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SEMI-U OVER SEMI-W STEREOSELECTIVITY IN ACID CLEAVAGES OF 1-METHOXYNORTRICYCLANE.[1]

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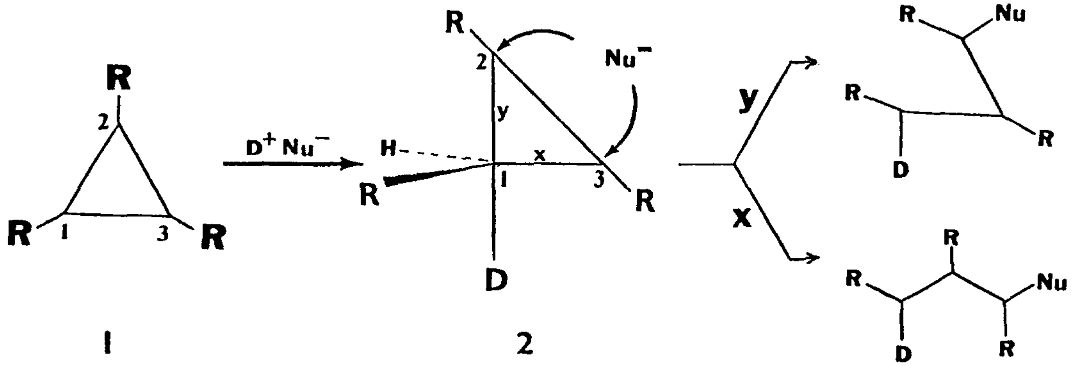
In a series of penetrating experiments, DePuy et al recently elucidated the intrinsic stereochemistry of proton cleavage of alkylated cyclopropanes, free of steric complications.[2] For rupture between two tertiary carbons (1) they found for acetic acid, methylene chloride, and trifluoroacetic acid solvents, a retention:inversion preference of ca. 2:1 for attack by the electrophile (D^+) and almost exclusive inversion (>90-95%) for attack by the nucleophile ($OAc^{\ominus}$, $Br^{\ominus}$, $CF_3CO_2^{\ominus}$).[3] DePuy proposed[2] an unsymmetrical, corner-protonated cyclopropane intermediate and likened it to a trigonal bipyramid (2), in which the two cyclopropyl bonds "x" and "y" formally occupy radial[4] and apical positions, respectively. (For clarity the trigonal bipyramid portrayed in 2 is idealized, with 120° angles between radial bonds, and with apical bonds orthogonal to them.) For D^+ attack at C-1 cleavage of bond "x" leads to retention at C-1, and cleavage of bond "y" gives inversion at C-1. This intermediate has appeal because it can relate the slightly different ease of cleavage of "x" and "y" to their different geometric character in the trigonal bipyramid.

An important unanswered question is whether this 2:1 stereoselectivity for D^+ attack depends upon collapse of the trigonal bipyramid by an S_N2-like inversion by nucleophile ($Nu^{\ominus}$) or whether it also holds for an ionic S_N1-like severance of a ring bond in this intermediate. Alkylated cyclopropanes cannot easily clarify this issue because it is difficult to ensure that cleavage of a ring-bond in the intermediate produces a discrete cation prior to nucleophilic attack. In this regard a study of alkoxy-substituted cyclopropanes, and in particular 1-methoxynortricyclane (4), should be informative because ring-opening in polar media would



