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ACID-CATALYZED REARRANGEMENTS OF TRICYCLO[4.3.2]PROPELLANE DERIVATIVES

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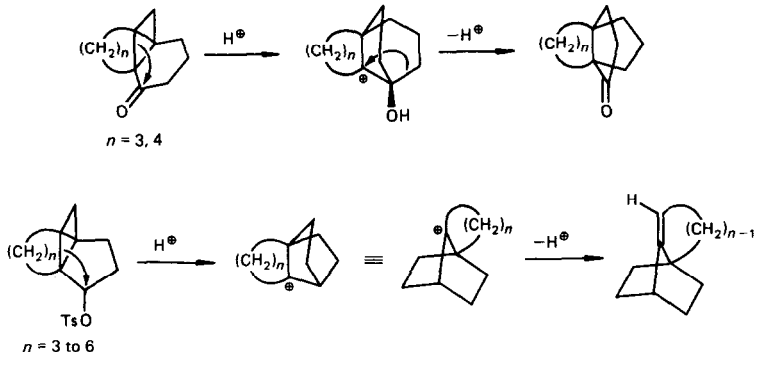
Abstract: The acid-catalyzed rearrangements of three model tricyclo[4.3.2] propellane derivatives have been explored. In each case the observed products are proposed to arise via a concerted 1,2-shift of the cyclobutane bond having an antiperiplanar alignment with the leaving group (i.e., stereoelectronic control).

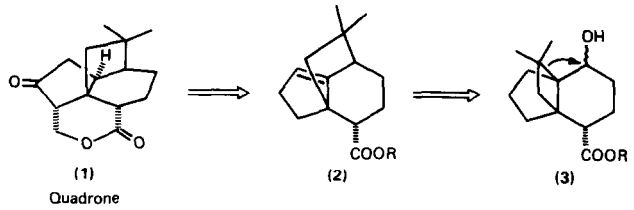
Rearrangements of cyclobutylcarbinyl systems have been studied extensively in recent years[2] and have found use in the synthesis of complex organic molecules.[3] Particularly interesting are the acid-catalyzed rearrangements of tricyclo[m.n.2]propellane derivatives (m ⩾ 3, n ⩾ 3) investigated by Cargill,[4] Tobe,[5] and Eaton.[6] In general, the rearrangements have been found to proceed via initial 1,2-migration of the external bond of the cyclobutane ring (Scheme I). Only recently have two examples been uncovered wherein the central bond undergoes migration.[5b,6]

Scheme I

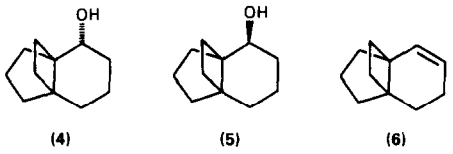


Our interest in the quadrone structure[7] led us to propose a synthetic strategy for the parent natural product quadrone[8] (1) wherein the key step would entail an acid-catalyzed rearrangement of propellane (3), or a closely related derivative, to afford olefin (2) possessing the requisite quadrone skeleton (see Scheme II).

Scheme II

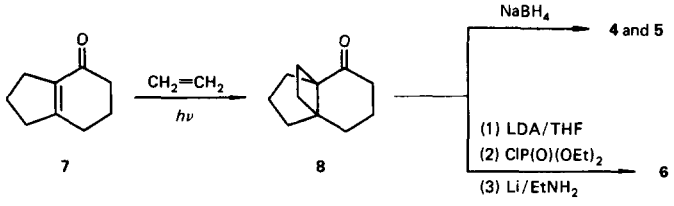


To explore the feasibility of such a strategy we examined the acid catalyzed rearrangement of three model propellanes (4, 5 and 6). We record here the result of that study.



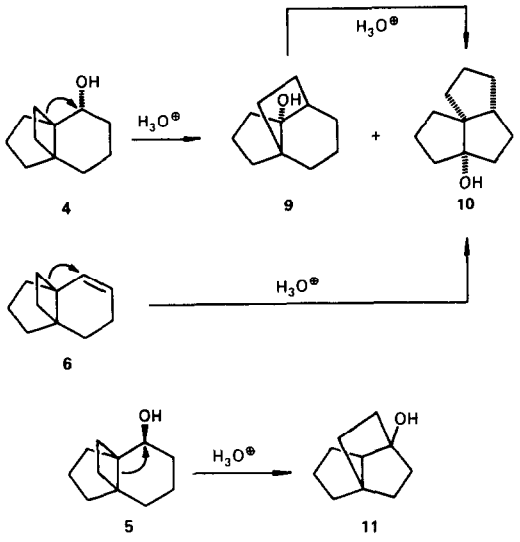
(4) (5) (6)

The tricyclo[4.3.2]propellane substrates (4, 5 and 6) were prepared using the methodology developed in connection with our recent modhephene synthesis.[9] Specifically, irradiation of a methylene chloride solution of enone 7[9] through pyrex in the presence of ethylene at -78° for 17 h afforded propellanone 8[10] in 86% isolated yield. Subsequent reduction of 8 with sodium borohydride afforded in near quantitative yield a 1:3.8 mixture of alcohols 4[10] and 5[10] respectively, which were separable by flash chromatography (10% EtOAc/hexane). Stereochemical assignments were based on chemical precedent.[11] Olefin 6, on the other hand, was prepared from 8 via the Ireland enol-phosphate protocol.[12] That is, capture of the enolate derived from 8 (LDA, THF, -78°) with diethylchlorophosphate gave the corresponding enol-phosphate, which was then reduced, albeit in poor yield, with lithium metal in ethylamine to afford highly volatile olefin 6.[9]



Treatment of the α-alcohol (4) with 40% aqueous sulfuric acid in THF [1:2(v/v)] at room temperature for 3 days afforded a mixture consisting of unreacted starting material and two isomeric alcohols, assigned structures 9[10] and 10[10] on the basis of chemical transformations to known compounds.[13] At higher temperature (60°C) 10 was isolated as the sole product. Pure 9 was also converted to 10 when subjected to the higher reaction temperature. Similarly, olefin 6 afforded 10 as the sole product when subjected to the rearrangement conditions (40°C). In both cases, the rearrangements are consistent with the expected initial peripheral bond migration (see Scheme I) leading to an intermediate which is then either captured by solvent (to give 9) or undergoes a secondary rearrangement (to give 10).

