The Synthesis of Cyclohexane Derivatives

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One possible way to build up the skeleton of a diterpenoid such as enmein[1] and its degradation products seems to be the Michael condensation of two appropriate cyclohexane derivatives. In this respect, the synthesis of three new cyclohexane derivatives, I, II and III, was attempted.

Dihydroresorcinol was converted, by the use of isobutanol and *p*-toluenesulfonic acid, into its isobutyl enol ether (IV)[2] (89% yield; bp 101—103°C/3 mmHg. Found: C, 71.11; H, 9.56%. Calcd for $C_{10}H_{16}O_2$; C, 71.39; H, 9.59%.), which, by Reformatsky reaction with zinc and ethyl α-bromopropionate at 120°C, yielded 50% of V (bp 99—101°C/3 mmHg. Found: C, 69.50; H, 9.42%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%.).

The hydrolysis of V with hydrochloric acid gave conjugate enone (a singlet vinyl proton at 4.16 τ in the NMR spectrum) (VI), 3-α-carbethoxyethylcyclohexene-2-one-1 (bp 123—127°C/4 mmHg. Found: C, 66.99; H, 8.40%. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22%; 2, 4-dinitrophenylhydrazone,[3] mp 121°C. Found: C, 54.25; H, 5.27; N, 14.72%. Calcd for $C_{17}H_{20}O_6N_4$: C, 54.25; H, 5.36; N, 14.89%.), which was hydrogenated over 5% palladised charcoal to give a saturated ketone (VII) (82.5% yield; bp 111—112°C/3.5 mmHg. Found; C, 68.48; H, 9.51%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%; semicarbazone (separated in 5 days at room temperature; mp 148°C. Found: C, 56.61; H, 8.42; N, 16.57%. Calcd for $C_{12}H_{21}O_3N_3$: C, 56.45; H, 8.29; N, 16.46%.).

Cyanohydrin (VIII) prepared by the reaction of the saturated ketone with hydrogen cyanide was dehydrated directly by treatment with thionyl chloride in a pyridine solution at room temperature overnight; a product (44.5% yield; bp 126.5—128.5°/3 mmHg. Found: C, 69.31, H, 8.31; N, 6.67%. Calcd for $C_{12}H_{17}O_2N$: C, 69.54; H, 8.27, N, 6.76%. $\nu_{C\equiv N}$ 2230 cm^{-1} in the IR spectrum[4]) was thus obtained, but it was difficult to separate it into fractions A and B (Fig. 2) by vapor-phase chromatography.

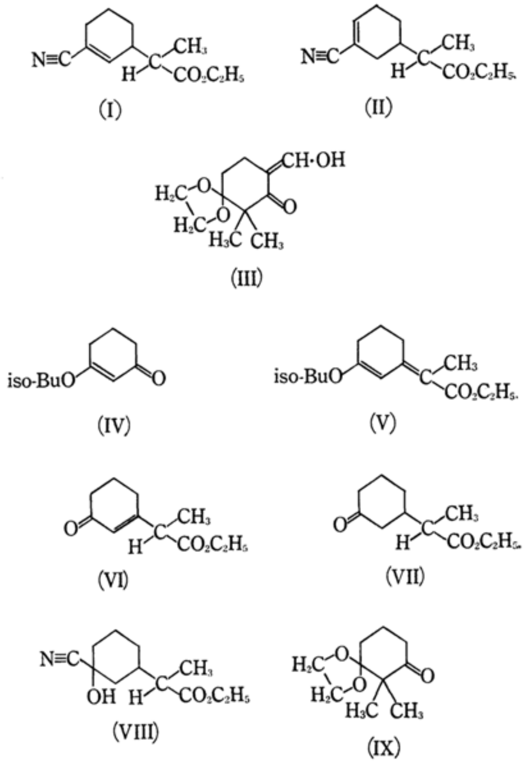

Fig. 1

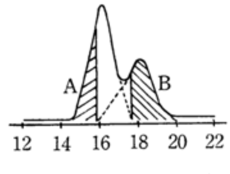

Fig. 2. V.p.c. separation of I and II.[6] (Column: Silicon DC 710; 227°C, N_2 gas)

A (doublet vinyl proton at 3.60 τ in the NMR spectrum) substantiated 1-cyano-3-α-carbethoxyethylcyclohexene (I) and B (tripletlike vinyl proton at 3.50 τ in the NMR spectrum)[5] sub-

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[1] T. Kubota, T. Matsuura, T. Tsutsui, T. Ikeda, M. Tomoeda, S. Kanetomo, S. Ueo, M. Takahashi, H. Irie, A. Numata, T. Fujita, T. Kosuga, S. Adachi, T. Okamoto, M. Natsume, Y. Kawazoe and K. Shuto, Abstracts of VIIth Symposium on Natural Organic Compounds, Kyushu University, p. 207 (1963).

[2] E. Eschenmoser, J. Schreiber and S. A. Julia, *Helv. Chim. Acta,* **36,** 482 (1953).

[3] Derivatives were prepared according to E. Funakubo, "Identification of Organic Compounds" (in Japanese), Yokendo, Tokyo (1944).

[4] L. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, New York (1954), p. 223.

[5] NMR spectra catalog, Vol. I, 15, Varian Associates, California.

[6] The author is grateful to Professor T. Matsuda, Mr. K. Sakai, Mr. M. Shito, and Miss. S. Tahara (Kyushu Univ.) for NMR and IR spectra, microanalysis and v.p.c. separation.

stantiated 1-cyano-5-α-carbethoxyethylcyclohexene (II).

Dimethyldihydroresorcinol⁷⁾ was converted into ethyleneketal (IX) (bp 100—104°C/4 mmHg); this, when treated with ethyl formate and sodium methoxide in a benzene solution overnight, yielded 2, 2-dimethyl-4-hydroxymethylenecyclohexane-dione-1, 3-monoethyleneketal (III) (24% yield; bp 106—110.5°C/4 mmHg. Found: C, 61.71; H, 8.70%. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60%; semicarbazone, mp 225°C, Found: C, 53.52; H 7.03; N, 15.76%. Calcd for $C_{12}H_{19}O_4N_3$: C, 53.52, H, 7.11; N, 15.60%.).

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7) S. Eskola, A. Aurinen, A. Hirvimies, T. Rinnv and R. Waris., *Chem. Abstr.*, **50**, 5558i (1956); I. Nazaroe, S. Zav'yalov, M. Burmistrova, I. Gurvich and L. Schmonina, *Chem. Abstr.*, **50**, 13847c (1956).