Wagner–Meerwein Rearrangements of Substituted 11-Oxatricyclo[6.2.1.0^{1,6}]undec-9-enes (2,4a-Epoxyoctahydronaphthalenes)

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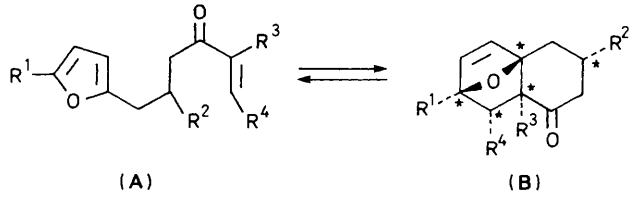
A variety of 11-oxatricyclo[6.2.1.0^{1,6}]undec-9-enes (**1**)—(**7**) undergo Wagner–Meerwein rearrangements when treated with either iodine/silver acetate/acetic acid or iodine/iodic acid/methanol.

We and others[1,2] 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.[1a]

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.[3] We therefore investigated the scope and limitations of the Wagner–Meerwin rearrangements on oxatricyclo adducts (**1**)—(**7**) and herein report our findings.

The oxatricyclo adducts (**1**)—(**3**) and (**5**)—(**7**) were prepared as previously described.[1a,b] Oxatricyclo adduct (**4**) was obtained by reducing the carbonyl group in compound (**1**) (Bu^i_2AlH, CH_2Cl_2, −78 °C) followed by acetylation (Ac_2O, 2-dimethylaminopyridine, CH_2Cl_2) 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 iodinium 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 $NaHCO_3$), 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**).

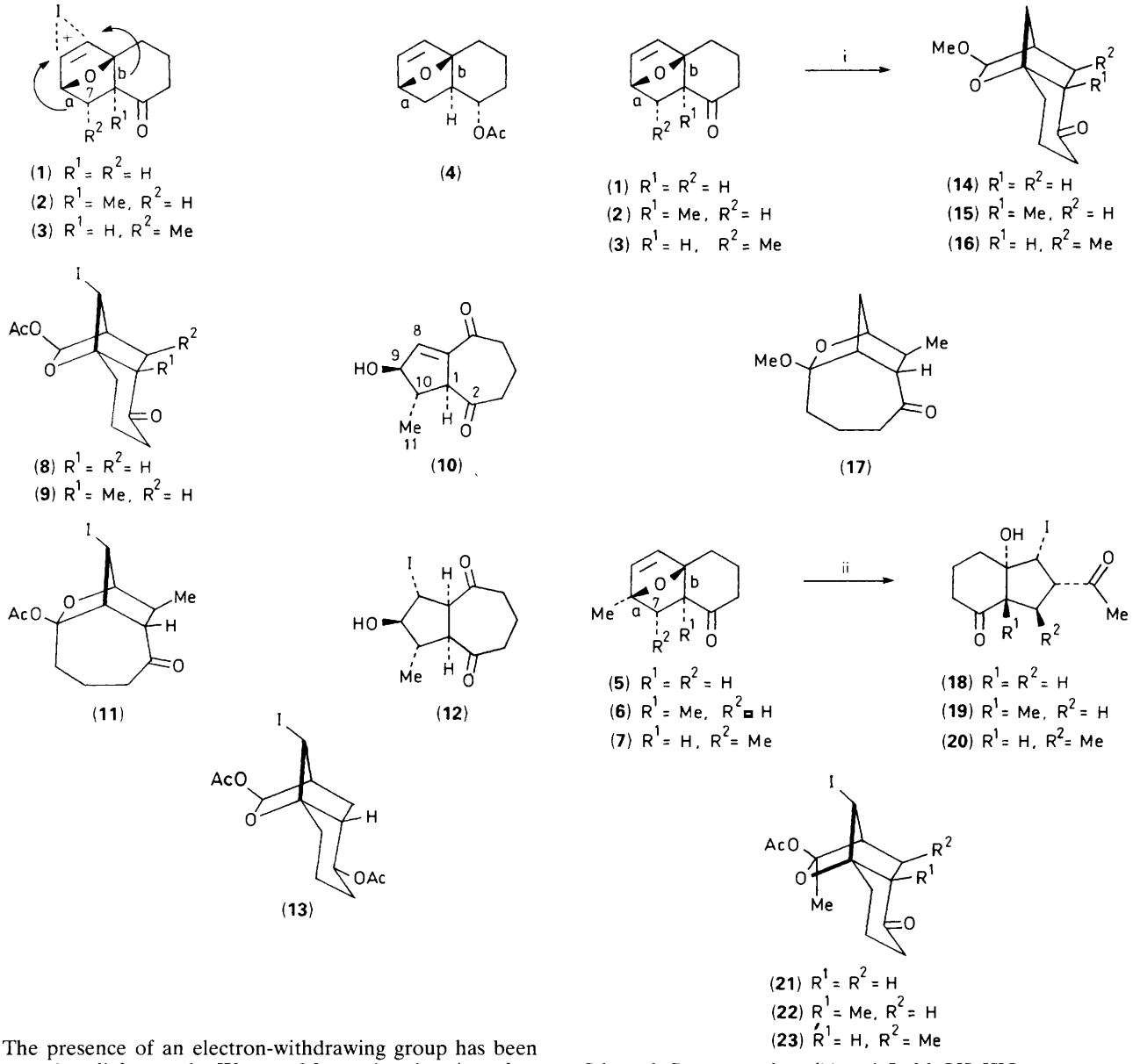


Scheme 1

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

The ^{1}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_{max} 3310, 1706, 1680 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 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, $J_{9\alpha,10\beta} = J_{1\beta,10\beta}$ = 3.1 Hz, $J_{10,11}$ 7.1 Hz, H-10), 2.6—2.82 (m, 4H), 3.60 (ddd, 1H, $J_{1\alpha,10\beta}$ 3.1, $J_{1\alpha,9\alpha}$ 1.0, $J_{1\alpha,8}$ 2.3 Hz, H-1), 4.32 (ddd, 1H, $J_{9\alpha,8}$ 2.3, $J_{1\alpha,9\alpha}$ 1.0, $J_{9\alpha,10\beta}$ 3.1 Hz, H-9), 6.8 (t, 1H, $J_{8,9\alpha}$ $J_{1\alpha,8}$ 2.3 Hz, H-8); ^{13}C NMR (75 MHz, $CDCl_3$): 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^+).



Scheme 2. *Reagents and conditions*: i, I_2, MeOH, HIO_3, room temp., then Bu_3SnH, *hν*; 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.[3b,c] 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[3a] 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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