combined extracts dried over Drierite. The solvent was distilled and the residue fractionated in vacuum. There was obtained 30.0 g. (28.1%) of diethyl 2-cyanoethylmalonate, b. p. 144–146° at 5 mm.[10] The residue, which crystallized on cooling, gave 31.1 g. (46.7%) of diethyl bis-(2-cyanoethyl)-malonate. Recrystallization from acetone gave white crystals, m. p. 61.5°.[10]

Acknowledgment.—The authors are grateful to the American Cyanamid Company for having contributed the β-chloropropionitrile used in this investigation.

Summary

1. Nine ketone anions (prepared from the ketones by reaction with sodium amide) have been cyanoethylated.

2. From each experiment a mixture of mono- and polycyanoethylated products has been obtained.

3. A possible course for the condensations has been suggested. The proposed mechanism assumes that two consecutive reactions occur, *i. e.*, an elimination reaction between the ketone anion and β-chloropropionitrile to give the ketone and acylonitrile, which then undergo a Michael condensation to give the cyanoethylated derivatives.

PITTSBURGH, PA. RECEIVED JANUARY 26, 1950

---

[10] Hesse and Bucking, *Ann.*, **563**, 31 (1949).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE]

The 1,3-Rearrangement. The Synthesis and Rearrangement of 4,4-Dimethyl-3-ethyl-2-pentanol[1a]

BY WILLIAM A. MOSHER AND JAMES C. COX, JR.[1b]

In 1933 Laughlin[2] observed the formation of 2,3,4-trimethyl-2-pentene in addition to expected products, in the copolymerization of *s*-butyl and *t*-butyl alcohols. This was regarded as such an unusual rearrangement that its discovery was not published until it had been repeatedly observed. This product can be accounted for by assuming a 1,3-rearrangement of a methyl group in the intermediate carbonium ion.

Drake, Kline and Rose[3] obtained 3,4,5,5-tetramethyl-2-hexene as one of the decenes from the acid treatment of methylisopropylcarbinol, but rejected the idea of a possible "1,3-shift" in the intermediate proposed by Whitmore. Whitmore and Mosher[4] confirmed the results of Drake, Kline and Rose.[3] Whitmore and Mosher[5] further encountered several such "1,3-shifts" in the course of their studies on the depolymerization of 3,4,5,5-tetramethyl-2-hexene and of 3,5,5-trimethyl-2-heptene.

From all cases reported, however, it has been impossible to conclude whether this rearrangement involves a single 1,3-shift or two successive 1,2-shifts, *i. e.*, the "double pinacol rearrangement" suggested by Wachter.[6]

The present investigation was undertaken with the highly-branched secondary alcohol, 4,4-dimethyl-3-ethyl-2-pentanol, which has both methyl and ethyl in rearrangeable positions.

The identification of 2,3,4-trimethyl-2-hexene as the dehydration product of this alcohol would indicate two successive 1,2-shifts. If 2,4-dimethyl-3-ethyl-2-pentene, however, resulted as the dehydration product, it would establish the rearrangement as a 1,3-shift. The possible routes that the dehydration reaction could take are represented in Fig. 1.

The dehydration of 4,4-dimethyl-3-ethyl-2-pentanol yielded 43% of 4,4-dimethyl-3-ethyl-2-pentene (I) and 57% of 2,4-dimethyl-3-ethyl-2-pentene (II). No 2,3,4-trimethyl-2-hexene (III) was found. This indicates that both normal (I) and rearranged (II) products were formed, and in the ratio of 3:4. These results indicate that the formation of the rearranged nonene (II) took place by means of a 1,3-rearrangement rather than by two successive 1,2-shifts.

The synthesis of 4,4-dimethyl-3-ethyl-2-pentanol presented difficulties, but was eventually accomplished from the lower boiling isomer of "diisobutylene," 2,4,4-trimethyl-1-pentene, proceeding through methyl neopentyl ketone and 4,4-dimethyl-3-ethylidene-2-pentanone, followed by reduction. The over-all yield was poor.

