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CATIONIC REARRANGEMENT OF A SECO-HOMOCUBANONE TO A BRENDANONE AND A PENTALENONE

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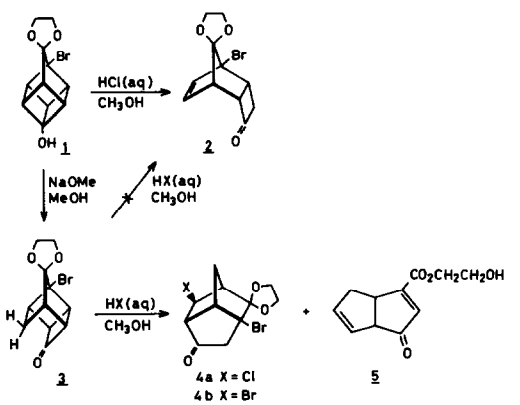
Bridgehead alcohols in strained cage systems such as homocuban-4-ols and 1,3-bishomocuban-5-ols readily undergo regio- and stereospecific homoketonization reactions under basic conditions[1,2]. Recently, we found that homocuban-4-ols are also quite reactive towards acidic reagents. Treatment of bridgehead alcohol 1-bromo-4-hydroxypentacyclo[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonan-9-one ethylene ketal 1 with aqueous HCl in methanol at 20°C slowly gave a new product to which, on the basis of spectroscopic data and comparison with an authentic sample, structure 2 was assigned (Scheme I). At first glance an acceptable pathway for this double cage opening seems to involve the intermediacy of half-cage ketone 3

Scheme I



However, as will be disclosed in this communication seco-homocubanone 1-bromotetracyclo[4.3.0.0^{2,5}.0^{3,8}]nonan-4,9-dione-9-ethylene ketal 3, under acid conditions, undergoes an unforeseen sequence of cationic rearrangements to brendanone 4 and pentalenone 5 (Scheme I).

Half-cage ketone 3, which is readily available from 1 via a base-induced homoketonization reaction[1], appeared to be extremely sensitive to acid. Upon treatment with aqueous HCl in methanol, ketone 3 rapidly reacted, yielding a mixture of two products. Spectroscopic and analytical data clearly revealed that

no tricyclononenone 2 had been produced. This result definitely rules out the intermediacy of half-cage ketone 3 during the acid-induced double-cage opening of homocubanol 1.

Separation of the two products from the mixture could be accomplished by rapid preparative TLC on silica, affording a crystalline compound 4a (m.p. 121-123°C) and an oily product 5, in 27% and 69% yield[3] respectively. At room temperature 4a was quite stable, but 5 decomposed rapidly making both separation and purification a laborious task. The spectral data of 4a [*m/e* 307, $C_{11}H_{12}O_3BrCl$; IR (KBr): ν_{max} 1750 (C=O), 1390 ($CH_2C=O$); ^{1}H-NMR ($CDCl_3$): δ 4.14 (m, 1H), 3.77-4.10 (m, 4H), 3.03-3.20 (m, 1H), 2.57-3.13 (m, AB pattern, 2H), 2.63-2.80 (d, 1H), 2.40-2.50 (m, 1H), 2.05-2.45 (m, AB pattern, 2H)] were indicative of a tricyclic structure. Careful analysis of the ^{1}H-NMR spectrum using shift reagents and double resonance techniques did not allow a definite assignment of the structure of 4a. However, the stereospecific incorporation of a chlorine substituent could be established unequivocally.

When ketone 3 was treated with aqueous HBr in methanol, a similar rearrangement occurred producing the bromo analog of 4a namely 4b in 80% yield[3]. Compound 5 was also formed in this reaction but only to a minor extent (14%)[3]. The striking change in product ratio by going from HCl to HBr indicated that the nucleophilicity of the acid used is of crucial importance. Substantial support for this view was obtained by treating ketone 3 with aqueous $HClO_4$ in methanol. An almost exclusive conversion of 3 into 5 was observed. No products structurally related to 4 could be detected. These results suggest that the formation of 4 and 5 is mechanistically related.

Crystals of 4b obtained by fractional crystallization from ethanol were subjected to an X-ray diffraction analysis providing an unambiguous assignment of its structure. As shown in Figure 1 dibromide 4b has the brendanone structure[4]. Accordingly, the tricyclic product (m.p. 121-123°C) obtained by

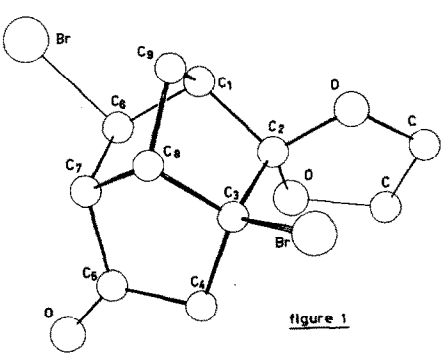


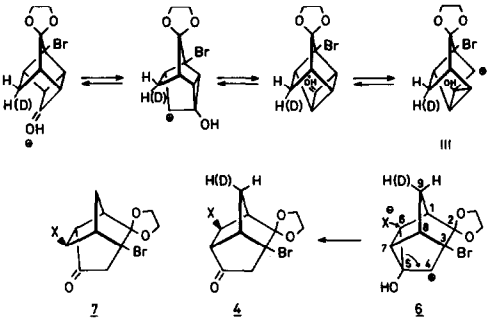
figure 1

using hydrochloric acid has structure 4a.

