Proximity Effects.[1] The Stereochemistry of the Lithium-Ammonia Reduction of Cyclic Styrenoid Systems containing a Neighbouring Carboxylic Acid Group

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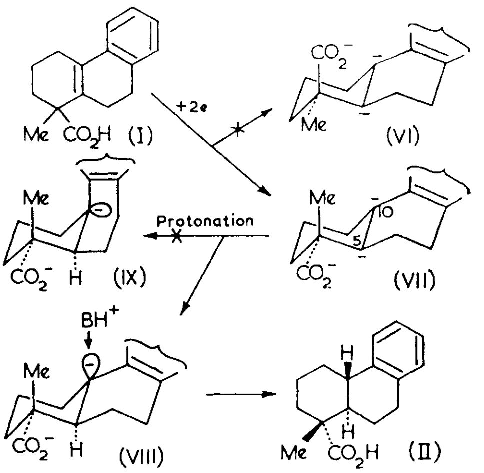
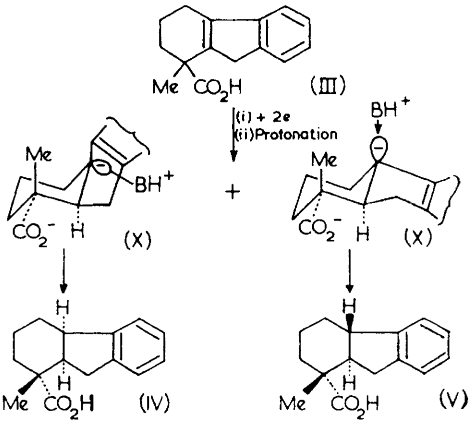
ALKALI METAL–AMMONIA reduction of cyclic styrenoid systems has been widely used in steroid syntheses.[2] In most cases[3] such reduction results in the most stable of the possible stereoisomers. To rationalise these stereochemical results, Smith[4] recently advanced an important mechanistic postulation, based on the considerations of conformational and steric approach factors controlling the protonation of the intermediate dianions and monoanions resulting from styrenoid systems by the addition of electrons from the metal[5] and stepwise additions of proton from ammonia.

Recently[6] we reported that the reduction of the styrenoid bond of the unsaturated acid (I) with an excess of lithium in liquid ammonia in the presence of ammonium chloride followed a remarkable stereospecific path, and afforded a single stereoisomeric acid (II),[7] in excellent yield. We have now observed that under similar reduction condition the unsaturated acid (III)[6] gave the saturated acids (IV),[8] m.p. 187—188°; λ_{max}(EtOH) 261 (log ϵ 3·007), 266 (log ϵ 3·05), and 273 mμ (log ϵ 3·014); and (V), m.p. 202—203°; λ_{max} (EtOH) 260 (log ϵ 2·95), 266 (log ϵ 3·07), and 273 mμ (log ϵ 3·05); in 53% and 23% yields respectively after separation through fractional crystallisation. The mechanistic implication of these results not only are nicely accommodated by consideration of the intermediate stages involved in the styrenoid bond reduction, following arguments similar to those of Smith,[4] but also explain the unique stereochemical control of a neighbouring asymmetric centre containing an anionic group. Accordingly, of the possible dianions (VI) and (VII), (carboxyl group evidently converted into carboxylate anion),





resulting from the addition of two electrons[4] to the styrenoid bond in the acid (I), the dianion (VI), having the axial carboxylate ion practically overlapping the anionic centre at C-10, is energetically unfavoured and thus can be reasonably excluded from further consideration. The protonation at the more basic homobenzylic position at C-5 in the dianion (VII) may give rise to two possible monoanions (VIII) and (IX). The entire product in this reduction in fact appears to originate from protonation at C-10 in the monoanion (VIII), favoured by conformational factors over the anion (IX). Similarly, the stereochemical course in the reduction[9] of (III) may be rationalised by considering the intermediate monoanions (X) and (XI). In this case *cis*-acid (IV) represents the major product of the reduction, arising from the anion (X), which is favoured both by conformational[10] and steric approach factors, over the anion (XI), giving rise to the *trans*-acid (V) through the final protonation step.

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[1] Previous Communication: U. R. Ghatak and J. Charkavarty, *Chem. Comm.*, 1966, 184.

[2] For an excellent critical Review, see H. Smith, "Organic Reactions in Liquid Ammonia", Interscience, 1963, pp. 226—230 and 307—308.

[3] For an exception, see W. S. Johnson, J. Ackerman, J. F. Eastham, and H. A. De Walt, *J. Amer. Chem. Soc.*, 1956, **78**, 6303; W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *ibid.*, 1960, **82**, 614.

[4] H. Smith, ref. 2, pp. 228—229. See also G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, 1964, **86**, 1761, and H. Zimmerman, *Tetrahedron*, 1961, **16**, 169.

[5] W. Nagata, T. Terasawa, S. Hirai, and H. Takeda, *Chem. and Pharm. Bull.* (*Japan*), 1961, **9**, 709; A. J. Birch, *Quart. Rev.*, 1950, **4**, 69.

[6] U. R. Ghatak, A. K. Banerjee, N. R. Chatterjee, and J. Chakravarty, *Tetrahedron Letters*, 1967, 247.

[7] Although only one enantiomer is illustrated, the compounds described are racemates.

[8] This and the remaining two epimeric acids have been synthesised through stereospecific routes: U. R. Ghatak, J. Chakravarty, and R. Das Gupta, unpublished results.

[9] *Cf.* J. Fried and N. A. Abraham, *Tetrahedron Letters*, 1965, 3505; R. J. Adamski and J. G. Cannon, *J. Org. Chem.*, **1964**, **29**, 3693.

[10] U. R. Ghatak, J. Chakravarty, and A. K. Banerjee, *Tetrahedron Letters*, 1965, 3145, and references cited therein.