

## Wagner–Meerwein Rearrangements of Substituted 11-Oxatricyclo[6.2.1.0<sup>1,6</sup>]undec-9-enes (2,4a-Epoxyoctahydronaphthalenes)

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A variety of 11-oxatricyclo[6.2.1.0<sup>1,6</sup>]undec-9-enes (1)–(7) undergo Wagner–Meerwein rearrangements when treated with either iodine/silver acetate/acetic acid or iodine/iodic acid/methanol.

We and others<sup>1,2</sup> have reported that the intramolecular Diels–Alder (IMDA) reaction of systems which contain a furan diene connected to a dienophile by four carbon atoms (A) provides only the oxatricyclo adducts (B) having the side arm orientated *exo* with respect to the oxygen bridge (Scheme 1). Therefore, depending on the positional substitution of a group(s) on the side chain and/or dienophile, the adduct (B) may contain from three to five asymmetric centres of known relative stereochemistry.<sup>1a</sup>

Since one of the challenges in the preparation of compounds containing two or more asymmetric centres is the development of the correct relative stereochemistry in a minimum number of transformations with maximum stereoselectivity, we sought methods for converting the oxatricyclo adducts (B) into useful synthetic intermediates.

Treatment of 7-oxabicyclo[2.2.1]heptenes under Prévost conditions has been reported to result in products having interesting carbon skeletons *via* a Wagner–Meerwein rearrangement.<sup>3</sup> We therefore investigated the scope and limitations of the Wagner–Meerwein rearrangements on oxatricyclo adducts (1)–(7) and herein report our findings.

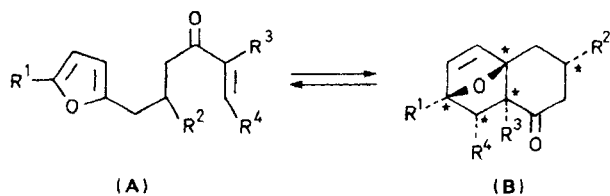
The oxatricyclo adducts (1)–(3) and (5)–(7) were prepared as previously described.<sup>1a,b</sup> Oxatricyclo adduct (4) was

obtained by reducing the carbonyl group in compound (1) (Bu<sub>2</sub>AlH, CH<sub>2</sub>Cl<sub>2</sub>, –78 °C) followed by acetylation (Ac<sub>2</sub>O, 2-dimethylaminopyridine, CH<sub>2</sub>Cl<sub>2</sub>) of the resulting alcohol. Compounds (1) and (2) (100 mg) when treated with a mixture of iodine/acetic acid/silver acetate (1.1 equiv./1 ml/1.1 equiv.) provided after work-up with sodium hydrogen carbonate the rearranged oxatricyclo compounds (8) (75%) and (9) (73%) respectively; compound (3) provided (10) (87%) under identical conditions.† Compounds (8) and (9) were formed *via* a Wagner–Meerwein rearrangement of an iodonium ion involving bond 'a' [see compound (1)] followed by trapping of the resulting oxonium ion with an acetate moiety. Compound (10), however, was formed *via* a similar rearrangement involving bond 'b' [see compound (1)] presumably to form (11). During work-up (aqueous NaHCO<sub>3</sub>), the acetate group in compound (11) was hydrolysed to a cyclic hemi-acetal which opened to the 5,7 ring fused system (12). Loss of hydrogen iodide then provided compound (10).

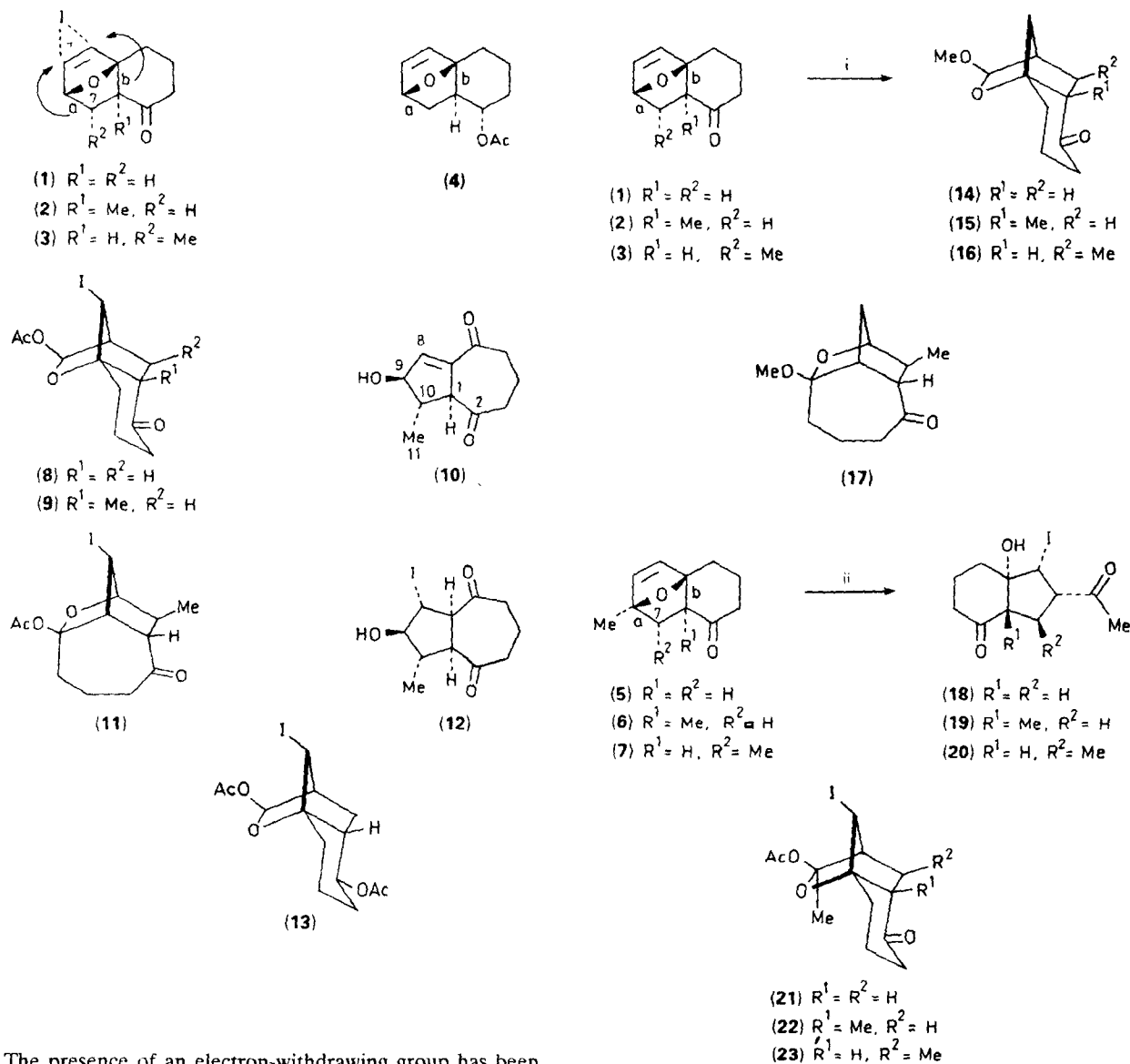
† All compounds provided analytical and/or spectroscopic data consistent with their structures.

