Pinacol–Pinacolone Rearrangement Induced By Aminium Salts

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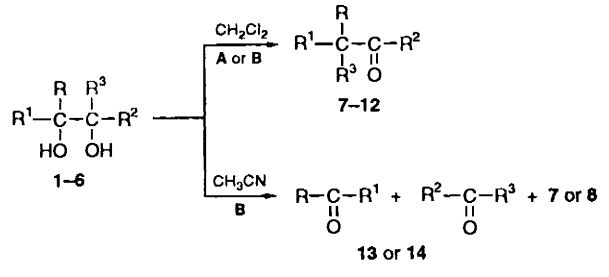
Catalytic amounts of aminium salts induce a quantitative and mild pinacol–pinacolone rearrangement of several vicinol diols in methylene dichloride solutions.

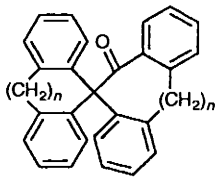
Aminium salt initiation has been found to represent a powerful protocol for Diels–Alder cycloadditions and several other reactions of electron-rich substrates.[1-3] The radical-cation chain mechanism invoked for all these reactions, modelled upon Ledwith[4] and Nelsen's[2] classic mechanisms, was debated by Gassman and Singleton,[5] who claimed that, in some systems (dienes, tetraenes), the aminium radical cations act mainly as an indirect source of protons, which are then utilized in the acid-catalysed process.[5] In this context, vicinal diols, by reaction with aminium salts, appear suitable substrates better to distinguish between a radical-cation chain mechanism, leading, through an oxidative C–C bond cleavage, to mixtures of simple carbonyl compounds,[6,7] and a protic acid-catalysed reaction, affording the corresponding pinacolones, through the well known rearrangement.[8]

Typical experimental conditions were as follows: catalytic amounts of aminium salts, such as tris(*p*-bromophenyl)aminium hexachloroantimonate [$(p\text{-BrC}_6\text{H}_4)_3\text{N}^{\bullet+}\text{SbCl}_6^-$] ($E^{red}$ = 1.16 V *vs.* SCE)[9] **A**, or tris(*o*,*p*-dibromophenyl)aminium hexachloroantimonate [$(o,p\text{-Br}_2\text{C}_6\text{H}_3)_2\text{N}^{\bullet+}\text{SbCl}_6^-$] ($E^{red}$ = 1.66 V *vs.* SCE)[9] **B**, were rapidly added to freshly distilled methylene dichloride solutions of the vicinal diols **1–6**,[10,11] with stirring at room temperature. The intensely blue or green colour of the solutions, depending on the aminium salts used, faded within a few minutes. Analyses of the reaction mixtures, monitored by TLC, GC and GC/MS until completion (< 1 h), showed the disappearance of starting materials and formation of new products **7–12**; the latter were isolated by column chromatography, and fully characterized on the basis of their physical characteristics, spectral results and comparison with authentic samples (see Experimental section). Similar reactions, carried out on substrates **1** and **2**, but in acetonitrile as solvent, required increasing amounts of the powerful oxidizing agent **B**; they afforded mixtures of triphenylmethylphenyl ketone **7** and benzophenone **13**, or 3,3-diphenylbutan-2-one **8** and acetophenone **14**, respectively (see Scheme 1).



Scheme 1 **1**:R = R^1 = R^2 = R^3 = Ph; **2**:R = R^3 = Ph, R^1 = R^2 = Me; **3a,b**: R = R^1 = R^3 = Ph, R^2 = H; **4**: R,R^1 = R^2,R^3 = $C_{13}H_8$ (fluorenyl); **5**: R,R^1 = R^2,R^3 = $C_{14}H_{10}$ (anthryl); **6**: R = Me, R^2 = [CH=CHC(O)Me], R^1,R^3 = $Me_2C(CH_2)_2CH_2$

