Observation of a New Rearrangement Pathway in the Silver(I) Catalysed Bond Reorganization of Cubyl-caged Systems. A Caveat on the Generality of the Homocubane → Norsnoutane Rearrangement

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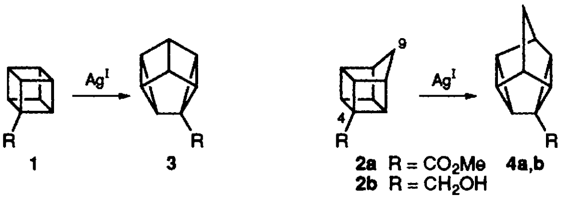
A new rearrangement of the homocubane framework to pentacyclo[4.3.0.0^{2,9}.0^{3,8}.0^{5,7}] nonane system spearheaded by the electronic effect of the substituent is described.

The generality of $\mathrm{Ag^I}$ catalysed reorganization of cubane **1** and homocubane **2** derivatives to cuneane **3** and norsnoutane **4** (homocuneane), respectively, is very well documented.[1] In particular, Paquette *et al.* have extensively studied the generality, preparative utility and mechanistic details of the **2** → **4** rearrangement employing various substituents, *e.g.* R = Me, CH_2OH, CO_2Me.[1d,e] However, we now report that the course of the $\mathrm{Ag^I}$ catalysed homocubane **2** → norsnoutane **4** reorganization is profoundly influenced by the substituents, and for **2a** (R = CO_2Me), a new reaction course leading to a new ring system is described, quite contrary to earlier structural formulation.[1d]

In connection with an ongoing research effort, we needed to access the pentacyclic keto ester **5**, which we felt, in the light of previous precedences, could be prepared through $\mathrm{Ag^I}$ catalysed rearrangement of homocubane ketal ester **6**. However, exposure ($AgNO_3$, aq. MeOH, heat or $AgClO_4$, C_6H_6, heat) of ketal ester **6**† (or the keto ester) to $\mathrm{Ag^I}$ led to a new keto ester (60–70%), with concomitant hydrolysis of the ketal group, whose eleven-line ^{13}C NMR spectrum clearly revealed that it was not the expected product **5**. Incisive analysis of the ^1H and ^{13}C NMR data and the $\nu(C{=}O)$ 1720 and 1724 cm^{-1} led to the formulation **7**‡,§ for this novel rearrangement product which was further unambiguously confirmed through single-crystal X-ray structure determination (Fig. 1).

At this stage, it was important to establish whether the deviation in the homocubane → norsnoutane type rearrangement observed in the case of **6** was due to the C_4-substituent, or C_9-functionality, or both. The ketal ester **6** was, therefore, reduced and the resulting ketal alcohol **8** was subjected to $\mathrm{Ag^I}$ rearrangement under the earlier employed conditions to furnish the 9-norsnoutanone alcohol **9**§ in quantitative yield and without any trace of **10** (Scheme 1). On the other hand, 9-hydroxy-homocubane ester **11** upon $\mathrm{Ag^I}$ exposure furnished the new skeleton **12** and not **13**. These observations firmly established the role of the C_4 ester substituent in homocubanes in deviating the rearrangement pathway away from the norsnoutane system. Concurrently, we also repeated the rearrangement of **2a** under the reported conditions and found that the product had a eleven-line ^{13}C NMR spectrum, similar to **7** and should be reformulated as **14**§, instead of **4a** as proposed earlier.[1d]



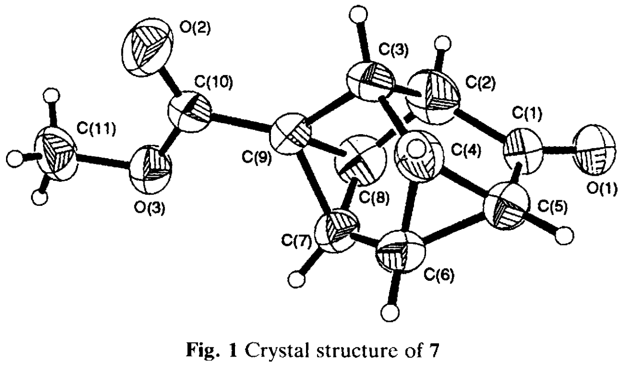
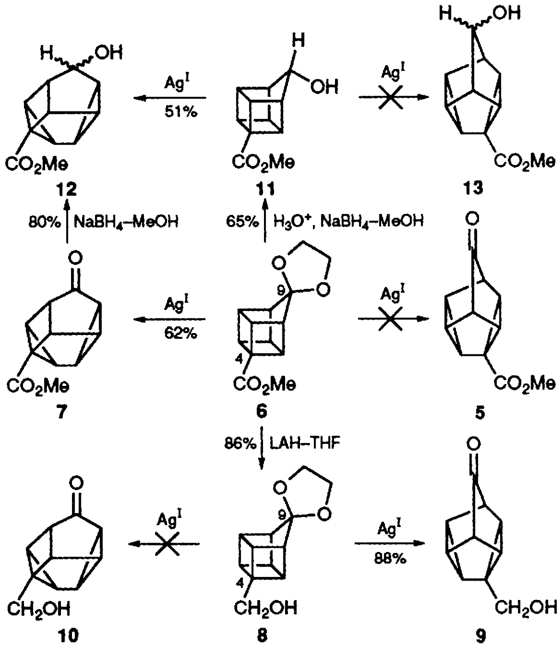
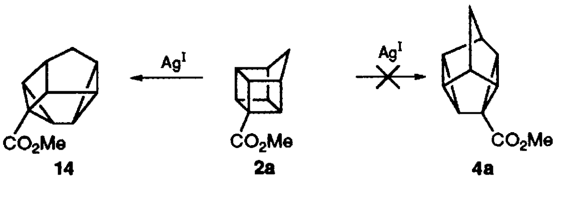


