), 2.26(s, 3H), 2.71(t, 2H, J = 6.8 Hz), 3.21(t, 2H, J = 6.8 Hz), 5.85 and 5.89(ABq, 2H, J = 3.0 Hz); ^{13}C NMR (50 MHz): 5.88(t), 13.42(q), 28.63(t), 31.72(t), 105.78(d), 106.28(d), 150.50(s), 151.94(s): mass spectrum: 250(51, $M^{\cdot+}$), 95(100, M − $(CH_2)_2I$). Exact Mass calcd. for $C_8H_{11}IO$: 249.9855; found: 249.9857.

6-(2-Furyl)-1-hexen-3-ol (24)

Using general procedure 2, iodide **22** (0.59 g, 2.50 mmol) was treated with *tert*-butyllithium (3.23 mL, 5.5 mmol) and acrolein (0.25 mL, 3.74 mmol) to produce compound **24** (0.22 g, 1.32 mmol) as a clear, colourless oil in 53% yield after purification by flash chromatography (5:1) and distillation; bp 60–68°C/0.04 Torr; IR (neat) cm^{-1}: 3385 (O-H); ^1H NMR (200 MHz): 1.52–1.84(overlapping m, 6H), 2.67(t, 2H, J = 7.1 Hz), 4.13(m, 1H, J = 6.2 Hz), 5.12(ddd, 1H, J = 1.3 Hz, J = 1.3 Hz, J = 10.3 Hz), 5.23(ddd, 1H, J = 1.3 Hz, J = 1.3 Hz, J = 17.2 Hz), 5.90(ddd, 1H, J = 6.2 Hz, J = 10.3 Hz, J = 17.2 Hz), 6.00(dd, 1H, J = 0.8 Hz, J = 3.1 Hz), 6.28(dd, 1H, J = 1.8 Hz, J = 3.1 Hz), 7.30(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 23.87(t), 27.80(t), 36.39(t), 72.93(d), 104.85(d), 110.05(d), 114.72(t), 140.77(d), 141.09(d), 155.98(s); mass spectrum: 166(9, $M^{\cdot+}$), 148(10, M − H_2O), 94(100, M − CH_2=C(OH)CH=CH_2). Exact Mass calcd. for $C_{10}H_{14}O_2$: 166.0994; found: 166.0994.

6-(2-Furyl)-2-methyl-1-hexen-3-ol (25)

Using general procedure 2, iodide **22** (0.51 g, 2.18 mmol) was treated with *tert*-butyllithium (2.82 mL, 4.79 mmol) and methacrolein (0.27 mL, 3.26 mmol) to produce compound **25** (0.22 g, 1.20 mmol) as a clear, colourless oil in 55% yield after purification by flash chromatography (5:1) and distillation; bp 130°C/0.1 Torr; IR (neat) cm^{-1}: 3397(OH); ^1H NMR (200 MHz): 1.55–1.80(m, 5H), 1.72(t, 3H, J = 1.1 Hz, J = 1.1 Hz), 2.67(t, 2H, J = 7.2 Hz, H-4), 4.08(br q, 1H), 4.85(qu, 1H, J = 1.6 Hz), 4.95(m, 1H, J = 1.0 Hz, J = 1.6 Hz), 5.99(dd, 1H, J = 0.8 Hz, J = 3.1 Hz), 6.28(dd, 1H, J = 1.8 Hz, J = 3.1 Hz), 7.30(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 17.45(q), 24.06(t), 27.76(t), 34.22(t), 75.85(d), 104.82(d), 110.03(d), 111.10(t), 140.75(d), 147.40(s), 156.00(s); mass spectrum: 180(10, $M^{\cdot+}$), 94(100, M − $CH_2CH(OH)C(Me)$=CH_2, McLafferty rearr.). Exact Mass calcd. for $C_{11}H_{16}O_2$: 180.1151; found: 180.1150.

(E-7-(2-Furyl)-2-hepten-4-ol (26)

Using general procedure 2, iodide **22** (0.60 g, 2.56 mmol) was treated with *tert*-butyllithium (3.32 mL, 5.64 mmol) and crotonaldehyde (0.32 mL, 3.84 mmol) to produce compound **26** (0.31 g, 1.72 mmol) as a clear, colourless oil in 67% yield after purification by flash chromatography (9:1) and distillation; bp 52–68°C/0.035 Torr; IR (neat) cm^{-1}: 3443(O-H); ^1H NMR (200 MHz): 1.47–1.84(m, 5H), 1.70(dd, 3H, J = 0.9 Hz, J = 6.0 Hz), 2.65(t, 2H, J = 7.1 Hz), 4.06(br q, 1H, J = 6.3 Hz), 5.48(ddq, 1H, J = 0.9 Hz, J = 6.0 Hz, J = 15.3 Hz), 5.67(ddq, 1H, J = 1.5 Hz, J = 6.8 Hz, J = 15.3 Hz), 5.99(dd, 1H, J = 0.8 Hz, J = 3.1 Hz), 6.28(dd, 1H, 1.9 Hz, J = 3.1 Hz), 7.30(dd, 1H, J = 0.8 Hz, J = 1.9 Hz); ^{13}C NMR (50 MHz): 17.62(q), 24.00(t), 27.81(t), 36.63(t), 72.84(d), 104.78(d), 110.02(d), 126.97(d), 134.11(d), 140.72(d), 156.05(s); mass spectrum: 180(8, $M^{\cdot+}$), 162(39, M − H_2O), 94(100, M − $CH_2CH(OH_2)$-CH=CHMe). Anal. calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95; found: C 73.10, H 9.02.

(E)-7-(2-Furyl)-3-methyl-2-hepten-4-ol (27)

Using general procedure 2, iodide **22** (1.56 g, 6.63 mmol) was treated with *tert*-butyllithium (8.58 mL, 14.58 mmol) and tiglic aldehyde (0.96 mL, 9.94 mmol) to produce compound **27** (0.58 g, 3.00 mmol) as a clear, colourless oil in 45% yield after purification by flash chromatography (7:1) and distillation; bp 72–78°C/0.1 Torr; IR (neat) cm^{-1}: 3365(O-H); ^1H NMR (200 MHz): 1.49(br, s, 1H), 1.50–1.80(m, 10H), 2.65(t, 2H, J = 5.0 Hz), 4.01(br m, 1H), 5.47(br q, 1H), 5.99(dd, 1H, J = 0.7 Hz, J = 3.1 Hz), 6.28(dd, 1H, J = 1.9 Hz, J = 3.1 Hz), 7.30(dd, 1H, J = 0.7 Hz, J = 1.9 Hz); mass spectrum: 194(23, $M^{\cdot+}$), 176(42, M − H_2O), 94(100, M − $CH_2CH(OH)C(Me)$=CHMe). Anal. calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 73.91, H 9.32.

6-(2-(5-Methylfuryl))-1-hexen-3-ol (28)

Using general procedure 2, iodide **23** (0.59 g, 2.34 mmol) was treated with *tert*-butyllithium (3.03 mL, 5.15 mmol) and acrolein (0.24 mL, 3.51 mmol) to produce compound **28** (0.25 g, 1.40 mmol) as a clear, colourless oil in 60% yield after purification by flash chromatography (5:1) and distillation; bp 130–135°C/12 Torr; IR (neat) cm^{-1}: 3400(C-O), 1021(C-O); ^1H NMR (200 MHz): 1.53–1.81(overlapping m, 6H), 2.26(s, 1H), 2.61(t, 2H, J = 7.2 Hz), 4.13(br, m, 1H, J = 6.2 Hz), 5.12(dt, 1H, J = 1.3 Hz, J = 1.3 Hz, J = 10.3 Hz), 5.23(dt, 1H, J = 1.3 Hz, J = 1.3 Hz, J = 17.2 Hz), 5.85(ABq, 2H), 5.87(ddd, 1H, J = 6.2 Hz, J = 10.3 Hz, J = 17.2 Hz); ^{13}C NMR (50 MHz): 13.41(q), 23.96(t), 27.85(t), 36.42(t), 72.93(d), 105.40(d), 105.73(d), 114.73(t), 141.10(d), 150.16(s), 154.08(s); mass spectrum: 180(31, $M^{\cdot+}$), 162(7, M − H_2O), 108 (100, M − CH_2=C(OH)CH=CH_2). Anal. calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95; found: C 73.08, H 9.21.

6-(2-(5-Methylfuryl))-2-methyl-1-hexen-3-ol (29)

Using general procedure 2, iodide **23** (0.52 g, 2.07 mmol) was treated with *tert*-butyllithium (2.67 mL, 4.55 mmol) and methacrolein (0.26 mL, 3.10 mmol) to produce compound **29** (0.28 g, 1.45 mmol) as a clear, colourless oil in 70% yield after purification by flash chromatography (5:1) and distillation; bp 69–77°C/0.04 Torr; IR (neat) cm^{-1}: 3405 (O-H); ^1H NMR (200 MHz): 1.55–1.70(m, 5H), 1.72(dd, 3H, J = 0.9 Hz, J = 1.2 Hz), 2.25(s, 3H), 2.61(t, 2H, 7.0 Hz), 4.08(br t, 1H, J = 7.5 Hz), 4.84(m, 1H, J = 1.7 Hz), 4.95(m, 1H, J = 0.8 Hz, J = 1.7 Hz), 5.85(ABq, 2H); ^{13}C NMR (50 MHz): 13.42(q), 17.44(q), 24.19(t), 27.84(t), 34.35(t), 75.66(d), 105.40(d), 105.79(d), 110.99(t), 147.48(s), 150.13(s), 154.16(s); mass spectrum: 194(14, $M^{\cdot+}$), 108(100, M − $CH_2CH(OH)C(Me)$=CH_2). Anal. calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 73.82, H 9.38.

(E)-7-(2-(5-Methylfuryl))-2-hepten-4-ol (30)

Using general procedure 2, iodide **23** (0.79 g, 3.18 mmol) was treated with *tert*-butyllithium (4.10 mL, 6.99 mmol) and crotonaldehyde (0.53 mL, 6.35 mmol) to produce compound **30**

(0.52 g, 2.66 mmol) as a clear, colourless oil in 84% yield after purification by flash chromatography (9:1) and distillation; bp 72–78°C/0.1 Torr; IR (neat) cm^{-1}: 3417(O-H); ^1H NMR (200 MHz): 1.50–1.70(m, 5H), 1.70(dd, 3H, J = 0.9 Hz, J = 6.3 Hz), 2.25(s, 3H), 2.58(t, 2H, J = 7.5 Hz), 4.06(br m, 1H), 5.46(ddq, 1H, J = 1.2 Hz, J = 6.8 Hz, J = 15.3 Hz), 5.68(ddq, 1H, J = 0.9 Hz, J = 5.9 Hz, J = 15.3 Hz), 5.85(ABq, 2H); ^{13}C NMR (50 MHz): 13.46(q), 17.82(q), 24.12(t), 27.88(t), 36.68(t), 72.88(d), 105.35(d), 105.72(d), 126.91(d), 134.14(d), 150.12(s), 154.20(s); mass spectrum: 194(16, $M^{+\cdot}$), 178(36, M − H_2O), 108(100, M − $CH_2CH(OH)CH{=}CHMe$). Anal. calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 73.86, H 9.29.

6-(2-Furyl)-1-hexen-3-one (1)

Compound **24** (0.19 g, 1.18 mmol) was oxidized according to general procedure 3 to provide compound **1** (0.18 g, 1.10 mmol) as a clear, colourless oil in 93% yield after purification by flash chromatography (20:1) and distillation; bp 50–55°C/0.08 Torr. The ^1H NMR spectrum always contained >10% bridged adduct **49**, therefore compound **1** was not analyzed but treated with either Florisil or methylaluminum dichloride to provide adduct **49**.

6-(2-Furyl)-2-methyl-1-hexen-3-one (2)

Compound **25** (0.65 g, 3.58 mmol) was oxidized according to general procedure 3 to provide compound **2** (0.60 g, 3.36 mmol) as a clear, colourless oil in 94% yield after purification by flash chromatography (20:1) and distillation; bp 58–60°C/0.045 Torr; IR(neat) cm^{-1}: 1677(C=O); ^1H NMR (200 MHz): 1.87(dd, 3H, J = 0.8 Hz, J = 1.4 Hz), 1.97(qu, 2H, J = 7.3 Hz), 2.67(t, 2H, J = 7.3 Hz), 2.72(t, 2H, J = 7.3 Hz), 5.75(dq, 1H, J = 0.8 Hz, J = 1.4 Hz), 5.92(m, 1H, J = 1.4 Hz), 6.00(dd, 1H, J = 0.8 Hz, J = 3.0 Hz), 6.28(dd, 1H, J = 2.0 Hz, J = 3.0 Hz), 7.30(dd, 1H, J = 0.8 Hz, J = 2.0 Hz); ^{13}C NMR(50 MHz): 17.55(q), 22.80(t), 27.27(t), 36.44(t), 105.18(d), 110.06(d), 124.27(t), 140.91(d), 144.53(s), 155.46(s), 199.52(s); mass spectrum: 178(21, $M^{+\cdot}$), 94(100, M − $CH_2{=}C(OH)C(Me){=}CH_2$, McLafferty rearr.). Exact Mass calcd. for $C_{11}H_{14}O_2$: 178.0994; found: 178.0998.