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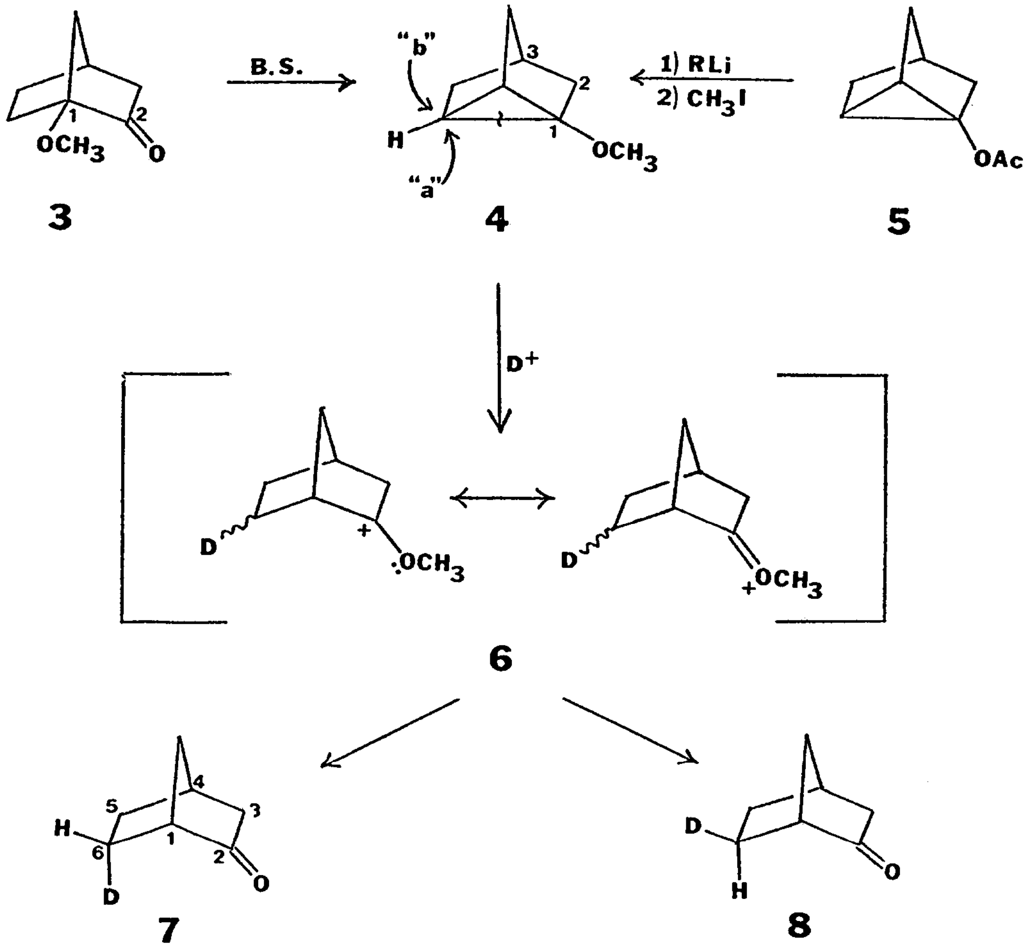
produce an exceptionally well-stabilized cation, whose ultimate fate could not influence the initial D^+ attack. Therefore stereochemistry of D^+ attack would not be linked to later events at the nucleofugal carbon.

We synthesized 1-methoxynortricyclane (4)[5] by an aprotic Bamford-Stevens (carbene insertion) reaction[6] on 1-methoxynorbornan-2-one (3)[7] and also by methylation (CH_3I) of the homoenolate ion liberated from 1-acetoxynortricyclane (5)[8] by treatment with CH_3Li or nBuLi.

In an unsymmetrical cyclopropyl compound like 4 the retention and inversion paths correspond to attack by D^+ on a nonmethoxylated carbon from directions "a" and "b", respectively. Slight steric differences in these two paths due to hindrance by OCH_3 should be unimportant because even larger steric differences have been shown not to play a major role in other cyclopropyl cleavages.[2] Cleavage of 4 by D^+ produces initially the strongly stabilized cation 6, which ultimately leads to 6-d-norbornan-2-one on aqueous work-up. The retention path ("a") produces the 6-endo-d-ketone 7 and the inversion path ("b") gives 6-exo-d-ketone 8, whose relative amounts were determined by ir comparison with known authentic mixtures.[8,9]



Seven deuterated solvent systems were examined; and sulfuric acid-d_2 was used to catalyze the ring opening in all runs except those in formic and trifluoroacetic acids (runs 8-14). Table I summarizes the results.