The reactions with substrates **1** and **3a,b**, followed by GC/MS showed the clear intermediate formation of the corresponding tetraphenylethylene and triphenylethylene oxides. In contrast, the reactions on substrates **4** and **5**, respectively, afforded spiro[9*H*-fluorene-9,9'(10'H)-phenanthren]-10'-one **10** and anthrapinacolin **11**, no trace of the eventual oxides, as intermediates, being detected.[12,13]



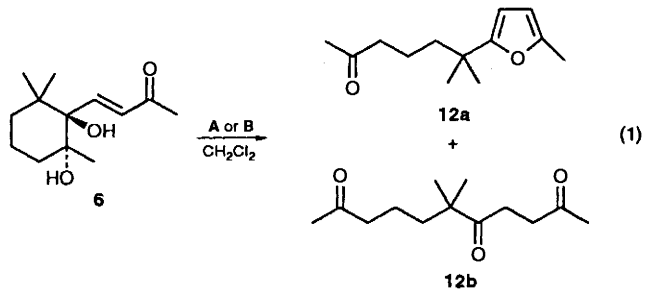
n = 0, **10**
n = 1, **11**

Given that our methylene dichloride solutions are strongly acidic, this new catalytic version of the pinacol–pinacolone rearrangement could easily be rationalized as a further acid-catalysed process,[8] mediated by aminium salts.[5]

Analogously, we could simply claim that the sole products of a single electron-transfer process should be **13** and **14**, as reported by Penn and co-workers on the same acetonitrile solutions of **1** and **2**, by using a different one-electron-oxidizing agent.[7] However, the idea that the choice of reagents, solvents and conditions could totally alter not only the course of the rearrangement, but also the mechanism, led us to investigate this process further.

The identity of the acid, developed in the reaction medium, which catalyses the process is currently unknown. Although it may be $HSbCl_6$, it is also possible that a chain-carrying cation radical intermediate fulfils the function.[5] In this regard, chemical proof that, under our conditions, a single-electron transfer mechanism is operating is as follows. (a) Similar reactions on compounds **1–5**, carried out in the presence of 2,6-di-*tert*-butylpyridine DBP (E^{ox} = 1.82 V *vs.* SCE),[14] a sterically hindered base with a nucleophilic reactivity restricted to protons, are not inhibited, and afford lower yields (60–70%) of the corresponding carbonyl compounds **7–11**, through an apparently slower process (2–4 h). (b) Similar reactions but modified by use of 1,4-diazabicyclo[2.2.2]octane, DABCO (E^{ox} = 0.64 V *vs.* SCE),[15] with an oxidation potential lower than those of the starting materials, are either totally inhibited or simply slowed down, depending on the relative amount (10–5 mol%) or DABCO used with respect to that of the aminium salt (10 mol%) employed. (c) Aminium salt-induced rearrangement of **3a,b** afforded triphenylacetaldehyde **9** (90%) together with minor amounts of benzhydrylphenyl ketone **9b** (10%). This latter compound, however, appears to be the sole, or main reaction product, when either **3a** or **3b** is refluxed in the presence of various strong acids.[8] Moreover, under our reaction conditions, the **9a**:**9b** ratio is unchanged along the reaction coordinate.[8] (d) Aminium salt-induced rearrangement of the vicinal diol 5,6-dihydroxy-5,6-dihydro-β-jonone **6**,[11] a non-aromatic substrate, which is much less susceptible to oxidation by an electron-transfer pathway, leads to a mixture of 6-methyl-6-(5-methyl-2-furyl)heptan-2-one **12a** (70%) and 6,6-dimethyl-undecane-2,5,10-trione **12b** (30%), through a plausible protic

acid-catalysed process.[11,16] [Eqn. (1)]. Thus, in sharp contrast



(1)

to earlier reactions, the DBP-modified reactions of **6** appear totally inhibited. Moreover, the same result has been already reported in a *bona fide* protic acid-catalysed process.[11] (e) In the protic acid (toluene-*p*-sulfonic acid, 0.06 mol, 10 mol%)-catalysed reactions, the concentration of the acid is too low to cause the rearrangement of our diols on the time-scale of our aminium-induced reactions. Finally, the preliminary results for reactions of the substrates **1** and **2**, conducted in acetonitrile as solvent, appear to be at variance with the observations by Penn and co-workers,[7] seeming to suggest that compounds **13** and **14**, as well as the pinacolones **7** and **8** might arise from the same radical cation intermediates. In fact, the formation of **7** and **8** is not inhibitied in the presence of DBP.

