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RING ENLARGEMENT—III

PINACOLIC DEAMINATION OF *CIS*-8-METHYL-1-EXO-AMINOMETHYL-HYDRINDAN-1-OL*

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Abstract—The pinacolic deamination of III yields *cis*-9-methyl-decal-1-one (IV) and *cis*-9-methyl-decal-2-one (V) in the ratio 97:3. The preponderance of IV is interpreted in terms of a chair transition state controlled reaction.

THE Schmidt reaction with *cis*-8-methyl-1-hydrindan-1-one showed[1] that the relative proportion of the products could be accounted for in terms of simultaneous action according to two possible mechanisms.[2]

These two parallel reactions, each with its distinct mechanism and stereospecificity, produce ring enlargment in different directions. The possibility of an alternative reaction mechanism allows the more substituted carbon atom to migrate without passing through an unfavourable steric transition state (boat).

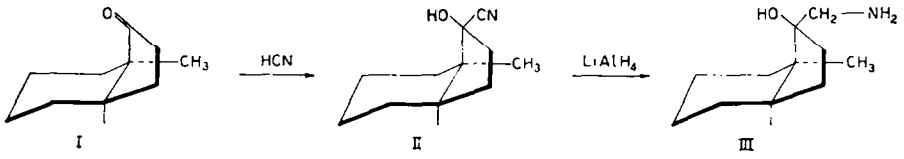
Consequently, the distribution of enlargement products for the same substrate in reactions without such a double mechanism in the expansion step were investigated.

A number of such ring enlargement reactions are known, for example the Baeyer-Villiger reaction, the homologation of cycloalkanones with diazomethane, the pinacolic deamination, the acidic transposition of cyclo-alkylazides, etc.

Some of these reactions using the same *cis*-8-methylhydrindanic system were investigated with the aim of obtaining a better understanding of the electronic and steric factors governing ring enlargement reactions.

In this paper the results of the pinacolic deamination of cis-8-*methyl*-1-exo-*aminomethylhydrindan*-1-*ol*[3] (III) is described.

Compound III was obtained from *cis*-8-methylhydrindan-1-one (I) via the *cyanohydrine* (II) which was reduced to the aminoalcohol (III) with LAH.



I II III

In accordance with the strong hindrance that a reactant experiences in approaching

* We thank the National Research Council for support.

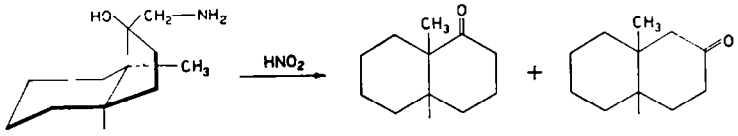
[1] G. Di Maio and V. Permutti, *Tetrahedron* **22**, 2053 (1966).

[2] P. de Mayo, *Molecular Rearrangements* p. 507. Interscience, New York (1963).

[3] Previously we attempted the homologation of *cis*-8-methylhydrindan-1-one with diazomethane and BF_3, but were unable to bring about any reaction.

the concave side of the molecule,[4] and bearing in mind the known conformation of the methyl group in 8-methylhydrindanic systems,[5] conformations II and III were assigned to the cyanohydrine and the aminoalcohol with the —CN and —CH_2NH_2 groups in the *exo* position and the methyl group in the equatorial position.

The aminoalcohol (III) on being subjected to the action of nitrous acid in acetic acid at 0°, yielded a mixture of *cis*-9-methyldecal-1-one (IV) and *cis*-9-methyldecal-2-one (V) in the ratio ~97:3 in almost theoretical yield.[6]

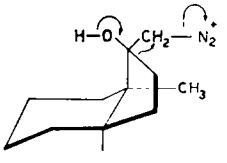


III IV V

The *cis*-9-methyldecal-1-one was identical by direct comparison of its semicarbazone with an authenitc specimen of the compound.[7]

The *cis*-9-methyldecal-2-one was not isolated but was identified in the reaction mixture by gas-chromatography by the enrichment technique, using an authentic specimen.[8]

The reaction proceeds by migration of the less substituted carbon atom and this can be explained by assuming that steric effects predominate[9] and favour a chair transition state (VI).[10]



VI

The almost exclusive production of α-decalone (IV) may be considered as a measure of the preponderance of the equatorial conformation for the angular methyl in hydrindanic systems.

[4] For other examples, see R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey and R. W. Kierstead, *Tetrahedron* **2**, 1 (1958).

[5] C. Djerassi, D. Marshall and T. Nakanà, *J. Amer. Chem. Soc.* **80**, 4853 (1958).

[6] GLC shows three peaks in addition to those corresponding to IV and V with areas amounting to 2% of the total area.

[7] W. S. Johnson, *J. Amer. Chem. Soc.* **65**, 1317 (1943).

[8] A. J. Birch and R. Robinson, *J. Chem. Soc.* 501 (1943).