The initial step of the synthesis, the oxidation of 2,4,4-trimethyl-1-pentene to methyl neopentyl ketone, was carried out with yields up to 56% of the ketone, considerably higher than reported previously for this reaction. This yield was obtained by the slow addition of the theoretical amount of concentrated sulfuric acid to a mixture of diisobutylene and potassium dichromate solution, the reaction temperature being maintained at 30–35°. Appreciable polymer was obtained under higher temperature conditions.

Acid dichromate was found to be a more effec-

---

[1] (a) Presented before the Division of Organic Chemistry, American Chemical Society, Atlantic City, September 20, 1949. From a dissertation presented by James C. Cox, Jr. in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Delaware, June, 1949. (b) E. I. du Pont de Nemours and Company Post Graduate Fellow in Chemistry, 1948–1949.

[2] (a) Laughlin, Ph.D. Thesis, The Pennsylvania State College; (b) Whitmore, Laughlin, Matuszeski and Surmatis, THIS JOURNAL, **63**, 576 (1941).

[3] Drake, Kline and Rose, THIS JOURNAL, **56**, 2076 (1934).

[4] Whitmore and Mosher, *ibid.*, **63**, 1120 (1941).

[5] Whitmore and Mosher, *ibid.*, **68**, 281 (1946).

[6] Wachter, *Ind. Eng. Chem.*, **30**, 822 (1938).

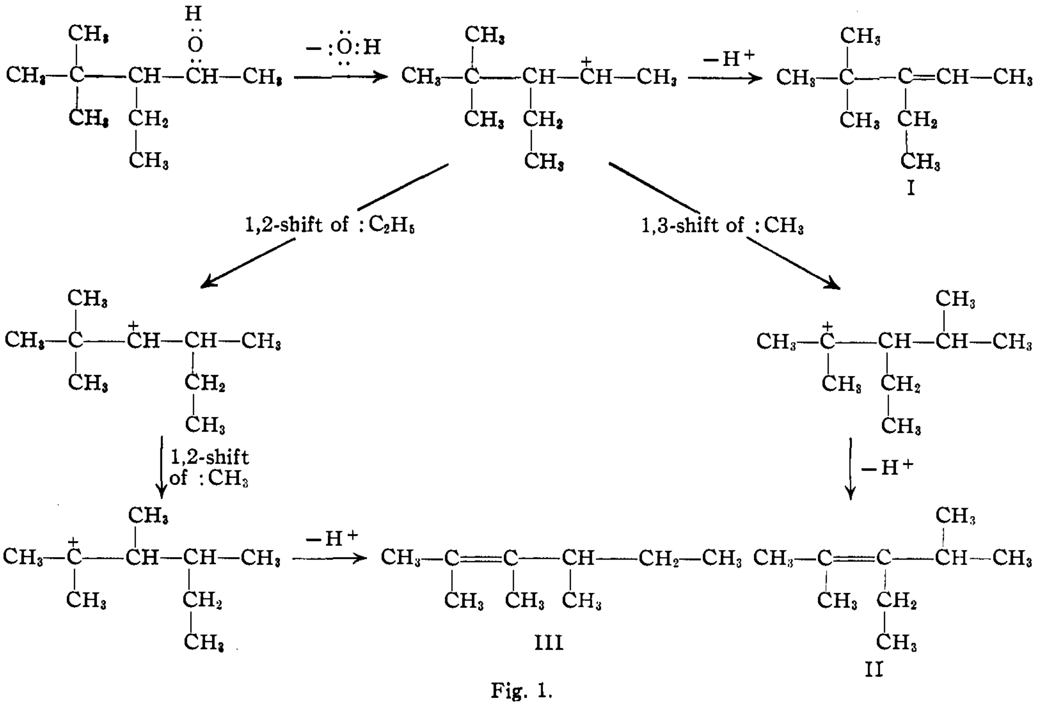


Fig. 1.

tive oxidizing agent in this case than potassium permanganate in acetic acid or in acetone and chromic acid in acetic acid. With the latter reagent a considerable amount of unreacted diisobutylene was recovered in every instance, even with an excess of the oxidizing agent.