(E)-7-(2-Furyl)-2-hepten-4-one (3)

Compound **26** (0.27 g, 1.48 mmol) was oxidized according to general procedure 3 to provide compound **3** (0.23 g, 1.29 mmol) as a clear, colourless oil in 88% yield after purification by flash chromatography (20:1) and distillation; bp 60–70°C/0.05 Torr; IR (neat) cm^{-1}: 1672 and 1696(C=O); ^1H NMR (200 MHz): 1.89(dd, 3H, J = 1.6 Hz, J = 6.8 Hz), 1.96(qu, 2H, J = 7.2 Hz), 2.57(t, 2H, J = 7.2 Hz), 2.66(t, 2H, J = 7.2 Hz), 6.00(dd, 1H, J = 0.6 Hz, J = 3.1 Hz), 6.11(dq, 1H, J = 1.6 Hz, J = 15.7 Hz), 6.28(dd, 1H, J = 1.9 Hz, J = 3.0 Hz), 6.83(dq, 1H, J = 6.8 Hz, J = 15.7 Hz), 7.30(dd, 1H, J = 0.6 Hz, J = 1.9 Hz); ^{13}C NMR (50 MHz): 18.09(q), 22.50(t), 27.26(t), 38.92(t), 105.18(d), 110.04(d), 131.91(d), 140.89(d), 142.31(d), 155.44(s), 199.74(s); mass spectrum (FI): 178(100, $M^{+\cdot}$). Anal. calcd. for $C_{11}H_{14}O_2$: C 74.13, H 7.92; found: C 74.18, H 7.98.

(E)-7-(2-Furyl)-3-methyl-2-hepten-4-one (4)

Compound **27** (0.69 g, 3.55 mmol) was oxidized according to general procedure 3 to provide compound **4** (0.62 g, 3.24 mmol) as a clear, colourless oil in 91% yield after purification by flash chromatography (20:1) and distillation; bp 60–70°C/0.045 Torr; IR (neat) cm^{-1}: 1666 (C=O); ^1H NMR (200 MHz): 1.77(d, 3H, J = 1.1 Hz), 1.84(d, 3H, J = 6.9 Hz), 1.96(qu, 2H, J = 7.2 Hz), 2.66 and 2.68(overlapping t, 4H, J = 7.2 Hz), 5.99(dd, 1H, J = 0.7 Hz, J = 3.1 Hz), 6.27(dd, 1H, J = 1.8 Hz, J = 3.1 Hz), 6.69(qq, 1H, J = 1.1 Hz, J = 6.9 Hz), 7.29(dd, 1H, J = 0.7 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 10.78(q), 14.51(q), 22.92(t), 27.19(t), 35.90(t), 104.94(d), 109.90(d), 136.88(d), 138.02(s), 140.68(d), 155.40(s), 200.94(s); mass spectrum (FI): 192(51, $M^{+\cdot}$), 94(100 − CH=C(OH)C(Me)=CHMe, McLafferty rearrangement). Anal. calcd. for $C_{12}H_{16}O_2$: C 74.97, H 8.39; found: C 74.85, H 8.43.

6-(2-(5-Methylfuryl)-1-hexen-3-one (5)

Compound **28** (0.24 g, 1.34 mmol) was oxidized according to general procedure 3 to provide compound **5** (0.15 g, 0.84 mmol) as a clear, colourless oil in 63% yield after purification by flash chromatography (20:1) and distillation; bp 60–70°C/0.04 Torr; IR (neat) cm^{-1}: 1684(C=O); ^1H NMR (200 MHz): 1.96(qu, 2H, J = 7.5 Hz), 2.25(s, 3H), 2.59–2.70(t, 2H each, J = 7.5 Hz), 5.85(m, 2H), 6.19(dd, 1H, J = 1.5 Hz, J = 16.5 Hz), 6.38(dd, 1H, J = 10.1 Hz, J = 16.5 Hz); ^{13}C NMR (50 MHz): 13.42(q), 22.33(t), 27.24(t), 38.57(t), 105.74(d), 105.86(d), 127.87(t), 136.50(d), 150.36(s), 153.36(s), 200.34(s); mass spectrum: 178(13, $M^{+\cdot}$), 108(100, M − $CH_2{=}C(OH)CH{=}CH_2$, McLafferty rearrangement).

6-(2-(5-Methylfuryl))-2-methyl-1-hexen-3-one (6)

Compound **29** (0.28 g, 1.45 mmol) was oxidized according to general procedure 3 to provide compound **6** (0.27 g, 1.42 mmol) as a clear, colourless oil in 98% yield after purification by flash chromatography (20:1) and distillation; bp 60–68°C/0.045 Torr; IR (neat) cm^{-1}: 1680(C=O); ^1H NMR (200 MHz): 1.87(dd, 3H, J = 0.7 Hz, J = 1.3 Hz), 1.94(qu, 2H, J = 7.3 Hz), 2.24(s, 3H), 2.61(t, 2H, J = 7.3 Hz), 2.73(t, 2H, J = 7.3 Hz), 5.75(m, 1H, J = 0.7 Hz, J = 1.4 Hz), 5.84(ABq, 2H), 5.93(m, 1H, J = 1.3 Hz, J = 1.4 Hz); ^{13}C NMR (50 MHz): 13.41(q), 17.54(q), 22.95(t), 27.37(t), 36.52(t), 105.78(d), 124.19(t), 144.57(s), 150.33(s), 153.56(s), 201.61(s); mass spectrum: 192(62, $M^{+\cdot}$), 108(100, M − $CH_2{=}C(OH)C(Me){=}CH_2$, McLafferty rearrangement). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1150; found: 192.1158.

(E)-7-(2-(5-Methylfuryl))-2-hepten-4-one (7)

Compound 30 (0.30 g, 1.54 mmol) was oxidized according to general procedure 3 to provide compound **7** (0.24 g, 1.23 mmol) as a clear, colourless oil in 80% yield after purification by flash chromatography (20:1) and distillation; bp 70–82°C/0.045 Torr; IR (neat) cm^{-1}: 1695–1670(C=O); ^1H NMR (200 MHz): 1.89(dd, 3H, J = 2.5 Hz, J = 7.5 Hz), 1.95(qu, 2H, J = 7.0 Hz), 2.25(s, 3H), 2.55(t, 2H, J = 7.0 Hz), 2.60(t, 2H, J = 7.0 Hz), 5.84(ABq, 2H), 6.11(dq, 1H, J = 1.6 Hz, J = 15.8 Hz), 6.83(dq, 1H, J = 6.8 Hz, J = 15.8 Hz); ^{13}C NMR (50 MHz): 13.39(q), 18.08(q), 22.59(t), 27.38(t), 38.96(t), 105.74(d), 105.78(d), 131.90(d), 142.24(d), 150.28(s), 153.49(s), 199.88(s); mass spectrum: 192(10, $M^{+\cdot}$), 108(100, M − $CH_2{=}C(OH)CH{=}CHMe$, McLafferty rearrangement). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1151; found: 192.1138.

1-Bromo-4-(2-furyl)butane (31)

Furan **18** (5.0 mL, 68.7 mmol) was dissolved in dry THF (80 mL) in an Ar-purged flask and cooled to −78°C in a Dry Ice – acetone bath. To this solution was added *n*-butyllithium (20.0 mL, 50.0 mmol), then the reaction was stirred at room temperature for 1 h. Freshly distilled 1,4-dibromobutane (10.0 g, 46.3 mmol) was added to the orange anion, and the reaction was stirred overnight. Saturated NH_4Cl (50 mL) was used to quench the reaction. The aqueous layer was extracted with ether (3 × 100 mL), then the combined organic layers were dried over Na_2SO_4, filtered, and the solvent removed *in vacuo*. The crude product was distilled using a fractionating column under aspirator pressure, collecting the fraction boiling from 95 to 100°C to give compound **31** (2.54 g, 12.5 mmol) in 25% yield; IR (neat) cm^{-1}: 2943–2864(C-H); ^1H NMR (200 MHz): 1.67–2.08(m, 4H), 2.68(t, 2H, J = 7.1 Hz), 3.43(t, 2H, J = 7.1 Hz), 6.02(dd, 1H, J = 0.8 Hz, J = 3.0 Hz), 6.30(dd, 1H, J = 1.7 Hz, J = 3.0 Hz), 7.33(dd, 1H, J = 0.8 Hz, J = 1.7 Hz); ^{13}C NMR (50 MHz): 26.56(t), 27.00(t), 32.04(t), 33.34(t), 105.03(d), 110.06(d), 140.88(d), 155.38(s); mass spectrum: 202 (6, $M^{+\cdot}$), 81(100, M − $(CH_2)_3Br$). Exact Mass calcd. for $C_8H_{11}BrO$: 201.9993; found: 201.9982.

7-(2-Furyl)-1-hepten-3-one (8)

General procedure 1 was used to convert bromide **31** (3.55 g, 17.5 mmol) to the corresponding iodide (4.16 g, 16.6 mmol) in 95% yield after distillation; bp 60–68°C/0.08 Torr; IR (neat) cm^{-1}:

2936–2860(C-H); ^{1}H NMR (200 MHz): 1.64–2.01(m, 4H), 2.68(t, 2H, J = 7.5 Hz), 3.21(t, 2H, J = 7.5 Hz), 6.02(dd, 1H, J = 0.7 Hz, J = 3.1 Hz), 6.29(dd, 1H, J = 1.7 Hz, J = 3.1 Hz), 7.31(dd, 1H, J = 0.7 Hz, J = 1.7 Hz); ^{13}C NMR (200 MHz): 6.50(t), 26.80(t), 28.87(t), 32.78(t), 105.03(d), 110.06(d), 140.88(d), 155.35(s); mass spectrum: 250(22, $M^{\cdot+}$), 123(30, M-I), 81(100, M − $(CH_2)_3$I). Exact Mass calcd. for $C_8H_{11}IO$: 249.9851; found: 249.9851.

Using general procedure 2, the above iodide (0.58 g, 2.32 mmol) was treated with *tert*-butyllithium (3.0 mL, 5.09 mmol) and acrolein (185 μL, 2.78 mmol) to produce the corresponding allylic alcohol (0.29 g, 1.61 mmol) as a clear, colourless oil in 69% yield after purification by flash chromatography (7:1) and distillation; bp 50–60°C/0.05 Torr; ^{1}H NMR (200 MHz): 1.39–1.75(m, 7H), 2.64(t, 2H, J = 7.2 Hz), 4.11(br, m, 1H), 5.11(dt, 1H, J = 1.2 Hz, J = 1.2 Hz, J = 10.3 Hz), 5.22(dt, 1H, J = 1.2 Hz, J = 1.2 Hz, J = 17.2 Hz), 5.91(ddd, 1H, J = 6.2 Hz, J = 10.3 Hz, J = 17.2 Hz), 5.99(dd, 1H, J = 0.7 Hz, J = 3.0 Hz), 6.28(dd, 1H, J = 1.9 Hz, J = 3.0 Hz), 7.30(dd, 1H, J = 0.7 Hz, J = 1.9 Hz).

The above allylic alcohol (133.9 mg, 0.74 mmol) was oxidized according to general procedure 3 to provide compound **8** (113.3 g, 0.64 mmol) as a clear, colourless oil in 86% yield after purification by flash chromatography (20:1) and distillation; bp 80°C/0.06 Torr; ^{1}H NMR (200 MHz): 1.56–1.83(overlapping m), 2.50–2.76(overlapping m), 5.83(dd, 1H, J = 2.5 Hz, J = 10.1 Hz), 5.98(dd, 1H, J = 0.7 Hz, J = 3.0 Hz), 6.20(d of ABq, 1H, J = 2.5 Hz, J = 17.5 Hz), 6.25(dd, 1H, J = 1.8 Hz, J = 3.0 Hz), 6.37(d of ABq, 1H, J = 10.1 Hz, J = 17.5 Hz), 7.30(dd, 1H, J = 0.7 Hz, J = 1.8 Hz).

4-Methyl-2-oxo-3-pentenenitrile (32)

Freshly distilled acid chloride of 3-methyl-2-butenoic acid (2.19 g, 18.5 mmol) was dissolved in dry acetonitrile (15 mL) under Ar. To this solution was added anhydrous CuCN (2 equiv.), and the suspension was heated to reflux (oil bath, 90°C) for 30 min, during which time a clear, brown solution was formed. The solution was cooled to room temperature, and the solvent was removed using a rotary evaporator (no heat), followed by an Ar back-purge. The desired compound was then distilled from the remaining brown solid, along with some acetonitrile. Conversion was confirmed by ^{1}H NMR, then the acyl cyanide **32** was used directly for the next step, bp 70–80°C/20 Torr; ^{1}H NMR (200 MHz): 2.07 and 2.30(s, 3H each), 6.25(s, 1H).

