pyridine was treated at 0° with 9 g. (130 mmoles) of vinyl isocyanate dissolved in 100 ml. of acetonitrile. The mixture was stirred and allowed to warm to room temperature slowly. After 18 hr., the mixture was concentrated under reduced pressure and the residue was dissolved in warm ethanol. Activated carbon was added and the mixture was filtered. Addition of water to the filtrate afforded an oil which slowly crystallized. After two further crystallizations from ethanol-water, using carbon for decolorization, pure material was obtained; yield 6.4 g. (61%), m.p. 136–137°, $[\alpha]_D^{28}$ +61.6° (*c*, 4.44, acetonitrile).

*Anal.* Calcd. for $C_9H_{12}N_6O_{17}$: C, 22.70; H, 2.54; N, 17.65. Found: C, 22.71; H, 2.61; N, 17.73.

DEPARTMENT OF CHEMISTRY
THE OHIO STATE UNIVERSITY
COLUMBUS 10, OHIO

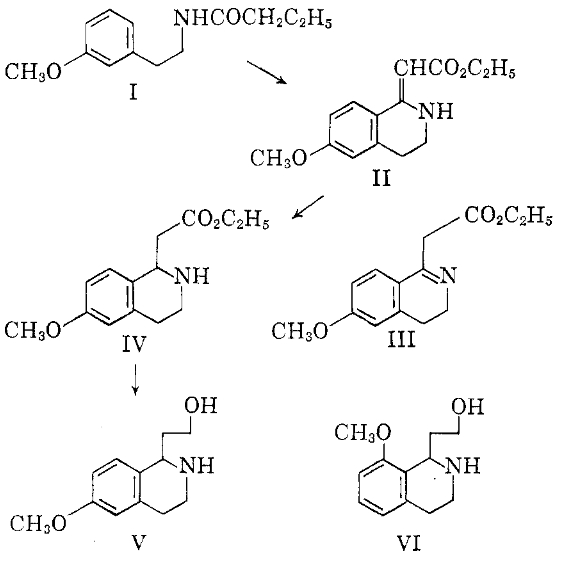
---

## 1-(β-Hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline[1]

N. A. NELSON,[2] K. O. GELOTTE, Y. TAMURA, H. B. SINCLAIR, J. M. SCHUCK, V. J. BAUER, AND R. W. WHITE

*Received November 29, 1960*

In work directed at the total synthesis of azasteroids, we had occasion to prepare 1-(β-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline (V), a substance possessing the A and B rings of an azasteroid nucleus. This note gives the details for the preparation of V and describes spectroscopic data which were used to distinguish alternative structures for the compounds produced.



Treatment of ethyl *N*-*m*-methoxyphenethylmalonamate (I) with phosphorus pentoxide in refluxing toluene[3] gave a noncrystalline red-colored product which resisted purification.[4] The infrared spectrum of the product is not consistent with structure III, which is the usual structure written for the product of a Bischler-Napieralski reaction.[3-6] For example, the spectrum exhibits an absorption band at 3320 cm.$^{-1}$ (presumably N—H stretching)[7] and no appreciable absorption in the range 1660–1800 cm.$^{-1}$ (indicating the absence of a normal ester carbonyl group). Structure II fits the spectral data and is also consistent with the known tendency of a β-imino-carbonyl compound (such as III) to exist in the tautomeric β-amino-α,β-unsaturated carbonyl system.[8]

Hydrogenation of the crude 1-carbethoxymethylene-6-methoxy-1,2,3,4-tetrahydroisoquinoline (II)[3] in acetic acid using Adams catalyst resulted in the absorption of one molecular equivalent of hydrogen and gave ethyl 6-methoxy-1,2,3,4-tetrahydro-1-isoquinolylacetate (IV). This material could be purified by distillation under highly reduced pressure, but ordinarily it was sufficiently pure to be used directly in the next step. Reduction of IV with lithium aluminum hydride yielded the crystalline 1-(β-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline (V). The ultraviolet spectrum of V is very similar to that of 6-methoxy-1,2,3,4-tetrahydroisoquinoline,[9] thus demonstrating the point of ring closure in the cyclization of the malonamate I. This result is in accord with the generally accepted fact that the Bischler-Napieralski reaction of *N*-*m*-methoxyphenethylamides results in cyclization at the position *para* to the methoxyl group.[6]

---

[1] This investigation was supported in part by research grants, CY-2999 (C1-C3), from the National Cancer Institute, Public Health Service.