The formation of 4 from half-cage ketone 3 can be rationalized as depicted in Scheme II. Protonation of the cyclobutanone carbonyl function initiates a series of consecutive cyclobutyl-cyclopropylcarbinyl rearrangements[5] leading to

the apparently most stable cyclopropylcarbinyl cation 6. Subsequent opening of

Scheme II



the cyclopropane ring in 6 by attack of the nucleophilic halogen at C_6 in a regio- and stereospecific process[6], furnishes brendanone 4. Formation of nortwistanone 7, which can be envisaged by attack of X^- on C_7 in 6, is unlikely on thermodynamical grounds, *viz.* 7 being 11 kcal/mol less stable then 4[7].

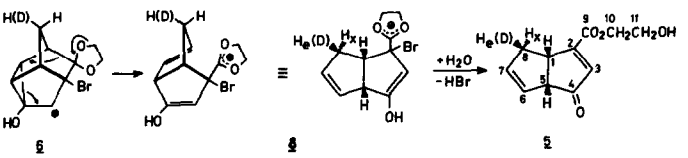
The spectral features of the oily product 5 show a high degree of unsaturation, and, in addition, reveal that no nucleophile has been incorporated. It should be recalled that its formation is mechanistically related to that of product 4 (*vide supra*). On the basis of these considerations and a logical breakdown of cation 6 (Scheme II) structure 5 was tentatively assigned to this oily material. Detailed analysis of the spectral data proved this assignment to be correct. The IR spectrum showed characteristic absorptions at 3450 (ν_{OH}),1705 (conjugated ester, ketone) and 1600 ($\nu_{C=C}$) cm^{-1}. The UV spectrum (CH_3OH) exhibited λ_{max} at 236 mμ, indicative of a cyclopenten-2-one system[8]. The ^{1}H-NMR spectrum ($CDCl_3$) displayed a characteristic doublet ($J_{H_3,H_1} \sim 1.5$ Hz) for olefinic proton H_3 at δ 6.59 and a broad singlet for olefinic protons H_6 and H_7 at δ 5.63 ppm. The ethylene glycolate protons were observed as a typical A_2B_2 pattern at δ 4.33 and 3.86 ppm. The bridgehead protons H_1 and H_5 appeared as a broad unresolved multiplet at δ 3.60 ppm. The methylene protons at C_8 exhibited the expected AB pattern as a doublet of broad doublets ($J_{H_{8e},8x} \sim 18$ Hz, $J_{H_{8e},H_1} \sim 10$ Hz, $J_{H_{8e},H_7} \sim 1$ Hz) at δ 2.8 for *endo*-proton H_{8e} and a doublet of triplets ($J_{H_{8x},H_{8e}} \sim 18$ Hz, $J_{H_{8x},H_1} \sim J_{H_{8x},H_7} \sim 2$ Hz) at δ 2.4 for *exo*-proton H_{8x}. The OH proton was found at δ 2.61 ppm. A high resolution mass spectral elemental map revealed a molecular ion peak of empirical formula $C_{11}H_{12}O_4$ (found: *m/e* 208,0734; calc.: 208,0736). As can be expected for 5, the most important mode of fragmentation is the formation of the tropylium cation (*m/e* 91)[9]. Confirmative evidence for the structure of 5 was provided by its ^{13}C-NMR spectrum in $CDCl_3$ [δ 35.63 (t, C_8), 42.28 (d, C_1), 59.40 (d, C_5), 60.28 (t, C_{11}), 66.72 (t, C_{10}), 126.76 (d, C_7), 131.89 (d, C_6), 135.93 (d, C_3), 164.10 + 164.95 (two s, C_2 and C_9), 208.72 (s, C_4)].The combination of the low field ^{13}C=O signal at

208.72 and an olefinic resonance at δ 164 ppm points to a cyclopenten-2-one structure[10]. The observation of a $^{13}C{=}O$ at ∿164 establishes the presence of an α,β-unsaturated ester[10].

Hydrogenation of 5 (Pd/C, 10%) gave the stable saturated compound $C_{11}H_{16}O_4$, the spectral properties of which were in full accord with the pentalone structure.

The formation of 5 from cyclopropylcarbinyl cation 6 can be explained as pictured in Scheme III. Most likely, the driving force of this rearrangement reaction is the generation of a relatively stable oxonium ion 8. Subsequent hydrolysis of this cation and dehydrobromination leads to the isolated pentalenone 5.

Scheme III



6 8 9

Substantial support for this mechanism is provided by the $HClO_4$-induced rearrangement of *endo*-monodeuterated seco-homocubanone 3 which led to monodeuterated pentalenone 5 in almost quantitative yield. The ^1H and ^{13}C-NMR spectra clearly reveal that deuterium has been incorporated at the C_8 *endo*-position exclusively. This result can only be reconciled with the reaction sequence given in Schemes II and III.

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