CHEMISTRY LETTERS, pp. 825-828, 1978. Published by the Chemical Society of Japan

REGIO- AND STEREOSELECTIVE CYCLOPROPANE RING OPENING IN A TETRACYCLIC COMPOUND. *exo*-4-ACETOXY-4-HOMOISOTWISTANE (*exo*-4-ACETOXYTRICYCLO[5.-3.1.$0^{3,8}$]UNDECANE) FROM 2,4-DEHYDRO-4-HOMOTWISTANE (TETRACYCLO[5.4.0.-$0^{2,4}$.$0^{3,9}$]UNDECANE) IN ACETIC ACID UNDER SULFURIC ACID CATALYSIS

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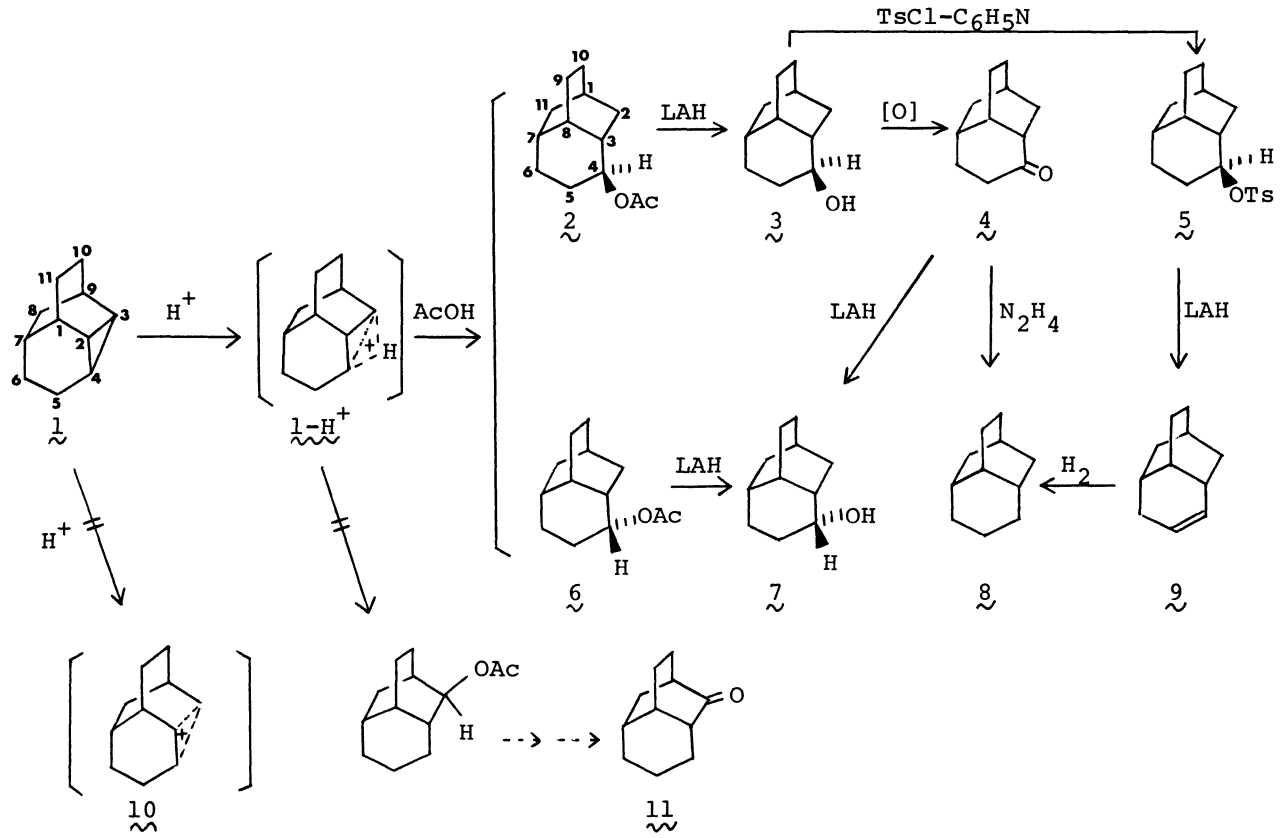
Sulfuric acid catalyzed reaction of 2,4-dehydro-4-homotwistane (1) with acetic acid gave predominantly *exo*-4-acetoxy-4-homoisotwistane (2). The result is best interpreted in terms of the edge-protonated cyclopropane intermediate 1-H$^+$, in which the ring opening occurs to give the most stable skeletal structure 8, while the regio- and stereoselectivity arise from the attack of AcOH at the least congested *exo*-4 site.