[2] Research Laboratories of the Upjohn Company, Kalamazoo, Mich.

(3) Using the procedure of A. R. Battersby, H. T. Openshaw, and H. C. S. Wood, *J. Chem. Soc.*, 2463 (1953).

(4) *Cf.* A. Brossi, H. Lindlar, M. Walter, and O. Schnider, *Helv. Chim. Acta*, **41**, 119 (1958).

(5) J. M. Osbond, *J. Chem. Soc.*, 3464 (1951).

(6) W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **VI**, 74 (1951). These authors also list some examples of products in which the newly created double bond is exocyclic.

(7) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace [*J. Am. Chem. Soc.*, **71**, 3337 (1949)], have described several *N*-alkyl-β-amino-α,β-unsaturated ketones in which no N—H stretching band was observed in the region of 3300 cm.$^{-1}$ They concluded that this absorption band was probably broadened and shifted to lower frequencies due to strong chelation and was thereby obscured by the C—H absorption bands. In our case this absorption band may be due to a weaker chelated N—H stretching, or the N—H stretching of the *trans* isomer of II. Since the position of absorption does not shift appreciably in going to very dilute solutions (0.01*M*), the former assignment is preferred. Finally, since the product is not crystalline, the possibility that this absorption band is caused by an impurity cannot be excluded.

(8) S. A. Glickman and A. C. Cope, *J. Am. Chem. Soc.*, **67**, 1017 (1945).

(9) Prepared as described by W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **VI**, 172 (1951). The sample had the following physical constants: b.p. 144° (9 mm.); $\lambda_{max}^{C_2H_5OH}$ 221.5 (ε 7200), 278.5 (ε 2010), and 287 mμ (ε 1800) with minima at 246 and 285 mμ.

In one experiment an effort was made to isolate the other possible amino alcohol VI which would be derived from a cyclization product in which ring closure occurred *ortho* to the methoxyl group. The residue remaining after isolation of the major product V was purified by distillation and chromatography. A forerun obtained in the distillation step appears to be 6-methoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline on the basis of spectral evidence and analytical data of its picrate derivative. Such a product could arise through loss of the ester function of I or II by hydrolysis and decarboxylation. Chromatographic purification of the high boiling fraction from the distillation yielded the isomeric 1-($\beta$-hydroxyethyl)-8-methoxy-1,2,3,4-tetrahydroisoquinoline (VI). The ultraviolet spectrum of VI, being quite similar to that of 5-methoxy-1,2,3,4-tetrahydronaphthalene[10] and related systems,[11] confirms the structural assignment.

## EXPERIMENTAL[12]

*1-($\beta$-Hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline* (V). To a boiling solution of 30 g. of crude ethyl *N-m*-methoxyphenethylmalonamate[13] in 450 ml. of toluene was added three 30-g. portions of phosphorus pentoxide at 10- to 15-min. intervals. The solid cake which formed was periodically broken up by means of a stirring rod. After heating the mixture at reflux for a total of 1 hr., it was cooled in an ice bath and 750 g. of ice and water was added in one portion with stirring. As soon as the red mass had dissolved, the mixture was filtered through a pad of 545 Celite. The layers of the filtrate were separated and the organic layer was extracted with dilute hydrochloric acid (work-up of the organic layer yielded 2.6 g. of unchanged starting material). All aqueous portions were combined without delay and washed with ether, cooled to 0°, and made basic with either solid potassium carbonate or 50% potassium hydroxide solution. The basic solution was extracted with ether and the ether extract dried and concentrated *in vacuo* giving 22.2 g. (79%) of crude II; $\nu_{\max}^{\mathrm{CCl_4}}$ 3320 (m, N—H), 1640 (s), 1630(s), 1605(s) and 1570 (s) cm.$^{-1}$ associated with the vibrational modes of the vinylogous urethan and aromatic systems (there is no absorption band in the range of 1660–1800 cm.$^{-1}$); $\nu_{\max}^{\mathrm{CCl_4}}$ (0.01 *M*, 1-cm. cell) 3320 (m, intramolecular hydrogen bonded N—H) cm.$^{-1}$ In another run this material decomposed when an attempt was made to purify it by distillation at 0.001 mm.