Further studies on other vicinal diols and aminium salts with different counteranions are underway better to define the scope and the mechanism operating in this procedure.

Experimental

Pinacol–Pinacolone Rearrangement of the Diols **1–6** *by Aminium Salts: General Procedure.*—The required catalytic amount of either aminium salt **A** or **B** (48–60 mg, 0.06 mmol, 10 mol%) was rapidly added with exposure to the air, at room temperature, to a stirred solution of the appropriate 1,2-diol **1–5** (234–145 mg, 0.6 mmol, 100 mol%) in dry CH_2Cl_2 (20 cm^3). The intensely green or blue colour of the solutions, depending on the aminium salts used, faded within a few minutes. The progress of the reactions was monitored by TLC, GC and GC/MS until completion (< 1 h). The solvent was removed under reduced pressure, and the reaction products **7** and **11** isolated by column chromatography (silica gel, light petroleum–diethyl ether 10 : 1 as eluent), have been fully characterized on the basis of their physical characteristics, spectral data and by comparison with authentic samples.

Compound **7** ($C_{26}H_{20}O$): yield 320 mg (95%), m.p. 179–180 °C (lit.,[18] 180–181 °C); $\nu_{max.}$(KBr)/cm^{-1} 3087, 1674 and 701; *m/z* (%) 243 (M^+ − PhCO, 100), 165 (54), 105 (9) and 77 (6).

Compound **8** ($C_{16}H_{16}O$): yield 200 mg (90%), m.p. 41 °C (lit.,[7,8] 41 °C); ν_{max}(KBr)/cm^{-1} 3058, 1709 and 701 cm^{-1}; *m/z* (%) 224 (M^+, 3), 181 (100), 165 (29), 103 (34), 77 (22) and 43 (17); δ($CDCl_3$) 7.38–7.21 (m, 10 H), 2.14 (s, 3 H) and 1.90 (s, 3 H); δ_C($CDCl_3$) 209.04, 143.52, 128.30, 126.85, 62.25, 27.55 and 26.36.

Compound **9a** ($C_{20}H_{16}O$): yield 210 mg (90%), m.p. 104–105 °C (lit.,[8] 104–105 °C); $\nu_{max.}$(KBr)/cm^{-1} 3058, 2724 and 1685; *m/z* (%) 243 (M^+ − CHO, 100) and 165 (56); δ_H($CDCl_3$) 10.28 (s, 1 H) and consistent aromatic resonances.

Compound **9b** ($C_{20}H_{16}O$): yield 19 mg (< 10%), m.p. 134–135 °C (lit.,[17] 133–135 °C); ν[$\mu_{max.}$Br)/cm^{-1} 3065, 2978 and 1683; *m/z* (%) 272 (M^+, 2), 167 (40), 105 (100) and 77 (19); δ_H($CDCl_3$) 8.03–7.95 (m, 2 H), 7.58–7.18 (m, 13 H) and 6.06 (s, 1 H); δ_C($CDCl_3$) 199.82, 139.35, 137.05, 133.21, 129.30, 129.11, 128.97, 127.83 and 59.43.

Compound **10** ($C_{26}H_{16}O$): yield 312 mg (> 90%), m.p. 262–263 °C (lit.,[12] 262 °C); ν_{max}(KBr)/cm^{-1} 3071, 1683, 1600, 1450, 1266, 1242, 857 and 752; *m/z* (%) 344 (M^+, 100), 316 (75), 315 (81), 289 (13), 157 (39) and 143 (16); δ_H($CDCl_3$) 8.21–7.01 (m, 15 H) and 6.57 (dd, 1 H, *J* 7.84); δ_C($CDCl_3$) 197.25, 147.07, 141.62, 139.32, 134.91, 130.10, 129.04, 128.57, 128.34, 128.11, 128.06, 127.95, 124.14, 123.24, 120.59 and 68.71.