TABLE I. Stereospecificity in Acid-Induced Ring Cleavage of 1-Methoxynortricyclane[a]

Run	Temp. ±3°	Solvent (approx. vol. ratio)	Conc. Molal		d-Assay[b] rel. %±1		Stereochemistry[b]	
			D_2SO_4	Substrate	d_0	d_1	% Inv.	% Ret.
1	27	CH_3OD	1.22	0.37	7	93	12.5	87.5
2	27	CH_3CO_2D-D_2O (1:1)	0.72	0.25	4	96	14	86
3	27	Dioxane-D_2O (2:1)	0.88	0.18	8	92	14	86
4	27	CH_3CO_2D	0.17	0.37	16	84	30	70
5	27	CH_3CO_2D	0.49	0.39	14	86	30	70
6	27	CH_3CO_2D	1.5	0.43	10	90	33	67
7	27	CH_3CO_2D	2.4	0.47	11	89	34	66
8	27	CF_3CO_2D	—	0.35	9	91	30	70
9	27	DCO_2D-D_2O (10:1)	—	0.39	3	97	25	75
10	33	DCO_2D-D_2O (10:1)	—	0.31	5	95	25	75
11	50	DCO_2D-D_2O (10:1)	—	0.57	4	96	30	70
12	27	DCO_2D	—	0.40	4	96	37	63
13	27-36	DCO_2D	—	0.53	13	87	35	65
14	50	DCO_2D	—	0.76	5	95	36	64

[a] All measured values are averages for two (or more) runs that agreed closely.

[b] Reproducibility ±1% for the repeated runs, but the infrared assay is probably not better than ±2%. Enolic deuterium was washed out before assay.[9]

Retention of configuration (i.e. Semi-U path[10]) was favored in all cases, which included three of the same solvents (methanol, acetic and trifluoroacetic acids) used by DePuy[2] in his study of alkylated cyclopropanes. Our results establish that cyclopropane opening that produces a cation prior to nucleophilic capture has about the same preference for retention in the D^+ attack (63-87.5%) as DePuy[2] *et al* found for simple alkylated cyclopropanes and as Hammons *et al* found (62%) for the hydrocarbon analog, 1-methylnortricyclane.[11] Furthermore, variation within this range can be brought about by solvent changes alone. Significantly, "inversion" (i.e. Semi-W path[10]) did not predominate in any of our openings of **4**, and this behavior contrasts sharply with the high inversion reported by others for cleavage of methoxycyclopropanes in more complex systems.[12] Their suggested rationale for inversion is therefore either not valid or, at least, not general.

Comparison of Table I with published results on homoketonization of 1-acetoxynortricyclane (**5**)[8] reveals a major difference in the behavior of **4** and **5** despite their structural similarity. Whereas in 1-methoxynortricyclane (**4**) the omission of water from the acetic or formic acids reduces slightly the preference for retention (*cf.* runs 4-7 with run 2; and compare runs 12-14 with runs 9-11) similar water omission from these solvents for 1-acetoxynortricyclane (**5**) dramatically *reverses* the stereochemistry from high retention (*ca.* 93%) to high inversion (94%).[8]

If our ring openings of **4** can be viewed as the microscopic reverse of γ-proton loss from alkoxycations to form three-membered rings,[13] then our results also show that *for the norbornyl system* the Semi-U is favored over the Semi-W geometry for such stepwise 1,3-eliminations.[10] Our findings are not subject to the usual classical *vs* nonclassical ambiguity[3b,13c,d,14] because methoxy-stabilized cations in the norbornyl systems are known to eschew carbon-bridging.[7]

REFERENCES AND FOOTNOTES

1. (a) Supported by the Petroleum Research Fund (administered by the American Chemical Society), the National Science Foundation (GP11919X), and the National Institutes of Health (GM06304); (b) Taken in part from the Ph.D. dissertation of J. J. F., The Johns Hopkins University, 1971.
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