A mixture of 22.2 g. of crude II in 175 ml. of glacial acetic acid was hydrogenated at 1–2 atm. pressure in the presence of 300 mg. of Adams catalyst. The hydrogen uptake ceased in about 40 min. when 1 molecular equivalent of hydrogen had been absorbed. Work-up of the reaction mixture[3] gave 21.2 g. of crude ethyl 6-methoxy-1,2,3,4-tetrahydro-1-isoquinolylacetate which was sufficiently pure to be used directly in the next step (see below).

In an earlier run, the crude product (17.9 g.) was purified by distillation giving 14.2 g. of IV as a colorless viscous oil, b.p. 98–103° (0.004 mm.), $n_{\mathrm{D}}^{25}$ 1.5362, $\nu_{\max}^{\mathrm{CCl_4}}$ 3350 (w, N—H) and 1735 (s, ester C=O) cm.$^{-1}$ [lit.[4] b.p. 132° (0.02 mm.)].

*Ethyl 6-methoxy-1,2,3,4-tetrahydro-1-isoquinolylacetate picrate* was prepared by heating equivalent amounts of the amino ester and picric acid for 5 min. at 115°. Addition of 95% ethanol gave 91% of the picrate, m.p. 164–166°, raised to 167.5–168° after several recrystallizations from ethanol.

*Anal.* Calcd. for $C_{20}H_{22}N_4O_{10}$: C, 50.21; H, 4.64; N, 11.71. Found: C, 50.39; H, 4.65; N, 11.50.

To a stirred solution of 4.0 g. of lithium aluminum hydride in 250 ml. of ether was added dropwise a solution of 10.0 g. of crude ethyl 6-methoxy-1,2,3,4-tetrahydro-1-isoquinolylacetate in 25 ml. of anhydrous tetrahydrofuran. The mixture was refluxed for 1 hr., then cooled in an ice bath. With vigorous stirring of the mixture there was added dropwise successively 4.0 ml. of water, 4.0 ml. of 15% sodium hydroxide solution, 12 ml. of water, and after 1 hr. a small amount of 545 Celite. The solid material was separated by filtration and washed with ether. The filtrate and washings were combined and concentrated *in vacuo* giving a red oil which was purified by chromatography on Florisil using benzene as the eluent. Fractions containing product were combined and recrystallized from cyclohexane giving 5.3 g. of 1-($\beta$-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline, m.p. 85–86°, $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 221 ($\epsilon$ 7850), 278 ($\epsilon$ 1970) and 286 m$\mu$ ($\epsilon$ 1860) with minima at 217, 247, and 283.5 m$\mu$, $\nu_{\max}^{\mathrm{CHCl_3}}$ 3300 (s, N—H and O—H) and 1605 (s), 1580 (m) and 1500 (s, aromatic C=C). The analytical sample melted at 87–88°.

*Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.42; H, 8.42; N, 7.07.

*1-($\beta$-Hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline picrate* was obtained in the usual way and recrystallized from ethanol, m.p. 143–144°.

*Anal.* Calcd. for $C_{18}H_{20}N_4O_9$: C, 49.54; H, 4.62; N, 12.84. Found: C, 49.55; H, 4.38; N, 12.67.

*1-($\beta$-Hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline hydrobromide*, obtained by passing hydrogen bromide into an ethereal solution of the amine, was recrystallized from ethanol-ether, m.p. 170–171°.

*Anal.* Calcd. for $C_{12}H_{18}BrNO_2$: C, 50.01; H, 6.29; N, 4.86. Found: C, 50.25; H, 6.11; N, 4.52.