Methyl 3-(2-furyl)-3-methylbutanoate (33)

A modification of the method of Ismail and Hoffmann (21) was used for the preparation of furan **33**. The acyl cyanide **32** (3.52 g, 32.3 mmol) was dissolved in CS_2 (120 mL) under Ar and cooled in an ice bath. To this solution was added $AlCl_3$ (1.08 g, 8.10 mmol), resulting in a gummy precipitate. After stirring for 1 h at room temperature, furan **18** (12.0 mL, 165.0 mmol) was added neat, and the reaction was stirred for 24 h, after which time anhydrous methanol (100 mL) was added to the solution. The reaction was then stirred for an additional 24 h. Evaporation of the CS_2, followed by removal of methanol *in vacuo*, resulted in a viscous brown material. The crude product was taken up in ether (200 mL) and water (100 mL) followed by washing with 10% Na_2CO_3 (2 × 100 mL), then water (2 × 100 mL), dried (Na_2SO_4), and the ether removed *in vacuo*. Distillation of the crude brown oil provided **33** (27% from 3-methyl-2-butenoic acid), bp 40–44°C/0.03 Torr (lit. (21) bp 40°C/0.03 Torr); IR (neat) cm^{-1}: 1738 (C═O), 1077 (C—O); ^{1}H NMR (200 MHz): 1.40(s, 6H), 2.61(s, 2H), 3.58(s, 3H), 6.01(dd, 1H, J = 0.8 Hz, J = 3.2 Hz), 6.26(dd, 1H, J = 1.9 Hz, J = 3.2 Hz), 7.32 (dd, 1H, J = 0.8 Hz, J = 1.9 Hz); ^{13}C NMR (50 MHz): 2 × 28.70(q), 34.96(s), 45.73(t), 51.11(q), 103.12(d), 108.80(d), 140.66(d), 161.27(s), 171.58(s); mass spectrum: 182(58, $M^{\cdot+}$), 109(100, M − CH_2CO_2Me). Exact Mass calcd. for $C_{10}H_{14}O_3$: 182.0942; found: 182.0935.

Methyl 3-(2-(5-methylfuryl))-3-methylbutanoate (34)

The acyl cyanide **32** (1.82 g, 16.7 mmol) was dissolved in CS_2 (60 mL) under Ar and cooled in an ice bath. To this solution was added $AlCl_3$ (0.56 g, 4.2 mmol), resulting in a gummy precipitate. After stirring for 1 h at room temperature, 2-methylfuran **19** (7.0 mL, 70.5 mmol) was added neat, and the reaction was stirred for 24 h, after which time anhydrous methanol (70 mL) was added to the crimson solution. The reaction was then stirred for an additional 24 h. Evaporation of the CS_2, followed by removal of methanol *in vacuo*, resulted in a viscous brown material. The crude product was taken up in ether (200 mL) and water (100 mL), followed by washing with 10% Na_2CO_3 (2 × 100 mL), then water (2 × 100 mL), dried (Na_2SO_4), and the ether removed *in vacuo*. Distillation of the crude brown oil provided **34** (66%), bp 100–120°C/15 Torr; IR (neat) cm^{-1}: 1738(C═O), 1385,1365(CMe_2) 1198(C—O); ^{1}H NMR (200 MHz): 1.37(s, 6H), 2.25(d, 3H, J = 0.75 Hz), 2.58(s, 2H), 3.60(s, 3H), 5.87(d of ABq, 2H, J = 0.8 Hz, J = 3.1 Hz); ^{13}C NMR (50 MHz): 13.43(q), 2 × 26.69(q), 34.89(s), 45.82(6), 71.08(q), 103.64(d), 105.57(d), 150.33(s), 159.568s), 171.77(s); mass spectrum: 196(53, $M^{\cdot+}$), 123(100, M − CH_2CO_2Me). Anal. calcd. for $C_{11}H_{16}O_3$: C 67.32, H 8.22; found: C 66.84, H 8.18.

3-(2-Furyl)-3-methyl-1-butanol (36)

To $LiAlH_4$ (0.51 g, 9.3 mmol), suspended in ether (25 mL) at 0°C under Ar, was added dropwise a solution of freshly distilled **33** (1.42 g, 7.8 mmol) in ether (8 mL). The reaction was warmed to room temperature and stirred for 12 h. After cooling to 0°C, the reaction was quenched using water (0.5 mL), 15% NaOH (0.5 mL), then water (1.5 mL). The white mixture was then filtered through Celite, and the solvent removed *in vacuo* to provide a clear, colourless oil. The oil was purified by flash chromatography (1:1), then distilled to yield compound **36** (92%), bp 48°C/0.07 Torr; IR (neat) cm^{-1}: 3333(OH), 1385,1363(CMe_2), 1077, 1059(C—O); ^{1}H NMR (200 MHz): 1.30(s, 6H), 1.51(s, 1H), 1.89(t, 2H, J = 7.2 Hz), 3.54(t, 2H, J = 7.2 Hz), 5.99 (dd, 1H, J = 0.9 Hz, J = 3.2 Hz), 6.28(dd, 1H, J = 1.5 Hz, J = 3.2 Hz) 7.32(dd, 1H, J = 0.9 Hz, J = 1.5 Hz); ^{13}C NMR (50 MHz): 2 × 27.20(q), 34.57(s), 44.61(t), 59.92(t), 103.24(d), 108.61(d), 140.64(d), 163.32(s); mass spectrum: 154(35, $M^{\cdot+}$), 109(100, M − $(CH_2)_2OH$). Anal. calcd. for $C_9H_{11}O_2$: C 70.09, H 9.15; found: C 69.66, H 9.00.

3-(2-(5-Methylfuryl))-3-methyl-1-butanol (37)

Compound **34** (2.03 g, 10.4 mmol) was reduced to alcohol **37** (1.76 g, 10.1 mmol) by the method described for compound **36** in 97.5% yield after distillation, bp 60–70°C/0.1 Torr; IR (neat) cm^{-1}: 3334(OH), 1384,1365(CMe_2), 1059,1021(C—O); ^{1}H NMR (200 MHz): 1.28(s, 6H), 1.38(br s, 1H), 1.87(t, 2H, J = 7.1 Hz), 2.26(d, 3H, J = 0.8 Hz), 3.58(t, 2H, J = 7.1 Hz), 5.85(ABq, 2H); ^{13}C NMR(50 MHz): 13.45(q), 2 × 27.22(q), 34.36(s), 44.55(t), 59.97(t), 103.62(d), 105.51(d), 150.31(s), 160.46(s); mass spectrum: 168(60, $M^{\cdot+}$), 123(100, M − $(CH_2)_2OH$). Anal. calcd. for $C_{10}H_{16}O_2$: C 71.39, H 9.59; found: C 71.37, H 9.43.

3-(2-Furyl)-1-iodo-3-methylbutane (38)

Distilled compound **36** (1.05 g, 6.80 mmol) was dissolved in dry CH_2Cl_2 (20 mL), and cooled in an ice bath. To this solution was added *p*-toluenesulfonyl chloride (2.59 g, 13.6 mmol) and DMAP (1.66 g, 13.6 mmol), and the reaction was stirred for 12 h. The mixture was poured into water (50 mL), then the organic layer was washed with 5% HCl (2 × 50 mL), and water (3 × 50 mL), then dried over Na_2SO_4. The solvent was removed *in vacuo* to yield a viscous clear oil, which was then purified by flash chromatography (7:1) to provide the tosylate of compound **36** (2.03 g, 6.58 mmol) in 98% yield. This decomposed when stored at room temperature; IR (neat) cm^{-1}: 3093–3035(C—H), 1364, 1187(SO_2st.); ^{1}H NMR (200 MHz): 1.25(s, 6H), 1.97(t, 2H, J = 7.3 Hz), 2.45(s, 3H), 3.93(t, 2H, J = 7.3 Hz), 5.91(dd, 1H, J = 0.7 Hz, J = 3.3 Hz), 6.22(dd, 1H, J = 1.8 Hz, J = 3.3 Hz), 7.25(d, 1H, J = 0.7 Hz, J = 1.8 Hz), 7.33 and 7.74(AA′XX′, 4H);

^{13}C NMR (50 MHz): 21.56(q), 2 × 27.02(q), 34.61(s), 40.34(t), 87.95(t), 103.78(d), 109.76(d), 127.64(d), 129.71(d), 133.40(s), 144.52(s), 141.05(d), 160.92(s); mass spectrum: 308(6, $M^{\cdot+}$), 109(100, M − $(CH_2)_2OTs$).

General procedure 1 was used to convert the above tosylate (2.00 g, 6.5 mmol) to iodide **38** (1.56 g, 5.91 mmol) in 91% yield after distillation, as a clear, colourless oil; bp 54–56°C/0.06 Torr; IR (neat) cm^{-1}: 1386, 1364(CMe_2); ^{1}H NMR (200 MHz): 1.28(s, 6H), 2.26(m, 2H), 2.96(m, 2H), 6.00(dd, 1H, J = 0.7 Hz, J = 3.2 Hz), 6.27(dd, 1H, J = 1.8 Hz, J = 3.2), 7.33(dd, 1H, J = 0.7 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 0.35(t), 2 × 26.41(q), 38.14(s), 47.22(t), 103.92(d), 109.78(d), 141.13(d), 160.82(s); mass spectrum: 264(36, $M^{\cdot+}$), 109(100, M − $(CH_2)_2I$). Anal. calcd. for $C_9H_{13}IO$: C 40.93, H 4.96; found: C 40.93, H 4.98.

*3-(2-(5-Methylfuryl))-1-iodo-3-methylbutane (**39**)*

The tosylate of alcohol **37** (2.70 g, 8.37 mmol) was prepared by the same method as above, in 87% yield after purification by flash chromatography (9:1) as a white, crystalline solid; mp 45–46°C; IR (KBr) cm^{-1}: 3087–3035(C—H), 1358 and 1191(SO_2); ^{1}H NMR (200 MHz): 1.22(s, 6H), 1.94(t, 2H, J = 7.3 Hz), 2.20(s, 3H), 2.46(s, 3H), 3.95(t, 3H, J = 7.3 Hz), 5.77(ABq, 2H), 7.33 and 7.75(AA'XX', 4H); ^{13}C NMR (50 MHz): 13.41(q), 21.55(q), 2 × 27.05(q), 34.45(s), 40.29(t), 66.14(t), 104.37(d), 105.54(d), 127.64(d), 129.70(d), 133.24(s), 144.49(s), 150.52(s), 159.07(s); mass spectrum: 322(6, $M^{\cdot+}$), 123(100, M − $(CH_2)_2OTs$).

General procedure 1 was used to convert the above tosylate (2.70 g, 8.37 mmol) to iodide **39** (2.09 g, 7.51 mmol) in 90% yield after distillation, as a clear, colourless oil; bp 40–44°C/0.04 Torr; IR (neat) cm^{-1}: 1385,1366(CMe_2); ^{1}H NMR (200 MHz): 1.25(s, 6H), 2.23(m, 2H), 2.26(d, 3H, J = 0.8 Hz), 2.99(m, 2H), 5.84(m, 2H); ^{13}C NMR (50 MHz): 0.71(t), 13.52(q), 26.42(q), 37.98(s), 47.19(t), 104.50(d), 105.56(d), 150.53(s), 158.95(s); mass spectrum: 278(30, $M^{\cdot+}$), 123(100, M − $(CH_2)_2I$). Exact Mass calcd. for $C_{10}H_{15}IO$: 278.0168; found: 278.0153.

*6-(2-Furyl)-6-methyl-1-hepten-3-ol (**40**)*

Using general procedure 2, iodide **38** (250.1 mg, 0.947 mmol) was treated with *tert*-butyllithium (1.16 mL, 1.96 mmol) and acrolein (72 μL, 1.08 mmol) to produce compound **40** (89.1 mg, 0.458 mmol) as a clear, colourless oil in 48% yield after purification by flash chromatography (5:1); IR (neat) cm^{-1}: 3356(OH), 1644(C=C), 1385,1363(*gem*-CH_3), 1012(C—O); ^{1}H NMR (200 MHz): 1.26(s, 6H), 1.28–1.80(m, 5H), 3.99(q, 1H, J = 6.5 Hz), 5.10(dt, 1H, J = 1.2 Hz, J = 10.6 Hz), 5.18(dt, 1H, J = 1.2 Hz, J = 17.1 Hz), 5.80(ddd, 1H, J = 7.0 Hz, J = 10.6 Hz, J = 17.1 Hz), 5.98(dd, 1H, J = 0.8 Hz, J = 3.1 Hz), 6.25(dd, 1H, J = 1.7 Hz, J = 3.1 Hz), 7.30(dd, 1H, J = 0.8 Hz, J = 1.7 Hz); ^{13}C NMR (50 MHz): 26.75(q), 26.87(q), 32.25(t), 35.42(s), 37.46(t), 73.41(d), 103.31(d), 109.63(d), 114.58(t), 140.62(d), 141.13(d), 162.59(s); mass spectrum: 194(9, $M^{\cdot+}$), 176(10, M − H_2O), 161(37, M − H_2O and CH_3), 109(100, M − $(CH_2)_2CH(OH)CH{=}CH_2$). Exact Mass calcd. for $C_{12}H_{18}O_2$: 194.1307; found: 194.1296.