Acetaldehyde was found to condense on the α-methylene carbon atom of methyl neopentyl ketone in alkaline media, although the yield of the resulting 4,4-dimethyl-3-ethylidene-2-pentanone in no case exceeded 20% due to competing polymerization reactions. No condensation of the aldehyde on the methyl carbon atom of the ketone was found. Alcoholic potassium hydroxide proved the most effective condensing agent, although anhydrous barium hydroxide was suitable. These results confirm those of Powell and co-workers.[7]

The reduction of 4,4-dimethyl-3-ethylidene-2-pentanone to the corresponding saturated alcohol proved difficult, but was effected in 44% yield using sodium and moist ether.[8] This highly-branched ketone could not be reduced to the corresponding saturated ketone by low-pressure hydrogenation over Adams' catalyst, or by a hot alkaline solution of nickel–aluminum alloy in a method adapted from that of Papa, Schwenk and Whitman.[9] The simultaneous reduction of the carbonyl bond and the carbon–carbon double bond of the less hindered mesityl oxide, however, was effected in 50% yield by the use of the latter procedure. Lithium aluminum hydride[10] gave no reduction of 4,4-dimethyl-3-ethylidene-2-pentanone or of mesityl oxide.

The structure of the 4,4-dimethyl-3-ethyl-2-pentanol obtained was established by oxidation with alkaline hypobromite to ethyl-*t*-butylacetic acid. This new acid was synthesized from *t*-butyllithium and α-bromobutyric acid and shown to be identical with that from the hypobromite oxidation.

Acknowledgment.—The authors express their sincere thanks to E. I. du Pont de Nemours and Company, Wilmington, Delaware, for its generous grant of funds which supported the major portion of this work.

Experimental

The Oxidation of 2,4,4-Trimethyl-1-pentene.—Three moles (336.6 g.) of technical diisobutylene, b. p. 101–104°, $n^{25}{}_D$ 1.4060 (80% 2,4,4-trimethyl-1-pentene) were added to four moles (1176.9 g.) of potassium dichromate in 800 ml. of water in a two-liter three-necked flask equipped with mechanical stirrer, dropping funnel and reflux condenser. Sixteen moles (1569 g.) of concentrated sulfuric acid was added with vigorous stirring over a period of five days, the temperature being maintained at 30–35° by the rate of addition. Stirring was continued for an additional day. On steam distillation and drying, 248.6 g. of crude methyl neopentyl ketone were obtained. Fractionation of the crude product through a 72 × 1.2 cm. Whitmore–Lux[11] total-condensation, partial take-off column packed with $^3/_{32}$ inch single-turn glass helices and equivalent to 25 theoretical plates, yielded 105.8 g. of methyl neopentyl ketone, b. p. 124–125° (760 mm.), $n^{25}{}_D$

---

[7] For leading references see Powell and Nielsen, THIS JOURNAL, **70**, 3627 (1948).

[8] This method was adapted from those used by Kerp, *Ann.*, **290**, 148 (1896), and by Clarke and Shreve, *Am. Chem. J.*, **35**, 515 (1906), in the reduction of mesityl oxide to methylisobutylcarbinol.

[9] Papa, Schwenk and Whitman, *J. Org. Chem.*, **7**, 587 (1942).

[10] Finholt, Bond and Schlesinger, THIS JOURNAL, **69**, 1199 (1947); Nystrom and Brown, *ibid.*, **69**, 1197 (1947).

[11] Whitmore and Lux, *ibid.*, **54**, 3451 (1932).

1.4018. The pressure was then reduced to 9 mm. and an additional 49.4 g. of methyl neopentyl ketone, b. p. 45–46° (9 mm.), $n^{25}D$ 1.4018, was obtained. The total amount of methyl neopentyl ketone obtained was 155.2 g. (56.0% of the theoretical amount).

The oil layer also yielded 23.2 g. (5%) of acetone, 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 126°, semicarbazone, m. p. and mixed m. p. 187°, and 12.2 g. of trimethylacetaldehyde, 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 210°. The residue from the distillation amounted to 24.5 g.