However, when the β-alcohol (5) was treated with 40% aqueous sulfuric acid in THF (60°C, 30 min), a new crystalline alcohol 11 (mp 74.5-75°C)[10] was isolated in 93% yield. X-ray crystallographic analysis confirmed the presence of a bridgehead hydroxyl group. In this case initial 1,2-migration of the central bond of the propellane ring takes place.



Unlike the results of Tobe,[5a] in which the same product results from the acid treatment of the isomeric tosylates (Scheme I), rearrangement of the isomeric hydroxy propellanes 4 and 5 leads to the formation of two different products. It is reasonable to suggest, therefore, that under the reaction conditions each alcohol undergoes solvolysis with concommitant shift of the properly aligned cyclobutyl bond in a concerted fashion.[14] Since alcohol 5 cannot assume a conformation with the leaving group antiperiplanar to the peripheral bond of the cyclobutane ring, the central bond, which can assume good alignment, is seen to migrate. The more planar olefin 6, upon protonation, would be expected to have the empty orbital of the cyclobutylcarbinyl system in good alignment with the external bond. In fact exclusive migration of the external bond is observed.

In summary, the above model studies suggest that rearrangement of propellane 2, or a closely related derivative, may provide a feasible approach to the quadrone skeleton. Studies to confirm this prediction are currently ongoing in our laboratory.

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10. (a) All new compounds gave high-field (250MHz) ^{1}H NMR, IR spectra and elemental composition data (C,H analysis and/or parent ion identification) in accord with the assigned structures. All yields recorded here are based upon isolated material which was ≥ 97% pure. NMR and IR spectra of representative intermediates are given below: 4: IR (CCl_4) 3625 (m), 3225-3525 (br, m), 2950 (br, s), 2875 (m), 1460 (m), 1275 (w), 1030 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.20-2.18 (m, 17 H), 4.04 (dd, J = 4.4, 9.9 Hz, 1 H); 5: IR (CCl_4) 3605 (w), 3325-3525 (br, m), 2920 (s) 2845 (m), 1445 (m), 1360 (w), 1250 (m), 1045 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.26-2.08 (m, 16 H), 2.09-2.24 (m, 1 H), 3.58 (dd, J = 5.5, 10.8 Hz, 1 H); 6: IR (CCl_4) 3075 (m), 2950 (s), 2875 (s), 1445 (m), 1235 (m), 1085 (br, s), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.22-1.54 (m, 4H), 7.56-1.90 (m, 8 H), 1.90-2.24 (m, 2 H), 5.83 ddd, J= 3.7, 5.1, 9.9 Hz, 1 H), 5.95 (d, J = 9.9 Hz, 1 H); 8: IR ($CHCl_3$) 3075 (w), 2950-3045 (s), 2925 (m), 1690 (m), 1435 (m), 1240 (w), 1220 (m), 1160 (m), 920 (m), 890 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.34-1.64 (m, 2 H), 1.66-2.34 (m, 13 H), 2.44-2.64 (m, 1H); 9: IR (CCl_4) 3615 (m), 2975 (s), 2860 (s) 1450 (m), 1150 (m), 1005 (m), 910 (m) cm^{-1}; NMR (250 Mhz, $CDCl_3$) δ 1.14-1.68 (m, 12H), 1.68-1.96 (m, 5H), 2.10 (d,d, J = 4,3.5 Hz, 1H); 10: IR (CCl_4) 3600 (m), 3325-3525 (m), 2950 (br, s), 2850 (s), 1445 (m), 1240 (m), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.14-1.30 (m, 6H), 1.30-2.04 (m, 12H); 11: IR 3610, 2940, 2870, 1450, 1125, 1050 cm^{-1}; NMR (250 MHz) 0.99 (s, 3H), 1.08 (s, 3H), 1.221.92 (comp. 16H).

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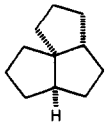
13. Alcohol 9 was chemically correlated with alcohol 11. Compound 10 was transformed into the known hydrocarbon 12; see: Takaishi, N.; Inamoto, Y.; Tsuchihashi, K.; Yashima, K.; Aigami, K. J. Org. Chem., 1975, 40, 2929.



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14. For a discussion of maximum continuous orbital overlap as applied to propellane rearrangements see: Kakiuchi, K.; Itoga, K.; Tsugaru, T.; Hato, Y.; Tobe, Y.; Odaira, Y., J. Org. Chem., 1984 49, 659 and references cited therein. For a general discussion on maxium continuous orbital overlap see: Schleyer, P. v. R.; Lam, L. K. M.; Raber, D. J.; Fry, J. L.; McKervey, M. A.; Alford, J. R.; Cuddy, B. D.; Keizer, V. G.; Geluk, H. W.; Schlatmann, J. L. M. A., J. Am. Chem. Soc. 1970, 92, 5246; Majerski, Z.; Schleyer, P. v. R.; Wolf, A. P. Ibid., 5731; and Nickon, A.; Weglein, R. C. J. Am. Chem. Soc. 1975, 97, 1271.

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