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Acid-catalyzed Rearrangement of Pentacyclic Cage Compound *via* a Strange By-path

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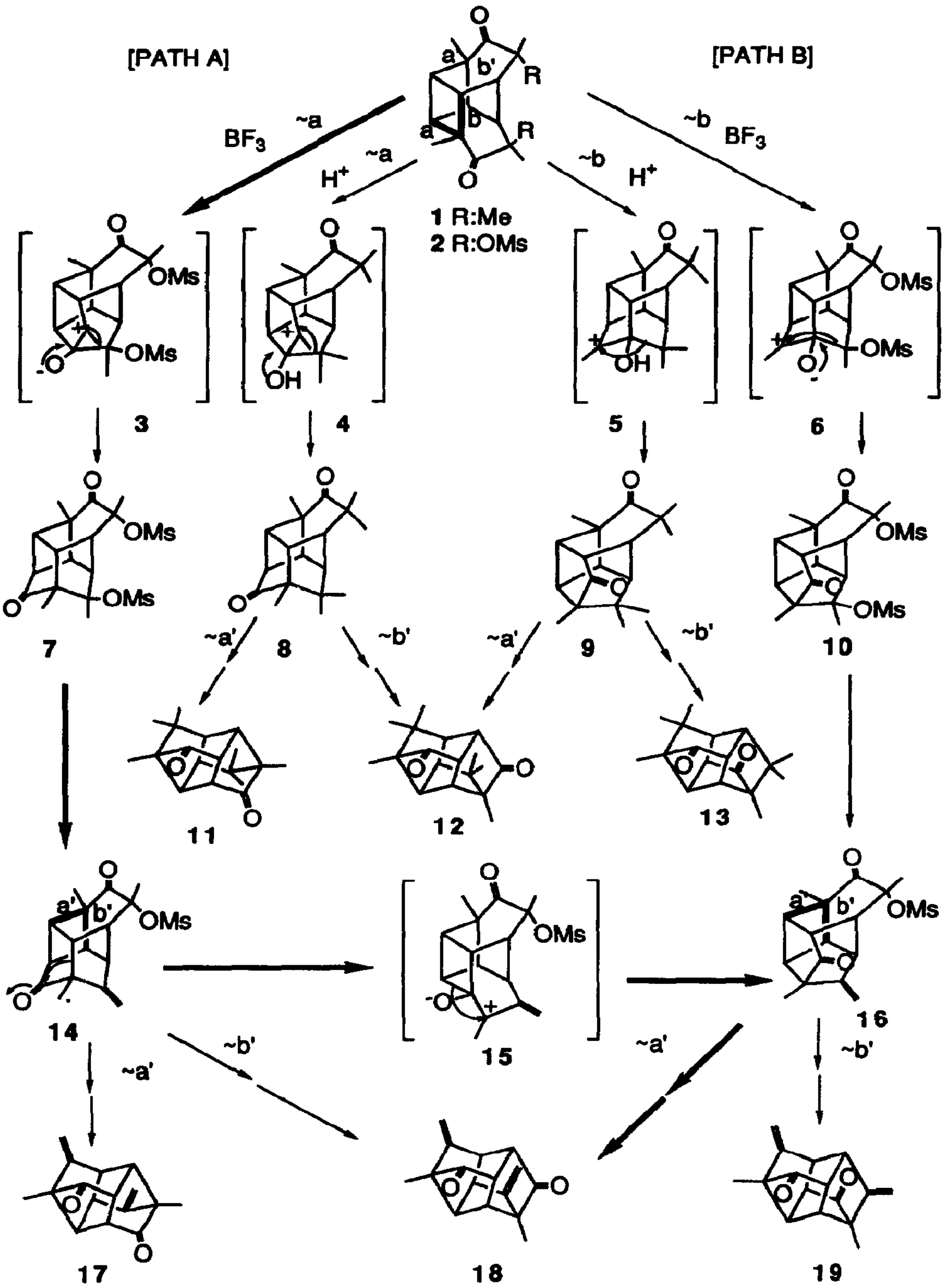
Abstract: The strange reaction pathway *via* an allyl cation **15** for the acid-catalyzed rearrangement of mesyloxy ketone **2** to diketones **18** and **19** is revealed by an X-ray crystallographic study of the intermediate enone **14**.