The Alkaline Condensation of Methyl Neopentyl Ketone with Acetaldehyde.—The following is a typical run using alcoholic potassium hydroxide: to 1 mole (114.4 g.) of ketone in 100 ml. of 1 *N* alcoholic potassium hydroxide in a 1 l. three-necked flask with stirrer, reflux condenser, and dropping funnel was added 1.5 moles (66 g.) of acetaldehyde (b. p. 21°) dropwise with vigorous stirring over a period of two hours. Addition of the acetaldehyde was adjusted to give gentle refluxing. About one hour after the addition of the aldehyde reflux began to drop off, but stirring was continued for eighteen hours more.

Slightly more than the calculated amount of powdered tartaric acid (16.0 g.) was stirred into the reaction mixture, the potassium acid tartrate precipitating filtered off, and the filtrate dried with anhydrous sodium sulfate. The intensely yellow liquid was fractionated through the column previously described. After stripping off the ethanol, 85.5 g. of methyl neopentyl ketone, $n^{25}D$ 1.4010, was recovered unreacted. No unreacted acetaldehyde was recovered. The distillation was continued under diminished pressure and 23.3 g. of a pleasant-smelling yellow liquid, $n^{25}D$ 1.4402, b. p. 101° (40 mm.), d_{25} 0.8546, were obtained. *Anal.* Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.15; H, 11.39. This material gave positive reactions with phenylhydrazine, bromine in carbon tetrachloride solution, and alkaline hypoiodite reagent, and was reduced to 4,4-dimethyl-3-ethyl-2-pentanol. The yield of 4,4-dimethyl-3-ethylidene-2-pentanone amounted to 16.6% of the theoretical. The distillation residue, 54.5 g., was not investigated. It was a dark brown semi-plastic material presumably a polymer of acetaldehyde.

Three crystalline derivatives of 4,4-dimethyl-3-ethylidene-2-pentanone were readily prepared: 2,4-dinitrophenylhydrazone, m. p. 186–187°; Calcd. for $C_{15}H_{21}O_4N_4$: N, 17.43. Found: N, 17.58: semicarbazone, m. p. 158° calcd. for $C_{10}H_{19}ON_3$: N, 21.30. Found: N, 21.42; and oxime, m. p. 153°, calcd. for $C_9H_{17}ON$: N, 8.95. Found: N, 9.04. Parachor values for 4,4-dimethyl-3-ethylidene-2-pentanone: 378.1 from empirical data, 383.2 from parachor equivalents; molar refraction, 43.1 from observed data, 43.3 from molar refraction equivalents.

The Reduction of 4,4-Dimethyl-3-ethylidene-2-pentanone.—After several unsuccessful attempts to reduce 4,4-dimethyl-3-ethylidene-2-pentanone to the corresponding saturated alcohol, by means of catalytic hydrogenation, nickel–aluminum alloy in hot alkali,[9] and lithium aluminum hydride[10] in anhydrous ether, the simultaneous reduction of the carbonyl bond and the carbon–carbon double bond was effected as following: A solution of 42.1 g. (0.3 mole) of 4,4-dimethyl-3-ethylidene-2-pentanone, $n^{25}D$ 1.4400, dissolved in 1025 ml. of anhydrous ether was added to a three-liter three-necked flask equipped with an efficient reflux condenser, dropping funnel and mechanical stirrer. The amount of water (71 g.) necessary to saturate the ether was added and vigorous stirring started. Over a period of three hours 90 g. of clean metallic sodium was added in very small pieces at such a rate that gentle refluxing was maintained. Stirring was continued for seventeen hours.