In a different run involving the reduction of 28.5 g. of crude ethyl 6-methoxy-1,2,3,4-tetrahydro-1-isoquinolylacetate(IV) the product was isolated without resort to chromatography by direct crystallization of it from ether giving 11.0 g. of 1-($\beta$-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline, m.p. 86–87.5°, and 1.25 g. with m.p. 84–85.5°. The filtrates from the crystallizations were combined and distilled giving two main fractions. The material from the first fraction amounted to 3.7 g. (12%) and had b.p. 92–105° (0.45 mm.), $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 220($\epsilon$ 7950), 277 ($\epsilon$ 2540), and 286 mu ($\epsilon$ 2180) with minima at 217, 246, and 283.5 m$\mu$. The infrared spectrum of this material is very similar to that of 1-($\beta$-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline (V) except for weaker absorption in the former case at 3300, 1060, and 930 cm.$^{-1}$ (implying lack of an alcoholic hydroxyl group) and stronger absorption at 1375 cm.$^{-1}$ (implying the presence of a C-methyl group). The infrared and ultraviolet spectral data are consistent for a 6-methoxy-1,2,3,4-tetrahydroisoquinoline system. It is possible that this side-reaction product is 6-methoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline. This side reaction product was characterized further by conversion to its picrate (crystallized from ethanol), m.p. 187.5–188.5°.

*Anal.* Calcd. for $C_{17}H_{18}N_4O_8$: C, 50.24; H, 4.47; N, 13.79. Found: C, 50.02; H, 4.30; N, 13.55.

The material from the second fraction amounted to 1.8 g. (6%) and had b.p. 167–170° (0.7 mm.), $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 278.5 m$\mu$ ($\epsilon$

---

[10] The sample had the following physical constants: b.p. 118–118.5° (12 mm.); $n_{\mathrm{D}}^{25}$ 1.5455; $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 270.5 ($\epsilon$ 1120) and 278 m$\mu$ ($\epsilon$ 1175) with minima at 244 and 275.5 m$\mu$.

[11] See, for example, W. S. Johnson *et al.*, *J. Am. Chem. Soc.*, **78**, 6289 (1956).

[12] The infrared spectra were determined with a Baird (model B) or Perkin-Elmer (models 21 or 137) spectrophotometer fitted with a sodium chloride prism. In reporting infrared spectra, (s) denotes strong, (m) medium, and (w) weak absorption. Ultraviolet spectra were determined with a Cary recording spectrophotometer (model 11 MS).

[13] Prepared by ammonolysis of diethyl malonate with *m*-methoxyphenethylamine,[3,4] $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 273 ($\epsilon$ 1960), 279.5 ($\epsilon$ 1830) and an inflection at 214 m$\mu$ ($\epsilon$ 9900).

1930) with an inflection at 272 mμ (ε 1670) and a shoulder at 285.5 mμ (ε 1160). The infrared spectrum of the material was similar to that of 1-(β-hydroxyethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinoline, but had a number of additional absorption bands in the finger-print region. One gram of this material was chromatographed on 170 g. of Florisil which had been washed with methanol and air dried briefly to give a free-flowing powder (the Florisil contained about 35% methanol). Elution with benzene gave several fractions amounting to 0.49 g. which had ultraviolet spectra ($\lambda_{\max}$ 271.5 and 278.5 mμ) characteristic of the 8-methoxy isomer VI. Distillation of this material and crystallization of the distillate from hexane gave 0.27 g. of *1-(β-hydroxyethyl)-8-methoxy-1,2,3,4-tetrahydroisoquinoline* (VI), m.p. 96–97°, $\lambda_{\max}^{C_2H_5OH}$ 223 (ε 7200), 271 (ε 1600), and 278.5 mμ (ε 1700) with minima at 246 and 276 mμ.

*Anal.* Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.50; H, 8.19; N, 6.98.

DEPARTMENT OF CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE 39, MASS.

---

## The Decomposition of 11-Cyano-12-tricosanone

C. C. COCHRANE AND H. J. HARWOOD[1]

*Received December 1, 1960*

Early investigations of the properties of low-molecular-weight dinitriles (I; diacetonitrile[2], R = H; dipropionitrile[3], R = $CH_3$) have shown that upon boiling with water these substances slowly decompose with the formation of ammonia, hydrogen cyanide, and a substance which is easily oxidized by ammoniacal copper and silver solutions. It was postulated that the easily oxidizable material was an α-hydroxy ketone (ketol or acyloin) which was formed in the following manner:

$$\underset{\text{I}}{RCH_2C(=NH)CHRCN} \xrightarrow{H_2O} \underset{\text{II}}{RCH_2COCHRCN} \xrightarrow{H_2O} \underset{\text{III}}{RCHCOCHOHR} + HCN$$

In this Laboratory it has been observed that crystallized 11-cyano-12-tricosanone (II. R = $C_{10}H_{21}$) upon standing in air slowly evolves hydrogen cyanide leaving a liquid residue. Analysis of this residue by gas chromatography indicates that it is a mixture of equimolar amounts of undecanoic and dodecanoic acids. In an atmosphere of dry nitrogen the keto nitrile undergoes no change. Presumably moisture and oxygen are required to bring about the decomposition with formation of the mixture of acids although this has not been proved.