Compound **11** ($C_{28}H_{20}O$): yield 336 mg (> 90%), m.p. 218–219 °C (lit.,[13] 218–219 °C); ν_{max}(KBr)/cm^{-1} 3062, 3029, 2955, 1683, 1598, 1482, 1239 and 743; *m/z* (%) 372 (M^+, 100), 353 (33), 265 (43) and 178 (30); δ_H($CDCl_3$) 8.35–8.31 (m, 1 H), 7.82–7.78 (m, 1 H), 7.40–6.51 (m, 14 H), 4.25 (AB system, q, 2 H, *J* 19.5) and 4.15 (s, 2 H); δ_C($CDCl_3$) 202.77, 144.11, 139.43, 139.25, 138.32, 136.64, 134.15, 130.59, 128.53, 128.23, 127.41, 127.30, 127.24, 127.19, 126.40, 126.31, 125.86, 69.44, 40.74 and 35.72.

Similar reactions, carried out in the presence of 2,6-di-*tert*-butylpyridine DBP (11.5 mg, 0.06 mmol, 10 mol%) afforded lower yields of the same reaction products, within (2–4 h). The reactions mediated by DABCO (7.1 mg, 0.06 mmol, 10 mol%) appeared totally inhibited. In contrast with reduced amounts of DABCO (3.55 mg, 0.03 mmol, 5 mol%), with respect to the aminium salt employed, a slow and partial conversion (< 20%) of the starting materials into the reaction products was detected by GC : MS analyses.

The same protocol has been followed for the substrate **6**, affording products **12a,b**, which were easily isolated and fully characterized.

Compound **12a** ($C_{13}H_{20}O_2$): yield 140 mg (< 70%), liquid, characterized by the following spectral data (see ref. 14): ν_{max}(KBr)/cm^{-1} 2920, 1715, 1565, 1360, 1156, 1010, 918, 882, 799 and 730; *m/z* (%) 208 (M^+, 9), 135 (7), 123 (100) and 43 (29); δ_H($CDCl_3$) 5.82–5.79 (m, 2 H), 2.32 (t, *J* 7.31, 2 H), 2.23 (d, *J* 0.90, 3 H), 2.07 (s, 3 H), 1.53–1.49 (m, 2 H), 1.45–1.39 (m, 2 H) and 1.21 (s, 6 H).

Compound **12b** ($C_{13}H_{22}O_3$): yield 65 mg (< 30%), liquid, characterized by the following spectral data (see ref. 14); ν_{max}(KBr)/cm^{-1} 3400, 2940, 1712, 1470, 1162 and 992; *m/z* (%) 142 (8), 127 (11), 109 (47), 99 (100), 71 (21), 69 (36) and 43 (90); δ_H($CDCl_3$) 2.75–2.71 (m, 2 H), 2.67–2.63 (m, 2 H), 2.39–2.35 (m, 2 H), 2.16 (s, 3 H), 2.09 (s, 3 H), 1.49–1.40 (m, 4 H) and 1.11 (s, 6 H); δ_C($CDCl_3$) 213.9, 208.4, 207.2, 47.2, 43.8, 38.3, 36.8, 31.0, 39.9, 29.7, 24.4 and 18.9.

The reactions on substrates **1** and **2** (183–121 mg, 0.5 mmol, 100 mol%), carried out in acetonitrile (20 cm^3) as solvent, required increasing amounts (262 mg, 0.25 mmol, 50 mol%) of the powerful oxidizing agent **B**. The reactions, monitored by GC/MS showed the formation of **7** (30%) together with benzophenone **13** (70%), or **8** (20%) together acetophenone **14** (80%). The percent amounts of the reaction products have been calculated by integration of the relative peaks in the presence of an appropriate internal standard, *i.e.* triphenylmethane.

Acknowledgements

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