*6-(2-Furyl)-2,6-dimethyl-1-hepten-3-ol (**41**)*

Using general procedure 2, iodide **38** (201.1 mg, 0.761 mmol) was treated with *tert*-butyllithium (0.93 mL, 1.58 mmol) and methacrolein (72 μL, 1.08 mmol) to produce compound **41** (108.7 mg, 0.522 mmol) as a clear, colourless oil in 68.6% yield after purification by flash chromatography (5:1) and distillation; bp 56°C/0.035 Torr; IR (neat) cm^{-1}: 3373(OH), 1650(C=C), 1384,1364(CMe_2), 1013(C—O); ^{1}H NMR (200 MHz): 1.26(s, 6H), 1.29–1.75(m, 5H), 1.64(s, 3H), 3.96(br t, 1H, J = 6.3 Hz), 4.83(overlapping dd, 1H, J = 1.5 Hz), 4.91(dd, 1H, J = 1.6 Hz), 5.97(d, 1H, J = 3.2 Hz), 6.26(dd, 1H, J = 1.8 Hz, J = 3.2 Hz), 7.31(d, 1H, J = 1.8 Hz); ^{13}C NMR (50 MHz): 17.29(q), 26.71(q), 26.98(q), 30.02(t), 35.45(s), 37.61(t), 76.27(d), 103.35(d), 109.67(d), 111.18(t), 140.64(d), 147.33(s), 162.66(s); mass spectrum: 208(13, $M^{\cdot+}$), 190(4, M − H_2O), 175(10, M − H_2O and Me), 109(100, M − $(CH_2)_2CH(OH)C(Me){=}CH_2$). Anal. calcd. for $C_{13}H_{20}O_2$: C 74.96, H 9.68; found: C 74.93, H 10.08.

*(E)-7-(2-Furyl)-7-methyl-2-octen-4ol (**42**)*

Using general procedure 2, iodide **38** (247.3 mg, 0.936 mmol) was treated with *tert*-butyllithium (1.21 mL, 2.06 mmol) and crotonaldehyde (116 μL, 1.40 mmol) to produce compound **42** (166.4 mg, 0.800 mmol) as a clear, colourless oil in 84% yield after purification by flash chromatography (5:1) and distillation; IR (neat) cm^{-1}: 3350(OH), 1673(C=C), 1077(C—O); ^{1}H NMR (200 MHz): 1.26(s, 6H), 1.27–1.76(m, 5H), 1.69(dd, 3H, J = 1.3 Hz, J = 6.2 Hz), 3.93(br. q, 1H, J = 4.4 Hz), 5.44(dq, 1H, J = 1.8 Hz, J = 6.9 Hz, J = 15.3 Hz), 5.64(dq, 1H, J = 0.7 Hz, J = 6.2 Hz, J = 15.3 Hz), 5.96(dd, 1H, J = 0.9 Hz, J = 3.2 Hz), 6.26(dd, 1H, J = 1.8 Hz, J = 3.2 Hz), 7.31(dd, 1H, J = 0.9 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 17.59(q), 26.79(q), 26.91(q), 32.56(t), 35.50(s), 37.70(t), 73.41(d), 103.31(d), 109.65(d), 126.78(d), 134.28(d), 140.64(d), 162.74(s); mass spectrum: 208(15, $M^{\cdot+}$), 190(17, M − H_2O), 175(43, M − H_2O and Me), 109(100, M − $(CH_2)_2CH(OH)CH{=}CHMe$). Anal. calcd. for $C_{13}H_{20}O_2$: C 74.96, H 9.68; found: C 74.85, H 9.79.

*(E)-7-(2-Furyl)-3,7-dimethyl-2-octen-4-ol (**43**)*

Using general procedure 2, iodide **38** (346.1 mg, 1.466 mmol) was treated with *tert*-butyllithium (1.90 mL, 3.23 mmol) and tiglic aldehyde (212 μL, 2.20 mmol) to produce compound **43** (193.3 mg, 0.869 mmol) as a clear, colourless oil in 59.3% yield after purification by flash chromatography (9:1) and distillation; bp 68–72°C/0.045 Torr; IR (neat) cm^{-1}: 3353(OH), 1671(C=C), 1382,1363(CMe_2), 1076(C—O); ^{1}H NMR (200 MHz): 1.25(s), 1.28–1.70(m, 5H), 1.52(dq, 3H, J = 1.0 Hz, J = 2.2 Hz), 1.61(dq, 3H, J = 0.9 Hz, J = 6.7 Hz), 3.88(br t, 1H, J = 6.0 Hz), 5.43(qq, 1H, J = 0.9 Hz, J = 6.7 Hz), 5.96(dd, 1H, J = 0.9 Hz, J = 3.2 Hz), 6.26(dd, 1H, J = 1.9 Hz, J = 3.2 Hz), 7.30(dd, 1H, J = 0.9 Hz, J = 1.9 Hz); ^{13}C NMR (50 MHz): 10.65(q), 12.97(q), 26.67(q), 27.00(q), 29.96(t), 35.47(s), 37.97(t), 78.37(d), 103.29(d), 109.64(d), 120.94(d), 137.79(s), 140.60(d), 162.74(s); mass spectrum: 222(38, $M^{\cdot+}$), 204(17, M − H_2O), 189(30, M − H_2O and Me), 109(100, M − $(CH_2)_2CH(OH)CMe{=}CHMe$). Exact mass calcd. for $C_{14}H_{22}O_2$: 222.1621; found: 222.1609.

*6-(2-(5-Methylfuryl))-6-methyl-1-hepten-3-ol (**44**)*

Using general procedure 2, iodide **39** (297.9 mg, 1.07 mmol) was treated with *tert*-butyllithium (1.40 mL, 2.36 mmol) and acrolein (143 μL, 2.14 mmol) to produce compound **44** (154.5 mg, 0.742 mmol) as a clear, colourless oil in 69% yield after purification by flash chromatography (7:1); IR(neat) cm^{-1}: 3408(OH), 1388,1365(CMe_2), 1019(C—O); ^{1}H NMR (300 MHz): 1.20(s, 6H), 1.29–1.66(m, 5H), 2.22(s, 3H), 3.98(br q, 1H, J = 6.3 Hz), 5.07(dt, 1H, J = 1.4 Hz, J = 10.4 Hz), 5.17(dt, 1H, J = 1.2 Hz, J = 17.2 Hz), 5.79(ABq, 2H), 5.7(ddd, 1H, J = 6.2 Hz, J = 10.4 Hz, J = 17.2 Hz); ^{13}C NMR (75 MHz): 13.54(q), 26.78(q), 26.89(q), 32.21(t), 37.37(t), 35.24(s), 73.53(d), 103.66(d), 105.38(d), 114.63(t), 141.08(d), 150.02(s), 160.76(s); mass spectrum: 208(11, $M^{\cdot+}$), 190(6, M − H_2O), 175(19, M − H_2O and CH_3), 123(100, M − $(CH_2)_2CH(OH)CH{=}CH_2$). Exact Mass calcd. for $C_{13}H_{20}O_2$: 208.1464; found: 208.1467.

*6-(2-(5-Methylfuryl))-2,6-dimethyl-1-hepten-3-ol (**45**)*

Using general procedure 2, iodide **39** (253.7 mg, 0.912 mmol) was treated with *tert*-butyllithium (1.20 mL, 2.01 mmol) and methacrolein (151 μL, 2.01 mmol) to produce compound **45** (113.4 mg, 0.510 mmol) as a clear, colourless oil in 56% yield after purification by flash chromatography (7:1) and distillation; bp 60°C/0.065 Torr; IR (neat) cm^{-1}: 3369(OH), 1652(C=C), 1384,1366(CMe_2), 1021(C—O); ^{1}H NMR (300 MHz): 1.20(s, 6H), 1.29–1.59(m, 5H), 1.62(t, 3H, J = 1.1 Hz), 2.22(d, 3H, J = 0.8 Hz), 3.94(br t, 1H), 4.81(m, 1H, J = 1.6 Hz), 4.88(m, 1H), 5.80(ABq, 2H); ^{13}C NMR (75 MHz): 13.53(q), 17.16(q), 26.67(q), 27.02(q), 29.84(t), 37.38(t), 35.27(s), 76.29(d), 103.89(d), 105.37(d), 111.33(t), 147.20(s), 149.98(s), 160.78(s); mass

spectrum (FI): 222.28. Exact Mass calcd. for $C_{14}H_{22}O_2$: 222.1620; found: 222.1620.

(E)-7-(2-(5-Methylfuryl))-7-methyl-2-octen-4-ol (46)

Using general procedure 2, iodide **39** (270.4 mg, 0.972 mmol) was treated with *tert*-butyllithium (1.26 mL, 2.14 mmol) and crotonaldehyde (161 μL, 1.94 mmol) to produce compound **46** (194.3 mg, 0.874 mmol) as a clear, colourless oil in 90% yield after purification by flash chromatography (9:1) and distillation; IR (neat) cm^{-1}: 3457–3427(OH), 1675(C=C), 1384, 1367(CMe_2), 1077(C—O); ^1H NMR (300 MHz): 1.20(s, 6H), 1.24–1.68(m, 5H), 1.66(dd, 3H, J = 0.9 Hz, J = 6.2 Hz), 2.22(s, 3H), 3.90(m, 1H, J = 6.6 Hz), 5.43(dd, 1H, J = 0.9 Hz, J = 6.6 Hz, J = 15.0 Hz), 5.57(dq, 1H, J = 6.2 Hz, J = 15.0 Hz), 5.79(s, 2H); ^{13}C NMR (75 MHz): 13.53(q), 17.62(q), 26.77(q), 26.89(q), 32.46(t), 37.53(t), 35.27(s), 73.44(d), 103.81(d), 105.37(d), 126.76(d), 134.19(d), 149.97(s), 160.88(s); mass spectrum: 222(13, $M^{\cdot+}$), 123(100, M − $(CH_2)_2CH(OH)CH$=CMe). Anal. calcd. for $C_{14}H_{22}O_2$: C 75.63, H 9.97; found: C 75.25, H 9.99.

6-(2-Furyl)-6-methyl-1-hepten-3-one (9)

Compound **40** (169.4 mg, 0.872 mmol) was oxidized according to general procedure 3 to provide compound **9** (118.8 mg, 0.618 mmol) in 71% yield as a clear, colourless oil after purification by flash chromatography (9:1) and distillation; bp 50–56°C/0.05 Torr; IR (neat) cm^{-1}: 1703 and 1680(C=O), 1615(C=C); ^1H NMR (200 MHz): 1.28(s, 6H), 1.88–1.96(m, 2H), 2.37–2.45(m, 2H), 5.77(ddd, 1H, J = 1.5 Hz, J = 10.6 Hz), 6.00(dd, 1H, J = 3.2 Hz), 6.11(dd, 1H, J = 1.5 Hz, J = 17.3 Hz), 6.28(dd, 1H, J = 10.6 Hz, J = 17.3 Hz), 6.30(m, 1H), 7.32(dd, 1H, J = 0.9 Hz); ^{13}C NMR (50 MHz): 2 × 26.46(q), 35.09(s), 35.26(t), 35.56(t), 103.47(d), 109.44(d), 127.38(t), 136.12(d), 140.81(d), 161.56(s), 200.34(s); mass spectrum: 192(18, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)CH$=CH_2). Anal. calcd. for $C_{13}H_{18}O_2$: C 75.69, H 8.80; found: C 75.45, H 9.26.

6-(2-Furyl)-2,6-dimethyl-1-hepten-3-one (10)

Compound **41** (83.1 mg, 0.399 mmol) was oxidized according to general procedure 3 to provide compound **10** (63.1 mg, 0.306 mmol) in 77% yield as a clear, colourless oil after purification by flash chromatography (9:1) and distillation; bp 50–56°C/0.04 Torr; IR (neat) cm^{-1} 1679,1672(C=O), 1630(C=C), 1385,1367(CMe_2); ^1H NMR (200 MHz): 1.28(s, 6H), 1.83(dd, 3H, J = 0.8 Hz, J = 1.4 Hz), 1.86–1.95(m, 2H), 2.46–2.54(m, 2H), 5.70(m, 1H), 5.81(m, 1H), 5.99(dd, 1H, J = 0.8 Hz, J = 3.2 Hz), 6.26(dd, 1H, J = 1.8 Hz, J = 3.2 Hz), 7.31(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 17.60(q), 2 × 26.79(q), 33.35(t), 35.44(s), 36.60(t), 103.67(d), 109.72(d), 124.09(t), 140.84(d), 144.40(s), 162.00(s), 202.03(s); mass spectrum: 206(7, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)C(Me)$=CH_2). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1283.