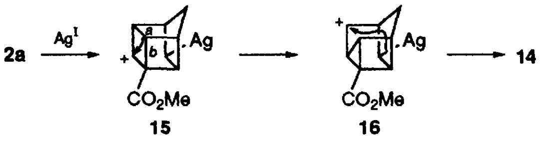
Fig. 1 Crystal structure of 7

It is quite intriguing that the electronic effect of the C_4-electron-withdrawing group guides the rearrangement to a thermodynamically less stable ring system and to a framework incorporating a bicyclo[2.1.0]pentane moiety.† Silver(I) catalysed rearrangements of strained ring systems are considered to be proceeding through carbocation intermediates with the metal ion functioning as a Lewis acid. A mechanism for the formation of **14** from **2a** is shown in Scheme 2, in which the electronic effect of the substituent dictates the course of the rearrangement. After the initial regioselective σ-bond cleavage away from the electron-withdrawing substituent to furnish the carbocation intermediate **15** (or its bicyclobutonium form), mechanistic bifurcation takes place through the



Scheme 1





Scheme 2

migration of the more electron rich *a* bond, in preference to the *b* bond, to result in a more stable carbocation **16** that eventually leads to the product **14**. However, when a C_4-electron-withdrawing group is not present, no such preference is mandated and the rearrangement adopts the favoured norsnoutane route. It is also worth mentioning that the mechanism outlined in Scheme 2 and the new rearrangement encountered here helps to further clarify the unusual product distribution observed earlier in the Ag^I catalysed rearrangement of mono- and 1,4-disubstituted cubanes to regioisomeric cuneanes.[1a]

Finally, in view of the results reported here, due caution should be exercised in generalizing the rearrangements in cubyl systems and in drawing mechanistic conclusions.[1] It needs to be emphasized that a substituent can be used as a powerful handle to further harness the latent ability of cubyl cages to rearrange particularly to new and synthetically useful polycycles.

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Footnotes

† Molecular mechanics calculations (MMX) indicated that the pentacyclo[4.3.0.0^{2,9}.0^{3,8}.0^{5,7}]nonane system present in **7** is *ca.* 3.5 kcal mol^{-1} less stable than the pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonane (norsnoutane) framework. (1 cal = 4.184 J).

‡ *Crystal data* for **7**: $C_{11}H_{10}O_3$, monoclinic, space group $P2_1/c$, a = 8.933(1), b = 11.098(1), c = 9.551(1) Å, β = 108.37(1)°, V = 898.62 Å^3, Z = 4, T = 293 K, D_c = 1.406 mg m^{-3}, crystal dimensions 0.18 × 0.15 × 15 × 0.16 mm, 1350 reflections measured, $2\theta_{max}$ = 45°, $0 \leqslant h \leqslant 9$, $0 \leqslant k \leqslant 11$, $-10 \leqslant l \leqslant 10$, 1182 unique reflections (R_{int} = 0.044, averaging double measured) and 1001 observed with $I \geqslant 3\sigma(I)$, μ = 0.07 mm^{-1}. Final R = 0.047 and R_w = 0.056 [127 parameters and $\omega = 1/\sigma^2(F_o) + 0.004074F_o^2$)], maximum shift/error = 0.001, $\Delta\rho_{max}$ = 0.16 eÅ^3, $\Delta\rho_{min}$ = −0.14 eÅ^3. Data were collected on a SIEMENS R3m/V single crystal diffractometer (ω–2θ scan technique) using Mo-Kα radiation (λ = 0.71073 Å). Data corrected for Lorentz and polarization but not for absorption. The structure was solved by direct methods (SHELXTL-PLUS) and anisotropically refined. The H-atoms calculated to their idealized positions and refined as riding atoms with fixed isotropic temperature factors (U = 0.08 Å^2). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for authors, Issue No. 1.

§ All new compounds reported here were characterized on the basis of spectral data and elemental analysis.

Selected data for **7**: ^{1}H NMR (200 MHz, CDCl$_3$): δ 3.67 (3H, s), 3.37 (1H, m), 2.87–2.98 (1H, m), 2.67–2.86 (3H, m), 2.48 (1H, m), 1.85–1.96 (1H, m); ^{13}C NMR (50 MHz, CDCl$_3$): δ 212.90, 171.22, 51.62, 41.49, 40.06, 39.74(2C), 39.18, 37.12, 30.86. For **9**: ^{1}H NMR (200 MHz, CDCl$_3$): δ 3.89 (2H, s), 2.55 (2H, m), 2.39 (1H, m), 2.04 (4H, m); ^{13}C NMR (50 MHz, CDCl$_3$): δ 204.36, 61.71, 50.23, 41.80, 33.79, 33.12, 28.60. For **14**: ^{1}H NMR (200 MHz, CDCl$_3$): δ 3.57 (3H, s), 3.07 (1H, m), 2.78 (1H, m), 2.10–2.25 (3H, m), 1.79 (1H, m), 1.65 (1H, m), 1.15–1.45 (2H, m); ^{13}C NMR (50 MHz, CDCl$_3$): δ 173.85, 51.30, 50.90, 45.54, 38.18, 35.30, 35.50, 31.91, 30.74, 26.63, 24.23.

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