A variety of reagents have been shown to add with concominant ring opening to the cyclopropane in polycyclic compounds, and the reaction often finds synthetic utility toward functionalized polycycloalkanes which otherwise could be prepared only with difficulty.[1] We now report regio- and stereoselective addition of acetic acid to 2,4-dehydro-4-homotwistane (tetracyclo[5.4.0.$0^{2,4}$.$0^{3,9}$]-undecane, 1)[2] in the presence of sulfuric acid. The product 4-acetoxy-4-homoisotwistanes (4-acetoxytricyclo[5.3.1.$0^{3,8}$]undecanes, 2 and 6) are sources of the corresponding 4-yl cation which was shown to be one of the key intermediates in later stages of the tricycloundecane rearrangement.[3]

The tetracycloundecane 1 (0.10 g) was stirred at ambient temperature for two days with acetic acid (5 ml) containing 98% sulfuric acid (0.05 g). Extraction with *n*-pentane followed by concentration gave a residue which was analyzed on a conventional VPC to show only one major peak (96% of the combined peak areas). Fractionation on preparative VPC gave 0.094 g (67% yield) of the product.[4]

The product was found to consist of two isomers (in 98:2 ratio) of an acetoxytricycloundecane upon Golay column GC-MS. The acetate mixture was reduced with lithium aluminum hydride to the corresponding alcohols which were separable on conventional VPC. Jones oxidation of the alcohol mixture afforded a single compound: IR (Nujol) 1710, 1290, 1250, 1070, 980, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.2 - 2.6 (complex m); ^{13}C NMR ($CDCl_3$) δ_C 23.52 (d), 24.62 (t), 25.08 (t), 29.11 (t), 29.69 (t), 31.25 (d), 31.38 (t), 31.97 (t), 33.40 (d), 48.15 (d), 215.19 (s); MS (*m/e*, rel intensity) 164 (100, M$^+$), 109 (54), 93 (36), 83 (54), 80 (96), 79 (83), 67 (83), 66 (54), 41 (49), 39 (41). Wolff-Kishner reduction led to 4-homoisotwistane (8). These results indicated the compound to be an asymmetrical 4-homoisotwistanone. Since only two structures, the 2-one (11) and the 4-one (4), were compatible with the above evidences, VPC and spectroscopic properties of


TsCl-C6H5N
LAH
[O]
H+
AcOH
LAH
N2H4
LAH
LAH
H2
OAc
OH
OTs
O
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1-H+
2
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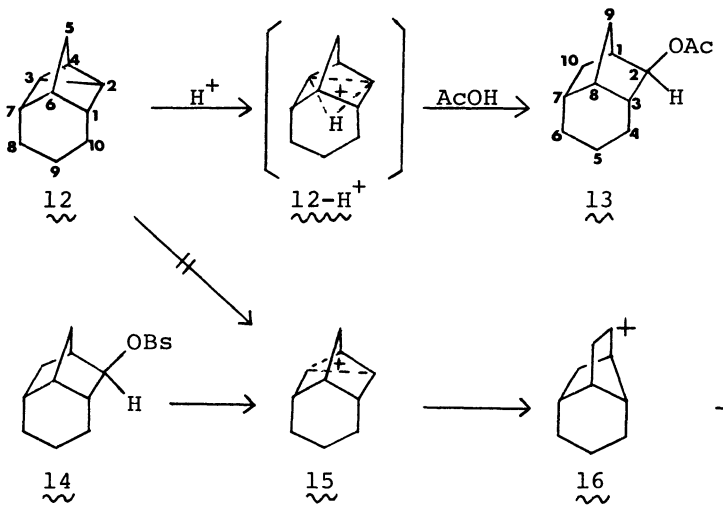
11


H+
AcOH
OBs
OAc
12
12-H+
13
14
15
16
17
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19
20

this ketone were compared with those of known 4-homoisotwistan-2-one (11)[5] to demonstrate disagreement between the two. Thus the structure of the ketone obtained here was unambiguously determined to be 4-homoisotwistan-4-one (4).