(E)-7-(2-Furyl)-7-methyl-2-octen-4-one (11)

Compound **42** (166.4 mg, 0.807 mmol) was oxidized according to general procedure 3 to provide compound **11** (124.7 mg, 0.604 mmol) in 76% yield as a clear, colourless oil after purification by flash chromatography (20:1) and distillation; IR(neat): 3143–3013(C—H), 2969–2871(C—H), 1697, 1673(C=O), 1634(C=C), 1379,1365(CMe_2); ^1H NMR(200 MHz): 1.26(s, 6H), 1.84(dd, 3H, J = 1.6 Hz, J = 6.8 Hz), 1.84–1.92(m, 2H), 2.29–2.37(m, 2H), 5.97(dd, 1H, J = 0.7 Hz, J = 3.2 Hz), 6.04(dq, 1H, J = 1.6 Hz, J = 15.8 Hz), 6.25(dd, 1H, J = 1.9 Hz, J = 3.2 Hz), 6.72(dq, 1H, J = 6.8 Hz, J = 15.8 Hz), 7.29(dd, 1H, J = 0.7 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 17.96(q), 2 × 26.68(q), 35.31(s), 35.76(t), 35.96(t), 103.59(d), 109.62(d), 131.72(d), 140.75(d), 142.00(d), 161.89(s), 200.22(s); mass spectrum: 206(36, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)CH$=CHMe). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1307.

(E)-7-(2-Furyl)-3,7-dimethyl-2-octen-4-one (12)

Compound **43** (153.2 mg, 0.689 mmol) was oxidized according to general procedure 3 to provide compound **12** (144.2 mg, 0.654 mmol) in 95% yield as a clear, colourless oil after purification by flash chromatography (20:1) and distillation; bp 80–90°C/0.06 Torr; IR(neat) cm^{-1}: 1667(C=O), 1644(C=C), 1379,1363(CMe_2); ^1H NMR (200 MHz): 1.28(s, 6H), 1.74(d, 3H, J = 1.0 Hz), 1.82(d, 3H, J = 6.9 Hz), 1.85–1.94(m, 2H), 2.42–2.5(m, 2H), 5.99(dd, 1H, J = 0.7 Hz, J = 3.2 Hz), 6.20(dd, 1H, J = 1.8 Hz, J = 3.2 Hz), 6.58(m, 1H, J = 1.0 Hz, J = 6.9 Hz), 7.32(dd, 1H, J = 0.8 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 10.98(q), 14.59(q), 2 × 26.77(q), 32.95(t), 36.87(t), 35.44(s), 103.60(d), 109.89(d), 136.66(d), 138.05(s), 140.77(d), 162.10(s), 201.76(s); mass spectrum: 220(45, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)CMe$=CHMe). Exact Mass calcd. for $C_{14}H_{20}O_2$: 220.1464; found: 220.1461.

6-(2-(5-Methylfuryl))-6-methyl-1-hepten-3-one (13)

Compound **44** (122.0 mg, 0.586 mmol) was oxidized according to general procedure 3 to provide compound **13** (80.9 mg, 0.392 mmol) in 67% yield as a clear, colourless oil after purification by flash chromatography (9:1) and distillation; bp 52–58°C/0.03 Torr; IR (neat) cm^{-1}: 1682(C=O), 1614(C=C); ^1H NMR (300 MHz): 1.22(s, 6H), 1.84–1.89(m, 2H), 2.22(d, 3H, J = 0.9 Hz), 2.37–2.42(m, 2H), 5.75(dd, 1H, J = 1.3 Hz, J = 10.4 Hz), 5.80(dq, 1H, J = 1.0 Hz, J = 3.0 Hz), 5.83(d, 1H, J = 3.0 Hz), 6.10(dd, 1H, J = 1.3 Hz, J = 17.6 Hz), 6.26(dd, 1H, J = 10.4 Hz, J = 17.6 Hz); ^{13}C NMR (75 MHz): 13.55(q), 2 × 26.62(q), 35.23(s), 35.62(t), 35.79(t), 104.34(d), 105.47(d), 127.76(t), 136.44(d), 150.37(s), 159.98(s), 201.01(s); mass spectrum: 206(24, $M^{\cdot+}$), 123(100, M − $(CH_2)_2C(O)CH$=CH_2). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1294.

6-(2-(5-Methylfuryl))-2,6-dimethyl-1-hepten-3-one (14)

Compound **45** (90.2 mg, 0.406 mmol) was oxidized according to general procedure 3 to provide compound **14** (88.3 mg, 0.401 mmol) in 99% yield as a clear, colourless oil after purification by flash chromatography (9:1) and distillation; bp 60°C/0.055 Torr; mp 27.5–30°C; IR (neat) cm^{-1}: 1677(C=O), 1625(C=C); ^1H NMR (300 MHz): 1.22(s, 6H), 1.81(d, 3H, J = 1.1 Hz), 1.82–1.87(m, 2H), 2.21(d, 3H, J = 0.8 Hz), 2.45–2.51(m, 2H), 5.68(m, 1H), 5.80(m, 3H); ^{13}C NMR (75 MHz): 13.53(q), 17.67(q), 2 × 26.63(q), 33.43(t), 36.56(t), 35.30(s), 104.28(d), 105.47(d), 124.29(t), 144.31(s), 150.29(s), 160.1(s), 202.39(s); mass spectrum: 220(18, $M^{\cdot+}$), 123(100, M − $(CH_2)_2C(O)C(Me)$=CH_2). Exact Mass calcd. for $C_{14}H_{20}O_2$: 220.1463; found: 220.1473.

(E)-7-(2-(5-Methylfuryl))-7-methyl-2-octen-4-one (15)

Compound **46** (199.8 mg, 0.899 mmol) was oxidized according to general procedure 3 to provide compound **15** (169.3 mg, 0.768 mmol) in 86% yield as a clear, colourless oil after purification by flash chromatography (20:1) and distillation, bp 62–64°C/0.055 Torr; IR (neat) cm^{-1}: 3034(CH), 2988–2869(CH), 1697, 1674(C=O), 1634(C=C), 1385, 1366(*gem*-Me); ^1H NMR (300 MHz): 1.25(s, 6H), 1.82–1.91(overlapping m, 5H), 2.25(s, 3H), 2.32–2.40(m, 2H), 5.84(m, 2H), 6.06(dq, 1H, J = 1.6 Hz, J = 15.7 Hz), 6.74(dq, 1H, J = 6.8 Hz, J = 15.7 Hz); ^{13}C NMR (75 MHz): 13.56(q), 18.16(q), 2 × 26.82(q), 35.27(s), 35.95(t), 36.01(t), 104.30(d), 105.45(d), 131.84(d), 142.22(d), 150.29(s), 160.12(s), 200.66(s); mass spectrum: 220(16, $M^{\cdot+}$), 123(100, M − $(CH_2)_2C(O)CH$=CHMe). Exact Mass calcd. for $C_{14}H_{20}O_2$: 220.1463; found: 220.1462.

6-(2-Furyl)-6-methyl-1-(trimethylsilyl)-1-heptyn-3-one (16)

Using general procedure 2, iodide **38** (285.1 mg, 1.08 mmol) was treated with *tert*-butyllithium (1.40 mL, 2.37 mmol) and aldehyde **47** (202.6 mg, 1.61 mmol) to produce the corresponding allylic alcohol (187.6 g, 0.71 mmol) as a clear, colourless oil in 66% yield after purification by flash chromatography (7:1) and distillation; bp 80–88°C/0.065 Torr; IR (neat) cm^{-1}: 3380(O—H), 1055(C—O); ^1H NMR (200 MHz): 0.18(s, 9H), 1.28(s, 6H), 1.47–1.81(overlapping m, 5H), 4.27(br q, 1H, J = 5.9 Hz), 5.99(dd, 1H, J = 0.8, J = 3.2 Hz), 6.27(dd, 1H, J = 1.9, J = 3.2 Hz),

7.31(dd, 1H, J = 0.8, J = 1.9 Hz); ^{13}C NMR (50 MHz): −0.14(q), 2 × 26.88(q), 33.24(t), 37.22(t), 63.12(d), 89.40(s), 106.80(s), 103.37(d), 109.66(d), 140.73(d), 162.43(s); mass spectrum: 264(4, $M^{\cdot+}$), 249(15, M − Me), 109(100, M − $(CH_2)_2CH(OH)$-C≡CSiMe$_3$). Exact Mass calcd. for $C_{15}H_{24}O_2Si$: 264.1546; found: 264.1535.

The above alcohol (123.3 mg, 0.47 mmol) was oxidized according to general procedure 3 to provide compound **16** (116.6 mg, 0.44 mmol) as a clear, colourless oil in 95% yield after purification by flash chromatography (20:1) and distillation; bp 68–74°C/0.04 Torr: IR (neat) cm^{-1}: 2151(C≡C), 1679(C=O); ^{1}H NMR (200 MHz): 0.25(s, 9H), 1.28(s, 6H), 1.90–2.04(m, 2H), 2.33–2.50(m, 2H), 6.00(dd, 1H, J = 0.8 and 3.0 Hz), 6.29(dd, 1H, J = 1.7 and 3.0 Hz), 7.33(dd, 1H, J = 0.8 and 1.7 Hz); ^{13}C NMR (50 MHz): 0.80(q), 2 × 26.73(q), 35.20(s), 35.38(t), 41.34(t), 97.50(s), 101.93(s), 103.82(d), 109.70(d), 140.99(d), 161.47(s), 187.51(s); mass spectrum: 262(5, $M^{\cdot+}$), 247(15, M − Me), 109(100, M − $(CH_2)_2C(O)C{\equiv}CSiMe_3$). Exact Mass calcd. for $C_{15}H_{22}O_2Si$: 262.1389; found: 262.1385.

7-(2-Furyl)-7-methyl-2-octyn-4-one (17)

Using general procedure 2, iodide **38** (601.5 mg, 2.28 mmol) was treated with *tert*-butyllithium (2.95 mL, 5.01 mmol) and aldehyde **48** (620.1 mg, 9.12 mmol) to produce the corresponding alcohol (378.8 g, 1.84 mmol) as a clear, colourless oil in 81% yield after purification by flash chromatography (7:1) and distillation; bp 70–80°C/0.045 Torr; IR (neat) cm^{-1}: 3520(O*H*), 1054(C—O); ^{1}H NMR (200 MHz): 1.28(s, 6H), 1.44–1.83(overlapping m, 5H), 1.84(d, 3H, J = 2.2 Hz), 4.22–4.25(br m, 1H), 5.98(dd, 1H, J = 0.7 Hz, J = 3.2 Hz), 6.26(dd, 1H, J = 1.8 Hz, J = 3.2 Hz), 7.31(dd, 1H, J = 0.7 Hz, J = 1.8 Hz); ^{13}C NMR (50 MHz): 3.37(q), 2 × 26.74(q), 33.46(t), 35.26(t), 37.19(t), 62.76(d), 80.37(s), 80.73(s), 103.24(d), 109.56(d), 140.59(d), 162.42(s); mass spectrum: 206(10, $M^{\cdot+}$), 109(100, M − $(CH_2)_2CH(OH)$-C≡CCH$_3$). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1307.

The above alcohol (213.1 mg, 1.03 mmol) was oxidized according to general procedure 3 to provide compound **17** (200.9 mg, 0.98 mmol) as a clear, colourless oil in 95% yield after purification by flash chromatography (20:1) and distillation; bp 76–80°C/0.08 Torr. IR (neat) cm^{-1}: 2218(C≡C), 1673(C=O); ^{1}H NMR (200 MHz): 1.27(s, 6H), 1.90–1.98(m, 2H), 2.00(s, 3H), 2.34(m, 2H), 5.99(dd, 1H, J = 0.8 Hz, J = 3.2 Hz), 6.27(dd, 1H, J = 1.9 Hz, J = 3.2 Hz), 7.32(dd, 1H, J = 0.8 Hz, J = 1.9 Hz); ^{13}C NMR (50 MHz): 3.96(q), 2 × 26.70(q), 35.22(s), 35.54(d), 41.44(d), 80.18(s), 89.78(s), 103.75(d), 109.70(d), 140.96(d), 161.61(s), 187.86(s); mass spectrum: 204(11, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)C{\equiv}CCH_3$) Exact Mass calcd. for $C_{13}H_{16}O_2$: 204.1150; found: 204.1151.