[9] M. F. Murray, B. A. Johnson, R. L. Pederson and A. C. Ott, *J. Amer. Chem. Soc.* **78**, 981 (1956).

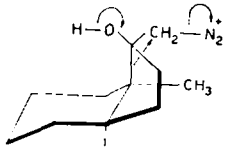
[10] M. Amorosa, L. Caglioti, G. Cainelli, H. Himmer, J. Keller, W. Wehrly, M. L. Milovic, K. Schaffer, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **45**, 2674 (1962) postulate that the 13-α-methyl-17-β-sterols, unlike their related 17-keto compounds, have the *C* ring in a boat conformation owing to the over-crowding that the hydroxyl causes on the concave side of the molecule.

Although this possibility also exists for both the aminoalcohol (III) and the cyanohydrine (II), this does not invalidate the hypothesis that the direction of ring enlargement derives from steric control of the boat-chair kind.

This is apparent on inspection of molecular models, for the angular methyl is oriented less axially than in a pure boat ring. Thus the 1,4-interaction in the six membered ring and the eclipsing of the methyl with the amino-methyl group are reduced allowing the five membered ring to attain an envelope conformation.

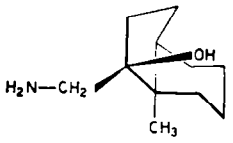
The origin of IV may be explained in one of two ways:

(1) It is formed by migration of methylated carbon in spite of a boat transition state VII

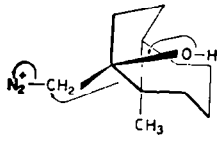


VII

(2) A portion (~3%) of the aminoalcohol subjected to reaction exists in the alternative *cis*-conformation (VIII) and on pinacolic deamination yields the β-decalone (V) through migration of methylated carbon (IX) which in this case is favoured also by boatchair steric as well as electronic effects.



VIII



IX

EXPERIMENTAL

cis-8-*Methylhydrindan*-1-*one cyanohydrine* (II). Anhydrous HCN (from 3 g KCN and 3 ml 50% H_2SO_4) was added to 1·23 g I at −15° with stirring. The mixture was stirred for 1 hr and allowed to stand overnight at − 15°. The excess of HCN was removed under red. press. at room temp and the residue extracted with a small amount of ether and the ethereal solution washed 3 times with a few ml water (acidified by adding a little H_2SO_4) and then with distilled water.

The ethereal solution was dried over Na_2SO_4 and evaporated to dryness. The residue (1·22 g) showed IR absorption bands due to —CN at 2242 cm^{-1} and to hydroxyl at 3330 cm^{-1}. The CO absorption band of unreacted ketone was also present.

It was not possible to purify this mixture, because every attempt to distill it gave the initial ketone. It was therefore used crude in the next step.

cis-8-*Methyl*-1-exo-*aminomethylhydrindan*-1-*ol* (III). The crude product was dissolved in 2·5 ml anhydrous ether and added (1 hr) to a suspension of 0·510 g LAH in 12 ml ether, with stirring and external cooling with ice.

The mixture was stirred at room temp for 20 hr, 4 ml water and 1·5 ml 20% NaOH aq were then added. After filtration, the solid residue was washed with ether. The ethereal solution was separated into neutral (545 mg) and basic (231 mg) fractions. The latter was a solid which after several sublimations at 70–75°/0·05 mm Hg gave m.p. 119–121°. The IR spectrum shows bands characteristic of hydroxyl (3330 cm^{-1}) and of —NH_2 (1603 cm^{-1}). (Found: C, 72·19; H, 11·63; N, 7·74. $C_{11}H_{21}NO$ requires: C, 72·08; H, 11·55; N, 7·64%.)

Pinacolic deamination of cis-8-*methyl*-1-*exo-aminomethylhydrindan*-1-*ol*. A cold solution of 280 mg $NaNO_2$ in 2·2 ml water was added (40 min) to an ice cold solution of 318 mg III in 0·5 ml of AcOH and 2·2 cc water.

The mixture was stirred for 1 hr, and after standing 15 hr at room temp, water was added and the solution extracted with ether. The extract was washed with 2N NaOH and then with water, dried over Na_2SO_4 and evaporated yielding a residue of 286 mg.

This residue was shown by GLC[11] to contain 5 products, two of which were identified as *cis*-9-methyldecal-1-one and *cis*-9-methyldecal-2-one (3 and 95% respectively of the total areas of the chromatogram).

The latter was isolated as its semicarbazone and identified by comparison (IR and mixed m.p.) with an authentic specimen.[8] (Found: C, 64·36; H, 9·54; N, 19·61. Calc. for $C_{12}H_{21}N_3O$: C, 64·54; H, 9·48; N, 18·82%.)

[11] With a Perkin–Elmer apparatus, with two different stationary phases: F.S. 1265; R (Polypropylene glycol).