Lithium aluminum hydride reduction reverted the ketone 4 back to a mixture of the same alcohols as were obtained from the acetoxytricycloundecanes 2 and 6. Ratio of the isomers, however, was greatly different in the two crops, the minor constituent (2%) of the alcohol mixture from the acetates 2 and 6 being the major one (76%) of that from the ketone 4. On the basis of the established preferable attack of lithium aluminum hydride from the less hindered exo side in polycyclic ketones,[5] the endo configuration 7 was assigned to the major product of ketone reduction: mp 97 - 98°C; IR (Nujol) 3600 - 3100, 1080, 1020, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 - 2.0 (complex m, 16H), 2.88 (s, 1H, O*H*), 3.3 - 3.7 (m, 1H, C*H*OH); ^{13}C NMR ($CDCl_3$) δ_C 23.92 (t), 24.24 (t), 26.07 (t), 26.31 (t), 26.52 (t), 29.40 (d), 30.21 (d), 31.76 (t), 32.12 (d), 37.97 (d), 72.57 (d); MS (*m/e*, rel intensity) 166 (23, M^+), 148 (99), 109 (79), 93 (36), 81 (43), 80 (100), 79 (58), 67 (66), 66 (42), 41 (45). Accordingly, the major product alcohol derived from the acetate mixture should have the exo configuration 3: mp 57.5 - 58.5°C; IR (Nujol) 3500 - 3100, 1100, 1010, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 - 2.2 (complex m, 16H), 2.52 (s, 1H, O*H*), 3.70 (s, 1H, C*H*OH); ^{13}C NMR ($CDCl_3$) δ_C 22.33 (t), 25.18 (t), 25.75 (d), 25.95 (t), 26.52 (t and t), 30.22 (d), 30.54 (d), 30.98 (t), 37.68 (d), 71.59 (d); MS (*m/e*, rel intensity) 166 (7, M^+), 148 (100), 119 (37), 109 (53), 93 (29), 81 (32), 80 (65), 79 (47), 67 (51), 66 (30).

The exo alcohol 3 was tosylated and treated with lithium aluminum hydride in the usual manner to produce an olefin, 4-homoisotwist-4-ene (9): IR (neat) 3020, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.7 - 2.4 (complex m, 14H), 5.2 - 6.0 (complex m, 2H, C*H*=C*H*); ^{13}C NMR ($CDCl_3$) δ_C 23.47 (d), 24.85 (t), 25.10 (t), 28.59 (d and d), 31.43 (d), 32.16 (t), 32.81 (t), 33.79 (t), 122.39 (d), 135.22 (d), MS (*m/e*, rel intensity) 148 (89, M^+), 119 (27), 105 (26), 92 (39), 91 (47), 81 (28), 80 (47), 79 (60), 44 (50), 41 (26), 32 (100). Hydrogenation of the olefin 9 over palladium on charcoal catalyst regenerated the saturated hydrocarbon 4-homoisotwistane (8), in agreement with the skeletal structure of 3.

A highly stereo- and regioselective cyclopropane ring rupture in 2,4-dehydro-4-homotwistane (1) seems to be best explained by presuming a product-determining attack of acetic acid on the edge-protonated intermediate[6] 1-H^+. Among the possible three products of the edge protonation on 1, which is considered to be rate-determining,[6] 1-H^+ leading to 4-homoisotwistane structure (2 and 6) would be formed predominantly under thermodynamic control.[7] The bridging proton in 1-H^+ is extended toward the endo side, so that the nucleophile should approach more preferably from the exo side to develop the observed high stereoselectivity to the less stable, axial isomer 2. On the other hand, the regiospecificity appears to arise from a larger steric congestion at *exo*-3 than at *exo*-4 in 1-H^+. In contrast to 1-H^+, the corner-protonated species 10 seems difficult to account for the selective formation of 2. The corner-protonated cyclopropanes are structurally identical with the corresponding carbon-bridged cations, and many of them have been found[6] to undergo intramolecular hydride transfer and skeletal rearrangement to a number of products.

The presumed intermediacy of the edge-protonated species 1-H^+ for the reaction of 1 is indirectly supported by the addition of acetic acid to 2,10-dehydro-4-homobrendane (tetracyclo[4.4.0.$0^{2,4}$.$0^{3,8}$]decane, 12),[1d] as compared to solvolyses of 4-homobrend-*exo*-2-yl (*exo*-2-tricyclo[5.2.1.$0^{3,8}$]decyl)brosylate (14).[8] The former reaction proceeded to afford exclusively 4-homobrend-*exo*-2-yl acetate (13), while the latter gave a variety of products derived from the cations 16 through 20. Since the brosylate 14 was shown to generate the bridged cation 15, which was the same species as the C-3 corner-protonated 12, formation of a single product 13 may be accounted for more reasonably with the intermediacy of the edge-protonated species 12-H^+.

In conclusion, the present reaction of 1, together with that of 12, suggests a possible mechanism involving the edge-protonated intermediate as the principal acceptor of the nucleophile. Deuterium labelling studies are now under way to confirm this mechanism.

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7) The products might be thought to arise via C-2-C-3 edge protonation followed by loosening of C-3-C-4 bond and attack of nucleophile at C-4, as proposed by DePuy.[6] However, this protonation would be rendered rather difficult because of steric congestion around C-2-C-3, as discussed in the text.

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(Received May 16, 1978)