(6α,8α-H)-11-Oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (49)

General procedure 5 was used for the Lewis acid-mediated IMDAF reaction of compound **1**. Thus, enone **1** (54.1 mg, 0.329 mmol) was treated with MeAlCl$_2$ (362 μL, 0.362 mmol) at −78°C for 1 h to provide adduct **49** (54.0 mg, 0.329 mmol) in 99% yield as white, crystalline solid; mp 25–27°C; IR (KBr) cm^{-1}: 1708(C=O), 1153(C—O); ^{1}H NMR (400 MHz): 1.47(dd, 1H, $J_{7\alpha,6\alpha}$ = 8.2 Hz, J_{gem} = 11.8 Hz, H-7α), 1.79–2.08(m, 2H), 2.28(dd, 1H, $J_{6\alpha,7\beta}$ = 3.0 Hz, $J_{6\alpha,7\alpha}$ = 8.2 Hz, H-6α), 2.49(ddd, $J_{7\beta,6\alpha}$ = 3.0 Hz, $J_{7\beta,8}$ = 4.8 Hz, J_{gem} = 11.8 Hz, H-7β), 2.20–2.58(m, 4H), 4.89(dd, 1H, $J_{8,9}$ = 1.6 Hz, $J_{8,7\beta}$ = 4.8 Hz, H-8), 6.27 (d, 1H, $J_{10,9}$ = 5.7 Hz, H-10), 6.42(dd, 1H, $J_{8,9}$ = 1.7 Hz, $J_{9,10}$ = 5.7 Hz, H-9); ^{13}C NMR(50 MHz): 21.73, 28.17, 29.10 and 41.66(t, C-2, C-3, C-4 and C-7), 50.30(d, C-6), 78.08(d, C-8), 90.40(s, C-1), 136.92 and 138.20(d, C-9 and C-10), 209.30(s, C-5); mass spectrum (FI): 164(100, $M^{\cdot+}$). Exact Mass calcd. for $C_{10}H_{12}O_2$: 164.0838; found: 164.0819.

(8α-H)-6α-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (50)

General procedure 5 was used to perform the Lewis acid-mediated reaction of compound **2**. Thus, enone **2** (66.6 mg, 0.374 mmol) was treated with MeAlCl$_2$ (411 μL, 0.411 mmol) at −78°C for 2.5 h to provide a SM:A ratio of 22.78 with 98% recovery of material. Adduct **50** was characterized as a pale yellow, crystalline solid, mp <22°C; IR (neat) cm^{-1}: 1707(C=O); ^{1}H NMR (400 MHz): 1.01(d, 1H, J_{gem} = 11.8 Hz, H-7α), 1.12(s, 3H, -CH$_3$), 1.91–2.03(m, 2H), 2.25–2.28(m, 2H), 2.42(dt, 1H, $J_{2\beta,3\alpha}$ = 2.9 Hz, $J_{2\beta,3\alpha}$ = 2.9 Hz, J_{gem} = 14.4 Hz, H-2β), 2.62(dd, 1H, $J_{3\alpha,4\alpha}$ = 14.4 Hz, J_{gem} = 19.4 Hz, H-4β), 2.86(dd, 1H, $J_{7\beta,8}$ = 5.1 Hz, J_{gem} = 11.8 Hz, H-7β), 4.82(dd, 1H, $J_{8,9}$ = 1.6 Hz, $J_{8,7\beta}$ = 5.1 Hz, H-8), 6.14(d, 1H, $J_{10,9}$ = 5.7 Hz, H-10), 6.49(dd, 1H, $J_{9,8}$ = 1.6 Hz, $J_{9,10}$ = 5.7 Hz, H-9); ^{13}C NMR (50 MHz): 20.94, 25.67, 37.34 and 38.28(t, C-2, C-3, C-4 and C-7), 22.44(q, -CH$_3$), 54.18(s, C-6), 78.03(d, C-8), 91.70(s, C-1), 135.13 and 138.81(d, C-9 and C-10), 213.00(s, C-5); mass spectrum: 178(14, $M^{\cdot+}$), 94(100, M − $CH_2{=}C(OH)C(Me){=}CH_2$, retro IMDAF–McLafferty rearr.). Exact Mass calcd. for $C_{11}H_{14}O_2$: 178.0994; found: 178.0990.

(6α,8α-H)-7α-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (51)

General procedure 5 was used to perform the Lewis acid-mediated reactions of compound **3**. Quantitative reaction: precursor **3** (107.6 mg, 0.604 mmol) was treated with MeAlCl$_2$ (664 μL, 0.664 mmol) at −78°C for 8 h to provide a SM:A ratio of 78:22 with quantitative recovery of material. Flash chromatography (7:1) provided starting material (40.8 mg) and adduct **51** (11.2 mg). Catalytic reaction: enone **3** (121.6 mg, 0.682 mmol) was treated with MeAlCl$_2$ (68 μL, 0.068 mmol) at −65°C for 2 h to provide a SM:A ratio of 31:69 with 99% recovery of material. Flash chromatography (9:1) provided precursor **3** (39.4 mg) and **51** (77.8 mg) as a clear, colourless oil; IR (neat) cm^{-1}: 1706(C=O); ^{1}H NMR (400 MHz): 0.93(d, 3H, J = 7.0 Hz, C-7-CH$_3$), 1.73(d, 1H, $J_{6\alpha,7\beta}$ = 4.0 Hz, H-6α), 1.82–2.01(m, 2H), 2.21(dt, 1H, $J_{2\alpha,3\alpha}$ = 4.7 Hz, $J_{2\alpha,3\beta}$ = 12.3 Hz, J_{gem} = 12.7 Hz, H-2α), 2.27–2.38(m, 2H), 2.47(ddt, 1H, $J_{4\beta,2\beta}$ = 1.6 Hz, $J_{4\beta,3\alpha}$ = 3.7 Hz, $J_{4\beta,3\beta}$ = 3.7 Hz, J_{gem} = 14.4 Hz, H-4β), 2.79(ddq, 1H, $J_{7\beta,6\alpha}$ = 4.0 Hz, $J_{7\beta,8}$ = 4.7 Hz, J = 7.0 Hz, H-7β), 4.69(dd, 1H, $J_{8,9}$ = 1.6 Hz, $J_{8,7\beta}$ = 4.7 Hz, H-8), 6.24(d, 1H, $J_{10,9}$ = 5.7 Hz, H-10), 6.37(dd, 1H, $J_{9,8}$ = 1.6 Hz, $J_{9,10}$ = 5.7 Hz, H-9); ^{13}C NMR (50 MHz): 17.23(q), 21.45, 28.50 and 41.54(t, C-2, C-3, and C-4), 37.40(d, C-7), 58.59(d, C-6), 81.80(d, C-8), 91.12(s, C-1), 135.80 and 138.32(d, C-9 and C-10), 209.76(s, C-5); mass spectrum: 178(16, $M^{\cdot+}$), 94(100, M − $CH_2{=}C(OH)CMe{=}CHMe$, retro IMDAF–McLafferty rearr.). Exact Mass calcd. for $C_{11}H_{14}O_2$: 178.0994; found: 178.1002.

(8α-H)-6α,7α-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (52)

General procedure 5 was used to perform the Lewis acid-mediated reaction of compound **4**. Quantitative reaction: enone **4** (38.1 mg, 0.198 mmol) was treated with MeAlCl$_2$ (218 μL, 0.218 mmol) at −65°C for 2 h to provide a SM:A ratio of 100:0. Catalytic reaction: compound **4** (143.8 mg, 0.747 mmol) was treated with MeAlCl$_2$ (75 μL, 0.075 mmol) at −65°C for 2 h to provide a SM:A ratio of 95:5 (99% recovery, 142.2 mg). Starting material **4** (130.0 mg) could be separated from the product **52** (6.0 mg), a yellow oil, using flash chromatography (9:1) (no bp due to decomposition); ^{1}H NMR (400 MHz): 0.78(d, 3H, J = 7.4 Hz, C-7-CH$_3$), 0.93(s, 3H, C-6-CH$_3$), 1.88–2.00(m, 2H), 2.20–2.26(m, 1H), 2.40(dt, 1H, $J_{4\beta,3\alpha}$ = 3.0 Hz, $J_{4\beta,3\beta}$ = 3.0 Hz, J_{gem} = 14.7 Hz, H-4β), 2.55–2.62(m, 1H), 2.64(dt, 1H, $J_{4\alpha,3\alpha}$ = 7.2 Hz, $J_{4\alpha,3\beta}$ = 14.7 Hz, J_{gem} = 14.7 Hz, H-4α), 2.99(dq, 1H, $J_{7\beta,8}$ = 4.8 Hz, $J_{7\beta,12}$ = 7.4 Hz, H-7β), 4.71(dd, $J_{8,9}$ = 1.7 Hz, $J_{8,7\beta}$ = 4.8 Hz, H-8), 6.22(d, 1H, $J_{10,9}$ = 5.8 Hz, H-10), 6.45(dd, 1H, $J_{9,8}$ = 1.7 Hz, $J_{9,10}$ = 5.8 Hz, H-9); ^{13}C NMR (50 MHz): 13.29(q), 17.86(q), 20.72, 26.18 and 38.20(t, C-2 to C-4), 39.27(d,

C-7), 60.35(s, C-6), 81.92(d, C-8), 92.68(s, C-1), 137.11(d, C-9 and C-10), 214.25(s, C-5).

(6α-H)-8α-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (53)

General procedure 5 was used to perform the Lewis acid-mediated reaction of compound **5**. Thus, enone **5** (58.9 mg, 0.33 mmol) was treated with $MeAlCl_2$ (0.36 mL, 0.36 mmol) at −78°C for 1 h to provide adduct **53** (58.9 mg, 0.33 mmol) in >99% yield as yellow oil (no bp due to decomposition on heating); IR (neat) cm^{-1}: 1710(C=O); ^{1}H NMR (400 MHz): 1.58(s, 3H, -CH_3), 1.61(dd, 1H, $J_{6\alpha,7\alpha}$ = 8.2 Hz, $J_{7\alpha,7\beta}$ = 11.8 Hz, H-7α), 1.88–2.04(m, 2H), 2.20(dd, 1H, $J_{7\beta,6\alpha}$ = 3.5 Hz, J_{gem} = 11.8 Hz, H-7β), 2.23(dt, 1H, $J_{2\alpha,3\alpha}$ = 5.2 Hz, $J_{2\alpha,3\beta}$ = 12.4 Hz, J_{gem} = 12.4 Hz, H-2α), 2.39(dd, 1H, $J_{6\alpha,7\beta}$ = 3.5 Hz, $J_{6\alpha,7\alpha}$ = 8.2 Hz, H-6α), 2.35–2.44(m, 2H), 2.52(dddt, 1H, $J_{4\beta,2\beta}$ = 1.6 Hz, $J_{4\beta,3\alpha}$ = 3.6 Hz, $J_{4\beta,3\beta}$ = 3.6 Hz, J_{gem} = 14.1 Hz, H-4β), 6.15 and 6.25(ABq, 1H, J = 5.6- Hz, H-9 and H-10); ^{13}C NMR (50 MHz): 18.71(q, -CH_3), 21.68, 28.54, 35.42, and 41.86(t, C-2, C-3, C-4, and C-7), 53.77(d, C-6), 85.96 and 90.83(s, C-1 and C-8), 137.69 and 141.18(d, C-9 and C-10), 209.70(s, C-5); mass spectrum (FI): 178. Exact mass calcd. for $C_{11}H_{14}O_2$: 178.0994; found: 178.0986.

6α,8α-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (54)

General procedure 5 was used to perform the Lewis acid-mediated reactions of compound **6**. 1.1 Equivalents of $MeAlCl_2$ reaction: precursor **6** (80.5 mg, 0.419 mmol) was treated with $MeAlCl_2$ (461 μL, 0.461 mmol) at −78°C for 8 h to provide a SM:A ratio of 19:81 with quantitative recovery of material. Flash chromatography (9:1) provided starting material (12.6 mg) and adduct **54** (59.0 mg). Catalytic reaction: enone **6** (37.4 mg, 0.192 mmol) was treated with $MeAlCl_2$ (19 μL, 0.019 mmol) at −65°C for 2 h to provide a SM:A ratio of <1:>99 with 99% recovery of material. Flash chromatography (9:1) provided precursor **6** (2.6 mg) and **54** (34.6 mg) as a clear, colourless oil; IR (neat) cm^{-1}: 1708(C=O); ^{1}H NMR (400 MHz): 1.08(s, 3H, C-6-CH_3), 1.10(d, 1H, $J_{7\alpha,7\beta}$ = 5.5 Hz, H-7α), 1.50(s, 3H, C-8-CH_3), 1.82–2.04(m, 2H), 2.16–2.23(m, 2H), 2.38(dt, 1H, $J_{3\beta,4\beta}$ = 3.2 Hz, $J_{3\alpha,4\beta}$ = 3.2 Hz, $J_{4\alpha,4\beta}$ = 14.4 Hz, H-4β), 2.51–2.67(m, 1H), 2.55(d, 1H, $J_{7\alpha,7\beta}$ = 11.8 Hz, H-7β), 6.13(d, 1H, $J_{10,9}$ = 5.6 Hz, H-10), 6.27(d, 1H, $J_{9,10}$ = 5.6 Hz, H-9); ^{13}C NMR (50 MHz): 18.87 and 22.24(q, -CH_3's), 20.84, 25.86, 38.22, and 43.66(t, C-2, C-3, C-4, and C-7), 57.41(s, C-6), 85.69 and 92.09(s, C-1 and C-8), 135.87 and 141.65(d, C-9 and C-10), 213.33(s, C-5); mass spectrum: 192(5, M$^{\cdot+}$), 108(100, M − CH_2=C(OH)C(Me)=CH_2, retro IMDAF–McLafferty rearr.). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1150; found: 192.1141.