If 11-cyano-12-tricosanone were to decompose according to the reaction proposed above it would lead to the formation of 11-hydroxy-12-tricosanone (III. R = $C_{10}H_{21}$) which differs from the acyloin 13-hydroxy-12-tetracosanone (lauroin) by only one carbon atom. So far as we are aware the acyloins derived from higher fatty acids are not susceptible to decomposition upon exposure to the atmosphere. Mild oxidizing agents such as iodine in acetic acid[4] or ferric chloride in acetic acid[5] oxidize these compounds to the diketone. Strong oxidizing agents such as chromic oxide are required to effect cleavage to the fatty acid.[5] We do not believe that the decomposition of the keto nitrile proceeds through the acyloin but do not have a reasonable alternative to offer.

### EXPERIMENTAL

*Dimeric lauronitrile.* To 9.2 g. (0.2 g.-atom) of 50% sodium dispersion in xylene, in 200 ml. of dry ether was added over 0.5 hr., with stirring 45 g. (0.25 mole) of lauronitrile. The ether refluxed gently after a short induction period during the addition. When the exothermic reaction had subsided, the mixture was stirred and refluxed for 24 hr. The supernatant liquid was decanted from residual sodium into a separatory funnel. The sodium was destroyed with methanol and the alcoholic solution was added to the separatory funnel. The organic extracts were washed three times with water, dried over anhydrous sodium sulfate, the solvent removed, and the residue distilled to give 2.1 g. lauronitrile, b.p. 88–89°/0.25 mm.; 22.9 of dinitrile b.p. 220–240°/0.15 mm. and a significant residue. Redistillation of the dinitrile afforded 20.9 g. b.p. 208–212°/0.10 mm.

*11-Cyano-12-tricosanone.* A mixture of 5 g. of dinitrile, 100 ml. of 95% alcohol and 2 ml. of concd. hydrochloric acid was warmed until solution was effected, then chilled overnight in the icebox. The solid was filtered and dried under vacuum in a desiccator, m.p. 46–47°[6] The keto nitrile was stable in an atmosphere of dry nitrogen. Left standing open to the air, an odor of hydrogen cyanide was evolved and the material passed from solid through semisolid to liquid during 1 week. Gas chromatography of the liquid[7] yielded two peaks of equal area, which were identical in position with those of a mixture of undecanoic and dodecanoic acids run under the same conditions. A sample sealed in an atmosphere of dry nitrogen underwent no change during a period of several years.

ARMOUR INDUSTRIAL CHEMICAL CO.
CHICAGO, ILL.

---

(1) Address communications to this author.

(2) R. Holtzwart, *J. prakt. Chem.*, **39**, 230 (1889).

(3) E. von Meyer, *J. prakt. Chem.*, **39**, 188 (1889).

(4) V. L. Hansley, *J. Am. Chem. Soc.*, **57**, 2303 (1935).

(5) F. Bonquet and C. Paquot, *Bull. soc. chim. France*, 1165 (1948).

(6) M. R. McCorkle, *Iowa State Coll. J. Sci.*, **14**, 64 (1939); *Chem. Abstr.*, **34**, 6220 (1940), reports the m.p. 44-45°.

(7) Through the courtesy of L. D. Metcalfe of this Laboratory. A phosphoric-acid-treated diethylene glycol–adipic acid polyester column was employed. *Cf.* L. D. Metcalfe, *Nature*, **188**, 142 (1960).

---

## Preparation and Reduction of 3-Nitro-*p*-terphenyl

ROBERT G. SPLIES

*Received December 9, 1960*

Three of the four possible mononitro derivatives of *p*-terphenyl have been reported.[1,2] The prepara-