The <sup>1</sup>H NMR spectrum of both (8) and (9) showed a 1H singlet at δ 5.60 and 5.52 respectively. These peaks were assigned to the cyclic acetal hydrogen; the absence of vicinal coupling to the adjacent bridge hydrogen indicated the placement of the acetoxy group *syn* to the one-carbon bridge.

Compound (10): IR (neat) ν<sub>max</sub> 3310, 1706, 1680 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 1.09 (d, 3H), 1.21 (s, 1H, –OH), 1.75–1.88 (m, 1H), 2.15–2.24 (m, 1H), 2.54 (ddq, 1H, J<sub>9α,10β</sub> = J<sub>1β,10β</sub> = 3.1 Hz, J<sub>10,11</sub> 7.1 Hz, H-10), 2.6–2.82 (m, 4H), 3.60 (ddd, 1H, J<sub>1α,10β</sub> 3.1 Hz, J<sub>1α,9α</sub> 1.0, J<sub>1α,8</sub> 2.3 Hz, H-1), 4.32 (ddd, 1H, J<sub>9α,8</sub> 2.3, J<sub>1α,9α</sub> 1.0, J<sub>9α,10β</sub> 3.1 Hz, H-9), 6.8 (t, 1H, J<sub>8,9α</sub> J<sub>1α,8</sub> 2.3 Hz, H-8); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 210.0, 197.6, 143.16, 140.5, 81.2, 63.5, 43.6, 42.8, 42.6, 20.6, 17.9; m/z 194, M<sup>+</sup>.



Scheme 1



Scheme 2. Reagents and conditions: i,  $I_2$ , MeOH,  $HIO_3$ , room temp., then  $Bu_3SnH$ ,  $h\nu$ ; ii,  $I_2$ , HOAc,  $AgOAc$ , then aq.  $Na_2CO_3$ .

The presence of an electron-withdrawing group has been reported to disfavour the Wagner-Meerwein migration of an adjacent C-C bond.<sup>3b,c</sup> The migration of bond 'b' in compound (3) was thus unexpected. Compound (4) was therefore prepared to determine the migratory aptitude of bonds 'a' and 'b' without the presence of an adjacent electron-withdrawing group. Under identical migration conditions to those above, only compound (13) was isolated (73%). These results indicate that bond 'a' in compounds (1), (2), and (4) is prone to migration, but that the presence of an *endo* substituent at C-7 of (3) may be responsible for the migration of the bond 'b'.

All attempts to isolate intermediate (11) failed. Therefore compounds (1)–(3) (100 mg) were subjected to an iodine/iodic acid/methanol (1.1 equiv./1.1 equiv./1 ml) mixture<sup>3a</sup> in an attempt to provide the corresponding cyclic methoxy acetals. Unfortunately, the rearranged products from compounds (1)–(3) containing iodine on the carbon bridge were unstable: addition of tri-*n*-butyltin hydride to the crude rearranged mixtures followed by photolysis provided the deiodized cyclic methoxyacetals (14)–(16) respectively. Interestingly, under these conditions bond 'a' in compound (3) migrated; compound (17) was not detected in the reaction mixture.

Wagner-Meerwein rearrangement (iodine/acetic acid/silver acetate) of compounds (5)–(7), which contain a methyl group at the oxygen bridge, provided the 5,6-ring fused bicyclo compounds (18)–(20) respectively; the expected oxatricyclo adducts (21)–(23) could be neither detected nor isolated. Surprisingly, bond 'a' in compound (7) migrated under conditions identical to those under which bond 'b' migrated in compound (3).

Further studies to rationalize the observed migratory aptitude of either bond 'a' or 'b' in these oxatricyclo adducts are pending.

We have therefore shown that oxatricyclo adducts (1)–(7) undergo Wagner-Meerwein rearrangements to provide interesting ring systems containing four or more asymmetric centres of known relative stereochemistry. Synthetic applications of these materials are currently under investigation.

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