(6α-H)-7α,8α-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (55)

General procedure 5 was used to perform the Lewis acid-mediated reaction of compound **7**. Quantitative reaction: enone **7** (63.7 mg, 0.331 mmol) was treated with $MeAlCl_2$ (364 μL, 0.364 mmol) at −78°C for 8 h to provide a SM:A ratio of 82:18 with 98% recovery of material. Flash chromatography (7:1) provided enone **7** (46.9 mg) and adduct **55** (15.2 mg). Catalytic reaction: compound **7** (51.4 mg, 0.267 mmol) was treated with $MeAlCl_2$ (27 μL, 0.027 mmol) at −65°C for 2 h to provide a SM:A ratio of 24:76 (92% recovery, 47.5 mg). Starting material **7** (10.7 mg) could be separated from the product **55** (32.1 mg), a yellow solid, using flash chromatography (9:1), mp 28–30°C; IR (KBr) cm^{-1}: 1709(C=O), 1136(C—O); ^{1}H NMR (400 MHz): 0.95(d, 3H, J = 7.1 Hz, C-7-CH_3), 1.52(s, 3H, C-8-CH_3), 1.89(d, 1H, $J_{6\alpha,7\beta}$ = 4.3 Hz, H-6α), 1.90–1.99(m, 2H), 2.17(ddd, 1H, $J_{2\alpha,3\alpha}$ = 5.3 Hz, $J_{2\alpha,3\beta}$ = 12.1 Hz, J_{gem} = 14.7 Hz, H-2α), 2.29–2.38(m, 2H), 2.46(dq, 1H, $J_{7\beta,6\alpha}$ = 4.1 Hz, J = 7.0 Hz, H-7β), 2.5(dddt, 1H, $J_{4\beta,2\beta}$ = 1.6 Hz, $J_{4\beta,3\alpha}$ = 3.7 Hz, $J_{4\beta,3\beta}$ = 3.7 Hz, J_{gem} = 14.3 Hz, H-4β), 6.20(d, 1H, $J_{9,10}$ = 5.6 Hz, H-10), 6.26(d, 1H, $J_{9,10}$ = 5.6 Hz, H-9); ^{13}C NMR (50 MHz): 17.07(q), 17.12(q), 21.38, 28.62, and 41.53(t, C-2, C-3, and C-4), 43.10(d, C-7), 61.51(d, C-6), 88.63 and 90.09(s, C-1 and C-8), 138.80 and 138.87(d, C-9 and C-10), 210.14(s, C-5); mass spectrum: 192(13, M$^{\cdot+}$), 108(100, M − CH_2=C(OH)CH=CHMe, retro IMDAF–McLafferty rearr.). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1151; found: 192.1132.

(6α,8α-H)-2,2-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (56)

The IMDAF reaction of compound **9** (52.9 mg, 0.275 mmol) was performed according to general procedure 4 to provide adduct **56** (46.5 mg, 0.242 mmol) after 12 h in 88% yield as a white solid, mp 57–60°C; IR (KBr) cm^{-1}: 1705(C=O), 1663(C=C), 1390, 1369(*gem*-Me); ^{1}H NMR (400 MHz): 1.08 and 1.36(s, 6H, 2 × CH_3), 1.55(dd, 1H, $J_{7\alpha,6\alpha}$ = 8.5 Hz, J_{gem} = 11.8 Hz, H-7α), 1.61(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.7 Hz, $J_{3\alpha,4\alpha}$ = 5.8 Hz, J_{gem} = 13.9 Hz, H-3α), 1.99(dt, 1H, $J_{3\beta,4\beta}$ = 4.3 Hz, $J_{3\beta,4\alpha}$ = 13.9 Hz, J_{gem} = 13.9 Hz, H-3β), 2.27(dd, 1H, $J_{6\alpha,7\beta}$ = 3.2 Hz, $J_{6\alpha,7\alpha}$ = 8.5 Hz, H-6α), 2.37–2.42(overlapping m, 2H, H-4β and H-7β), 2.58(dt, 1H, $J_{4\alpha,3\alpha}$ = 5.8 Hz, $J_{4\alpha,3\beta}$ = 15.1 Hz, $J_{4\alpha,4\beta}$ = 15.1 Hz, H-4α), 4.88(dd, 1H, $J_{8,9}$ = 1.5 Hz, $J_{8,7\beta}$ = 4.9 Hz, H-8), 6.24(d, 1H, $J_{10,9}$ = 5.8 Hz, H-10), 6.43(dd, 1H, $J_{9,8}$ = 1.5 Hz, $J_{9,10}$ = 5.8 Hz, H-9); ^{13}C NMR (50 MHz): 24.24 and 25.96(q, -CH_3), 30.98, 34.88, and 37.84(t, C-3, C-4, and C-7), 31.98(s, C-2), 47.90(d, C-6), 77.90(d, C-8), 95.90(s, C-1), 133.47, 138.83(d, C-9 and C-10), 210.20(s, C-5); mass spectrum: 192(48, M$^{\cdot+}$), 109(100, M − $(CH_2)_2$C(O)CH=CH_2). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1150; found: 192.1148.

(8α-H)-2,2,6α-Trimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (57)

The IMDAF reaction of compound **10** (221.2 mg, 1.07 mmol) was performed according to general procedure 4 to provide after 96 h precursor **10** (186.4 mg, 0.903 mmol) and adduct **57** (19.8 mg, 0.096 mmol) after purification by flash chromatography (9:1) in 93% total recovery.

General Procedure 5 was used to perform the Lewis acid-mediated reactions of compound **10**. Thus, enone **10** (55.3 mg, 0.268 mmol) was treated with quantitative $MeAlCl_2$ (295 μL, 0.295 mmol) at −78°C for 8 h to provide a SM:A ratio of 68:32 with a quantitative recovery of material. Enone **10** (161.9 mg, 0.785 mmol) was treated with catalytic $MeAlCl_2$ (79 μL, 0.079 mmol) (according to general procedure 5) at −65°C for 2 h to provide a SM:A ratio of 40:60 with quantitative recovery. Flash chromatography (9:1) provided enone **10** (64.5 mg) and adduct **57** (92.3 mg) in 97% recovered yield. Adduct **57** was characterized as a white solid, mp 44–55°C; IR (KBr) cm^{-1}: 3078, 3021(C-H), 2982–2858(C-H), 1699(C=O), 1389, 1369(*gem*-Me); ^{1}H NMR (200 MHz): 0.99(d, 1H, J = 11.7 Hz, H-7α), 1.03(s, C-6-CH_3), 1.16 and 1.39(s, 3H each, 2 × CH_3), 1.61(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.8 Hz, $J_{3\alpha,4\alpha}$ = 5.8 Hz, $J_{3\alpha,3\beta}$ = 13.4 Hz, H-3α), 2.01(dt, 1H, $J_{3\beta,4\beta}$ = 4.1 Hz, $J_{3\beta,4\alpha}$ = 14.3 Hz, $J_{3\beta,3\alpha}$ = 13.6 Hz, H-3β), 2.35(ddd, 1H, $J_{4\beta,3\alpha}$ = 2.8 Hz, $J_{4\beta,3\beta}$ = 4.0 Hz, $J_{4\beta,4\alpha}$ = 15.3 Hz, H-4β), 2.82(dt, 1H, $J_{4\beta,3\beta}$ = 5.8 Hz, J_{gem} = 14.5 Hz, H-4α), 2.85(dd, 1H, $J_{7\beta,8}$ = 3.8 Hz, $J_{7\beta,7\alpha}$ = 11.8 Hz, H-7β), 4.77(dd, 1H, $J_{8,9}$ = 1.6 Hz, $J_{8,7\beta}$ = 5.2 Hz, H-8), 6.33(d, 1H, $J_{10,9}$ = 5.9 Hz, H-10), 6.48(dd, 1H, $J_{9,8}$ = 1.7 Hz, $J_{9,10}$ = 5.9 Hz, H-9); ^{13}C NMR (50 MHz): 23.85(q), 24.44(q), 27.48(q), 32.70(s, C-2), 35.10, 35.29, and 39.78(t, C-3, C-4, and C-7), 54.18(s, C-6), 77.39(d, C-8), 97.10(s, C-1), 132.15 and 138.70(d, C-9 and C-10), 213.94(s, C-5); mass spectrum: 206(10, M$^{\cdot+}$), 109(100, M − $(CH_2)_2$C(O)CMe=CH_2). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1290.

(6α,8α-H)-2,2,7α-Trimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (58)

The IMDAF reaction of compound **11** (54.9 mg, 0.266 mmol) was performed according to general procedure 4 to provide a SM:A ratio of 87:13 with quantitative recovery of material after 192 h. General procedure 5 was used to perform the Lewis acid–mediated reactions of compound **11**. Thus, enone **11** (104.1 mg, 0.504 mmol) was treated with quantitative $MeAlCl_2$ (555 μL, 0.555 mmol) at −78°C for 8 h to provide a SM:A ratio of 73:27

and enone **11** (60.5 mg) and adduct **58** (24.7 mg) with 82% recovery after separation by flash chromatography (9:1). Enone **11** (124.7 mg, 0.604 mmol) was treated with catalytic $MeAlCl_2$ (60 μL, 0.060 mmol) at −65°C for 2 h according to general procedure 5 to provide a SM:A ratio of 27:73 with a quantitative recovery of material. Adduct **58** was characterized as a solid, mp 35–37°C; IR (KBr) cm^{-1}: 3012(CH), 2968–2871(CH), 1698(C=O), 1389, 1368(*gem*-Me); ^1H NMR (200 MHz): 0.98(d, $J_{7\beta,14}$ = 7.0 Hz, C-7-CH_3), 1.07 and 1.31(s, 3H each), 1.59(ddd, 1H, $J_{3\alpha,4\beta}$ = 3.1 Hz, $J_{3\alpha,4\alpha}$ = 5.7 Hz, $J_{3\alpha,3\beta}$ = 13.4 Hz, H-3α), 1.77(d, 1H, $J_{6\alpha,7\beta}$ = 4.0 Hz, H-6α), 2.01(dt, 1H, $J_{3\beta,4\beta}$ = 5.2 Hz, $J_{3\beta,4\alpha}$ = 13.4 Hz, $J_{3\alpha,3\beta}$ = 13.4 Hz, H-3β), 2.40(ddd, 1H, $J_{3\alpha,4\beta}$ = 3.1 Hz, $J_{3\beta,4\beta}$ = 5.2 Hz, $J_{4\alpha,4\beta}$ = 16.3 Hz, H-4β), 2.54(ddd, 1H, $J_{3\alpha,4\alpha}$ = 6.6 Hz, $J_{3\beta,4\alpha}$ = 13.4 Hz, $J_{4\beta,4\alpha}$ = 16.2 Hz, H-4α), 2.74(ddq, 1H, $J_{7\beta,6\alpha}$ = 4.2 Hz, $J_{7\beta,8}$ = 4.8 Hz, $J_{7\beta,14}$ = 7.0 Hz, H-7β), 4.73(d, 1H, $J_{7\beta,8}$ = 4.6 Hz, H-8), 6.40(ABq, 2H, H-9 and H-10); ^{13}C NMR (50 MHz): 17.51(q), 24.23(q), 25.78(q), 31.91(s, C-2), 34.47 and 37.55(t, C-3 and C-4), 39.72(d, C-7), 56.28(d, C-6), 81.57(d, C-8), 96.47(s, C-1), 134.95, 136.32(d, C-9 and C-10), 211.29(s, C-5); mass spectrum: 206(20, $M^{\cdot+}$), 109(100, M − $(CH_2)_2C(O)CMe{=}CH_2$). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1305.

*(6α-H)-2,2,8α-Trimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (**60**)*

The IMDAF reaction of compound **13** (62.1 mg, 0.301 mmol) occurred at 0°C as a neat oil to provide adduct **60** (62.1 mg, 0.301 mmol) as a white, crystalline solid, mp 52–54°C; IR (KBr) cm^{-1}: 1707(C=O); ^1H NMR (300 MHz): 1.08 and 1.33(s, 3H each), 1.55(s, 3H C-8-CH_3), 1.60(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.7 Hz, $J_{3\alpha,4\alpha}$ to 5.8 Hz, $J_{3\alpha,3\beta}$ = 13.9 Hz, H-3α), 1.68(dd, 1H, $J_{7\alpha,6\alpha}$ = 8.4 Hz, $J_{7\alpha,7\beta}$ = 11.8 Hz, H-7α), 2.01(dt, 1H, $J_{3\beta,4\beta}$ = 4.3 Hz, $J_{3\beta,4\alpha}$ = 13.9 Hz, $J_{3\beta,3\alpha}$ = 13.9 Hz, H-3β), 2.12(dd, 1H, $J_{7\beta,6\alpha}$ = 3.3 Hz, $J_{7\beta,7\alpha}$ = 11.8 Hz, H-7β), 2.38(dd, 1H, $J_{6\alpha,7\beta}$ = 3.3 Hz, $J_{6\alpha,7\alpha}$ = 8.4 Hz, H-6α), 2.40(ddd, 1H, $J_{4\beta,3\alpha}$ = 2.8 Hz, $J_{4\beta,3\beta}$ = 4.3 Hz, $J_{4\beta,4\alpha}$ = 13.2 Hz, H-4β), 2.56(dt, 1H, $J_{4\alpha,3\alpha}$ = 5.8 Hz, $J_{4\alpha,4\beta}$ = 13.2 Hz, $J_{4\alpha,3\beta}$ = 13.9 Hz, H-4α), 6.25(ABq, 2H, H-9 and H-10); ^{13}C NMR (75 MHz): 18.77(q), 24.08(q), 26.05(q), 32.10(s, C-2), 34.88, 37.40, and 37.89(t, C-3, C-4, and C-7), 51.24(d, C-6), 85.63 and 96.09(s, C-1 and C-8), 134.16 and 141.77(d, C-9 and C-10), 210.83(s, C-5); mass spectrum: 206(43, $M^{\cdot+}$), 191(13, M − Me), 123(100, M − $(CH_2)_2C(O)CH{=}CH_2$). Exact Mass calcd. for $C_{13}H_{18}O_2$: 206.1307; found: 206.1297.