Some years ago, we found an efficient method for the synthesis of the bisnordiamantane skeleton **11**[1] by the completely regiospecific rearrangement of the pentacyclic cage compound **1**[2] using a Brønsted acid (CF_3CO_2H or *p*-TsOH) as a catalyst. The regiospecificity of the reaction (**1**→ **4**; preferable rearrangement of bond a) was attributed to the favorable formation of the cationic intermediate **4** ([PATH A]) over the formation of **5** ([PATH B]) on the basis of inspection of molecular models.[1] The carbocation **4** then readily isomerizes to the OH-stabilized intermediate **8H**$^+$, which is then deprotonated to **8**. Another set of analogous two-fold rearrangements involving bond a' occurs to give the bisnordiamantane **11**. Later, this proposal was supported by the convincing explanation by using empirical force field calculations.[3]

This acid-catalyzed reaction was intended for application to the preparation of other cage systems.[4] When the pentacyclic mesyloxy ketone **2** was treated with BF_3-ether in benzene, no trace amounts of expected **17** (having the skeleton corresponding to **11**) were detected, but two unexpected diketones **18** (corresponding to **12**, 47%) and **19** (corresponding to **13**, 10%) were obtained. The loss of high regiospecificity observed during the rearrangement of **1** and the alteration of the route from [PATH A] to [PATH B], which includes intermediaries **10** and **16**, have been ascribed to the steric hindrance of the mesylate groups to the bulky BF_3 catalyst.[4] However, it is necessary to modify this assumption in the following way.

In order to look more closely at the reaction of the mesyloxy ketone **2** with BF_3, the reaction products other than **18** and **19** have been studied. Among the products, a set of isomeric enones (in 13 and 0.4% yields) has been obtained. The analysis of the spectral data of these isomeric enones reveals that the structures should be **14** and **16**.[5] If the reaction of **2** with BF_3 proceeds by the presumed mechanism previously described (i.e. through [Path B]), the major enone (obtained in 13% yield) and the minor enone (obtained in 0.4% yield) should be **16** and **14**, respectively. Because the distinction between the two cannot be unambiguously deduced from the spectral data, the confirmation of the structure of the major enone has been made by X-ray analysis. In contrast to our anticipation, the structure, shown in Fig. 1[6] is indeed that of **14**. When **2** and **14** were treated with BF_3



Scheme 1. Acid-catalyzed rearrangements of 1 and 2

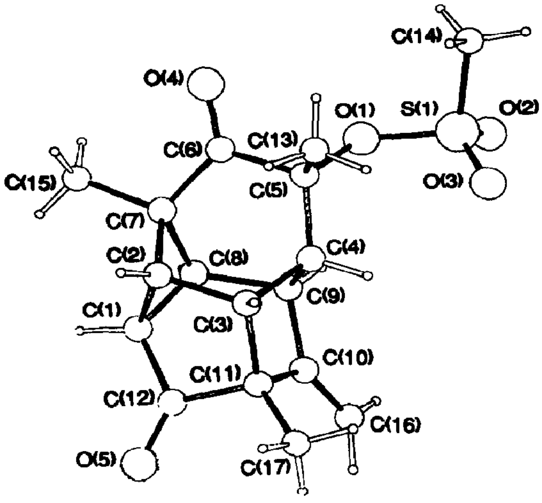
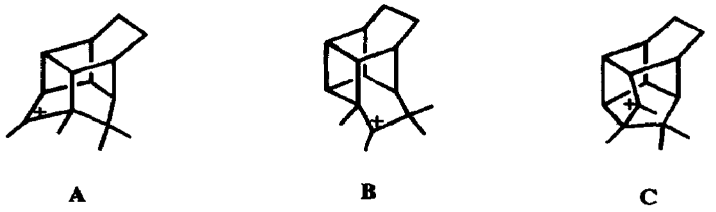


Fig. 1. Molecular structure of 14

etherate under the same conditions,[4] both gave the rearrangement products, 18 and 19, at the same ratio of 2 :1, respectively.[7] These results have strongly suggested that 14 is an intermediate of the reaction of 2 to 18 and 19. Thus, the formation route of 18 and 19 from 2 involves a strange by-path from 14 to 16 *via* an allyl cation 15. In addition, according to the empirical force field calculations,[3] the estimated enthalpies ($\Delta\Delta Hf$) of intermediate cations A (14^+), B (15), and C (16^+) (Scheme 2) are 27.89, 18.09, and 12.97 kcal mol^{-1},[†] respectively. Thus, it is possible that 14 (A type) can isomerize into 16 (C type) by way of the allyl cation 15



Scheme 2.