*2,2,6α,8α-Tetramethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (**61**)*

The IMDAF reaction of compound **14** (58.4 mg, 0.265 mmol) was performed according to general procedure 4 to provide a SM:A ratio of 88:12 in 82% recovery of material after 336 h. Starting material (40.9 mg) and adduct (6.8 mg) were isolated by flash chromatography (9:1). General procedure 5 was used to perform the Lewis acid-mediated reactions of compound **14**. Thus, enone **14** (48.8 mg, 0.222 mmol) was treated with quantitative $MeAlCl_2$ (244 μL, 0.244 mmol) at −78°C for 8 h to provide a SM:A ratio of 78:22 with quantitative recovery of material. Enone **14** (30.1 mg) and adduct (9.0 mg) were isolated by flash chromatography (9:1). Enone **14** (32.7 mg, 0.148 mmol) was treated with catalytic $MeAlCl_2$ (15 μL, 0.015 mmol) (according to general procedure 5) at −65°C for 2 h to provide a SM:A ratio of 23:77 with quantitative recovery. Adduct **61** was characterized as a solid; IR (KBr) cm^{-1}: 2986–2873(C—H), 1708(C=O), 1384,1371(*gem*-Me); ^1H NMR (300 MHz): 1.01(s, 3H, C-6-CH_3), 1.09(d, 1H, $J_{7\alpha,7\beta}$ = 11.7 Hz, H-7α), 1.12 and 1.33(s, 3H each), 1.46(s, 3H, C-8-CH_3), 1.56(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.7 Hz, $J_{3\alpha,4\alpha}$ = 5.8 Hz, $J_{3\alpha,3\beta}$ = 13.6 Hz, H-3α), 1.99(dt, 1H, $J_{3\beta,4\beta}$ = 4.1 Hz, $J_{3\beta,3\alpha}$ = 13.6 Hz, $J_{3\beta,4\alpha}$ = 14.4 Hz, H-3β), 2.32(ddd, 1H, $J_{4\beta,3\alpha}$ = 2.7 Hz, $J_{4\beta,3\beta}$ = 4.1 Hz, $J_{4\beta,4\alpha}$ = 15.3 Hz, H-4β), 2.53(d, 1H, J = 11.7 Hz, H-7β), 2.77(ddd, 1H, $J_{4\alpha,3\alpha}$ = 5.8 Hz, $J_{4\alpha,3\beta}$ = 14.4 Hz, $J_{4\alpha,4\beta}$ = 15.3 Hz, H-4α), 6.25(d, 1H, $J_{10,9}$ = 5.7 Hz, H-10), 6.30(d, 1H, $J_{9,10}$ = 5.7 Hz, H-9); ^{13}C NMR (75 MHz): 18.93(q), 23.75(q), 24.27(q), 27.51(q), 32.78(s, C-2), 35.00 and 35.31(t, C-3 and C-7), 46.21(t, C-4), 57.37(s, C-6), 84.76 and 97.29(s, C-1 and C-8), 132.76 and 141.69(d, C-9 and C-10), 214.39(s, C-5); mass spectrum: 220(18, $M^{\cdot+}$), 123(100, M − $(CH_2)_2C(O)CMe{=}CH_2$). Exact Mass calcd. for $C_{14}H_{20}O_2$: 220.1464; found: 220.1462.

*(6α-H)-2,2,7α,8α-Tetramethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (**62**)*

General procedure 5 was used to perform the Lewis acid-mediated reactions of compound **15**. Thus, enone **15** (14.6 mg, 0.066 mmol) was treated with catalytic $MeAlCl_2$ (6.6 μL, 0.066 mmol) at −65°C for 2 h to provide a **15**:**62** ratio of 69:31 with 72% recovery; IR (KBr) cm^{-1}: 2960–2868(C-H), 1706(C=O), 1384,1368(*gem*-Me); ^1H NMR (400 MHz): 0.97(d, 3H, $J_{14,7\beta}$ = 7.0 Hz, H-14), 1.08 and 1.28(s, 3H each), 1.50(s, 3H, C-8-CH_3), 1.56(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.8 Hz, $J_{3\alpha,4\alpha}$ = 6.0 Hz, $J_{3\alpha,3\beta}$ = 13.5 Hz, H-3α), 1.88(d, 1H, $J_{6\alpha,7\beta}$ = 4.1 Hz, H-6α), 2.01(dt, 1H, $J_{3\beta,4\beta}$ = 4.8 Hz, $J_{3\beta,4\alpha}$ = 13.6 Hz, $J_{3\beta,3\alpha}$ = 13.6 Hz, H-3β), 2.35(dq, 1H, $J_{7\beta,6\alpha}$ = 4.1 Hz, $J_{7\beta,14}$ = 7.0 Hz, H-7β), 2.40(ddd, 1H, $J_{4\beta,3\alpha}$ = 2.8 Hz, $J_{4\beta,3\beta}$ = 4.8 Hz, $J_{4\beta,4\alpha}$ = 16.2 Hz, H-4β), 2.51(ddd, 1H, $J_{4\alpha,3\alpha}$ = 6.0 Hz, $J_{4\alpha,3\beta}$ = 13.6 Hz, $J_{4\alpha,4\beta}$ = 16.2 Hz, H-4α), 6.20(d, 1H, $J_{10,9}$ = 5.7 Hz, H-10), 6.37(d, 1H, $J_{9,10}$ = 5.7 Hz, H-9); ^{13}C NMR (50 MHz): 17.20(q), 17.40(q), 24.06(q), 25.86(q), 31.94(s, C-2), 34.40 and 37.55(t, C-3 and C4), 45.65(d, C-7), 59.21(d, C-6), 88.25 and 95.38(s, C-1 and C-8), 135.41 and 139.34(d, C-9 and C-10), 211.59(s, C-5); mass spectrum: 220(8, $M^{\cdot+}$), 123(100, M − $(CH_2)_2C(O)CH{=}CHMe$). Exact Mass calcd. for $C_{14}H_{20}O_2$: 220.1464; found: 220.1465.

*(7β,9α-H)-12-Oxatricyclo[7.2.1.0^{1,7}]dodec-10-en-6-one (**63**)*

General procedure 5 was used to perform the Lewis acid-mediated reaction of compound **8**. Thus, enone **8** (63.5 mg, 0.356 mmol) was treated with $MeAlCl_2$ (36 μL, 0.036 mmol) at −78°C for 2 h to provide a SM:A ratio of 8:92 with 98% recovery of material. Some retro-IMDAF reaction occurred upon attempted purification by flash chromatography (9:1). Adduct **63** was characterized as a white crystalline solid; ^1H NMR (200 MHz): 1.38–1.67(m, 2H), 1.75–2.30(overlapping m, 6H), 2.38–2.70(overlapping m, 2H), 3.20(dd, 1H), 4.90(dd, 1H, H-9), 6.02(d, 1H, $J_{11,10}$ = 6.2 Hz, H-11), 6.41(dd, 1H, $J_{10,9}$ = 1.2 Hz, $J_{10,11}$ = 6.2 Hz, H-10).

*2,2-Dimethyl-7-(trimethysilyl)-11-oxatricyclo[6.2.1.0^{1,6}] undec-6,9-dien-5-one (**65**)*

General procedure 5 was used for the Lewis acid-mediated IMDAF reaction of compound **16**. Thus, enone **16** (100.9 mg, 0.384 mmol) was treated with $MeAlCl_2$ (423 μL, 0.423 mmol) at −50°C for 2.5 h to provide a SM:A ratio of 12.88. Adduct **65** (76.4 mg, 0.482 mmol) was obtained in 89% yield (based on recovered starting material) as a golden crystalline solid, after purification by flash chromatography; mp 85–94°C; IR (Kbr) cm^{-1}: 1660(C=O); ^1H NMR (200 MHz): 0.19(s, 9H), 1.09 and 1.22(s, 3H each, C-2-CH_3's), 1.79(ddd, 1H, $J_{3\alpha,4\beta}$ = 2.6 Hz, $J_{3\alpha,4\alpha}$ = 6.6 Hz, J_{gem} = 14.2 Hz, H-3α), 1.95(ddd, 1H, $J_{3\beta,4\beta}$ = 5.6 Hz, $J_{3\beta,4\alpha}$ = 12.5 Hz, J_{gem} = 14.2 Hz, H-3β), 2.43(ddd, 1H, $J_{4\beta,3\alpha}$ = 2.6 Hz, $J_{4\beta,3\beta}$ = 5.6 Hz, J_{gem} = 19.1 Hz, H-4β), 2.63(ddd, 1H, $J_{4\alpha,3\alpha}$ = 6.6 Hz, $J_{4\alpha,3\beta}$ = 12.5 Hz, J_{gem} = 19.1 Hz, H-4α), 5.60(d, 1H, $J_{8,9}$ = 1.9 Hz, H-8), 6.98(dd, 1H, $J_{9,8}$ = 1.9 Hz, $J_{9,10}$ = 5.4 Hz, H-9), 7.05(d, 1H, $J_{10,9}$ = 5.4 Hz, H-10); ^{13}C NMR (50 MHz): −2.15(q), 25.76(q), 22.29(q), 31.63(s, C-2), 34.20 and 36.16(t, C-3 and C-4), 86.48(d, C-8), 99.87(s, C-1), 144.16 and 144.44(d, C-9 and C-10), 160.77 and 174.23(s, C-6 and C-7), 195.64(s, C-5); mass spectrum: 262(15, $M^{\cdot+}$), 247(50, M − Me), 109(100, M − $C_8H_{16}OSi$). Exact Mass calcd. for $C_{15}H_{22}O_2Si$: 262.1389; found: 262.1376.

*2,2,7-Trimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-6,9-dien-5-one (**66**)*

General procedure 5 was used for the Lewis acid-mediated IMDAF reaction of compound **17**. Thus, enone **17** (99.1 mg, 0.485 mmol) was treated with $MeAlCl_2$ (553 μL, 0.553 mmol) at −60°C for 0.5 h to provide adduct **66** (98.5 mg, 0.482 mmol) in

99% recovery as a white, crystalline solid, which could not be purified by flash chromatography without isomerization of the C-6, C-7 double bond; IR (neat) cm^{-1}: 1666(C=O); ^1H NMR (200 MHz): 1.10 and 1.21(s, 3H each), 1.75(ddd, 1H, $J_{3\alpha,4\beta}$ = 3.0 Hz, $J_{3\alpha,4\alpha}$ = 6.7 Hz, J_{gem} = 12.9 Hz, H-3α), 1.89(dt, 1H, $J_{3\beta,4\beta}$ = 3.0 Hz, $J_{3\beta,4\alpha}$ = J_{gem} = 12.9 Hz, H-3β), 2.31(s, 3H, C-8-CH_3), 2.43(ddd, 1H, $J_{4\beta,3\alpha}$ = 3.0 Hz, $J_{4\beta,3\beta}$ = 3.0 Hz, J_{gem} = 16.3 Hz, H-4β), 2.50–2.75(m, 1H, H-4α), 5.10(d, 1H, $J_{8,9}$ = 1.8 Hz, H-8), 7.04(dd, 1H, $J_{9,8}$ = 1.8 Hz, $J_{9,10}$ = 5.4 Hz, H-9), 7.09(d, 1H, $J_{10,9}$ = 5.4 Hz, H-10); ^{13}C NMR (50 MHz): 15.63(q), 22.02(q), 25.44(q), 31.64(s, C-2), 34.20(t), 36.16(t), 86.12(d, C-8), 99.28(s, C-1), 142.04 and 145.57(d, C-9 and C-10), 171.98(s, C-6 and C-7), 196.32(s, C-5); mass spectrum: 204(14, $M^{\cdot+}$), 163(24, M − HC≡CH), 109(100, M − $(CH_2)_2C(O)C{\equiv}CCH_3$). Exact Mass calcd. for $C_{13}H_{16}O_2$: 204.1150; found: 204.1146.

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