(B type).[8] Taking into account the fact that 11 is the sole product and no 12 is obtainable by the acid-catalyzed reaction of 1 and furthermore, no 17 is detected by the reaction of 2, the possibility of the direct formation of 18 from 14 may be ruled out, although its possibility cannot be thoroughly excluded by the available results. Finally, the calculations[3] also clarify the loss of regiospecificity of the further rearrangement of 16 to 18 and 19. Both processes of the shift of bond a' and b' leading to 18 and 19, respectively, having negative $\Delta\Delta Hf$ values are favourable. However, the probability of occurrence of the former (-4.87 kcal mol^{-1}) is larger than that of the latter (-0.88 kcal mol^{-1}).[†,3]

In conclusion, the Lewis acid-catalyzed reaction of **2** does not proceed through **10** → **16**, but through **7** → **14** → **15** → **16** → **18** and **19** as shown in Scheme 1 by the boldface arrows.

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† 1 kcal = 4.184 kJ

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5. *Spectral and physical data* for **14**: m.p. 142-143 °C (Found: C, 60.96; H, 6.01; S, 9.50. $C_{17}H_{20}O_5S$ requires C, 60.71; H, 5.99; S, 9.50%); ν_{max} (Nujol)/cm^{-1} 1730, 1660, 1340, 1180, and 920; δ_H(400 MHz; $CDCl_3$) 1.37 (3H, s), 1.48 (3H, s), 1.63 (3H, s), 2.6 (1H, m), 2.7 (1H, m), 2.8 (1H, bs), 3.0 (1H, m), 3.19 (3H, s), 3.4 (1H, bs), 3.5 (1H, bs), 4.85 (1H, s) and 5.06 (1H, s); δ_C(100 MHz; $CDCl_3$) 13.02 (q), 16.26 (q), 22.26 (q), 41.08 (q), 43.31 (d), 44.46 (d), 45.47 (s), 47.81 (d), 52.51 (d), 52.76 (d), 55.19 (d), 61.63 (s), 85.52 (s), 105.83 (t), 155.87 (s), 206.12 (s), and 208.30 (s); m/z 336 (M^+, 7%), 240 (85), 225 (90), 212 (42), 197 (53), and 43 (100).
   Spectral and physical data for **16**: m.p. 97-99 °C(decomp); ν_{max} (Nujol)/cm^{-1} 1740, 1720, 1660, 1350, 1180, and 920; δ_H(400 MHz; $CDCl_3$) 1.38 (3H, s), 1.48 (3H, s), 1.68 (3H, s), 2.8 (1H, m), 3.0 (2H, m), 3.4 (1H, m), 3.13 (3H, s), 3.4 (1H, m), 4.83 (1H, m), and 4.97 (1H, m); δ_C(100 MHz; $CDCl_3$) 13.04 (q), 16.31 (q), 22.53 (q), 40.89 (q), 44.86 (d), 45.26 (d), 45.89 (s), 47.15 (d), 51.17 (d), 53.40 (d), 55.07 (d), 61.52 (s), 83.67 (s), 104.97 (t), 156.40 (s), 205.74 (s), and 208.27 (s); m/z 336 (M^+, 7%)(Found: 336.104. $C_{17}H_{20}O_5S$ requires 336.103), 257 (4), 240 (100), 225 (42), 212 (51), 197 (55), and 43 (67).
6. *Crystal data* for **14**: $C_{17}H_{20}O_5S$, M = 336.39. Monoclinic, space group $P2_1/a$, a = 19.764(5), b = 11.6233(2), c = 6.825(1) Å, β = 94.55(2)°, V = 1562.8(6) Å^3, Z = 4, Dc = 1.430 g cm^{-1}, Mo-Kα radiation (λ = 0.71073 Å, graphite-monochromatized), μ (Mo-Kα) = 2.2 cm^{-1}, F(000) = 712. Intensity data were measured using a Rigaku automated four-circle diffractometer. Within the range $2 < 2\theta < 55°$, 2974 unique reflections were obtained with $|Fo| > 3\sigma(|Fo|)$. Structure was solved by the direct method using MULTAN78 and refined by the block-diagonal least-squares method on a FACOM M-1800 computer (programs UNICS-III program system).[9] Final R = 0.045, R_w = 0.043. Sources of atomic scattering factors and Δf' and Δf" values are given in ref 10.
7. The ratio, **18** to **19**, was determined by HPLC analysis.
8. The calculated ΔΔHf value of **B** underestimates the actual enthalpy, because the ion **15** is stabilized by delocalization involving the adjacent double bond; this point is under investigation.
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