The excess sodium was decomposed by the dropwise addition of 270 ml. of water over four hours. After separating the ether layer, the water layer was extracted with ether. The combined ethereal layer and extracts were dried over anhydrous sodium sulfate. After filtering off the drying agent, fractionation of the material through the 25-plate column gave 15.1 g. of a colorless liquid, b. p. 90–92° (10 mm.), $n^{25}D$ 1.4320, along with 27.5 g. of a polymeric substance. The colorless liquid showed no unsaturation to bromine in carbon tetrachloride or to potassium permanganate solution and gave a positive test for alcohol with metallic sodium and with ceric nitrate reagent. The yield of saturated alcohol represented 44% of the theoretical amount. A total of 130.2 g. of the 4,4-dimethyl-3-ethyl-2-pentanol was prepared in this manner. Calcd. for $C_9H_{20}O$: C, 74.93, H, 13.98. Found: C, 75.06; H, 13.86.

Two derivatives of 4,4-dimethyl-3-ethyl-2-pentanol were prepared: phenylurethan, m. p. 121° (Calcd.: N, 5.31. Found: N, 5.27), and 3,5-dinitrobenzoate, m. p. 115–116°, which was not analyzed. Parachor values for 4,4-dimethyl-3-ethyl-2-pentanol: from empirical data, 407.1; from parachor equivalents, 405.2. Molar refraction values: from empirical data, 44.2; from molar refraction equivalents, 44.9.

Oxidation of 4,4-Dimethyl-3-ethyl-2-pentanol.—The oxidation of the 4,4-dimethyl-3-ethyl-2-pentanol to ethyl-*t*-butylacetic acid was carried out according to a method adapted from that used by Meister, Lucius and Bruning.[12] A solution of 25 g. of sodium hydroxide in 1248 ml. of water was added to a two-liter flask equipped with reflux condenser and dropping funnel. Following the addition of 96 g. of bromine, the mixture was shaken well and 30 g. (0.2 mole) of 4,4-dimethyl-3-ethyl-2-pentanol was added. The alcohol was not at first completely soluble in the mixture, but as the reaction progressed complete solution was attained. The mixture was heated on a steam-bath for 14 hours. The mixture stood for 24 hours. After separating the bromoform, the filtrate was acidified with dilute sulfuric acid. The oil layer was separated and the water layer extracted with six successive 50-ml. portions of ether. The oil and ether extracts were combined and dried over anhydrous sodium sulfate. The drying agent was filtered off and the ether evaporated from the crude acid. Fractionation yielded 11.3 g. of an acid with a nauseating odor, b. p. 113–115° (10 mm.), $n^{25}D$ 1.4252, neutral. equiv. calcd., 144.2; found, 143.6. The amide and the anilide derivatives of this acid were prepared; melting points 115–116°; calcd. for $C_8H_{17}ON$: N, 9.88. Found: 10.02 and 92–93°, calcd. for $C_{14}H_{21}ON$: N, 6.39. Found: N, 6.30, respectively.

The Synthesis of Ethyl-*t*-butylacetic Acid.—The *t*-butyllithium was obtained by the action of *t*-butyl chloride on lithium sand prepared according to the method of Bartlett, Swain and Woodward.[13] One and one-half atoms (10.5 g.) of lithium sand was added along with 250 ml. of anhydrous ether under an atmosphere of nitrogen to a one-liter three-necked flask equipped with stirring mechanism, dropping funnel and reflux condenser. With continuous stirring 81 g. (0.875 mole) of anhydrous *t*-butyl chloride was added dropwise over a period of six hours, a current of nitrogen being maintained during the operation. One and one-half moles (126.0 g.) of α-bromobutyric acid, b. p. 99–103°, $n^{25}D$ 1.4700 (Eastman Kodak Company), were stirred into the mixture at a dropwise rate over a period of four hours. After a short induction period a reaction set in and the ether refluxed gently. Stirring was continued for an additional 20 hours after the completion of the addition of the α-bromobutyric acid.

The small amount of oxide-coated lithium that remained was then destroyed by carefully adding 100 ml. of water. The resulting solution was acidified and the water layer drawn off and extracted with three successive 50-ml. portions of ether. The ether layer and extracts were combined and dried over anhydrous sodium sulfate. Fractionation of the dried product yielded 5.2 g. of a colorless unpleasant-smelling acid, b. p. 111–115° (10 mm.), $n^{25}D$ 1.4253, identical with the material obtained by the hypobromite oxidation of 4,4-dimethyl-3-ethyl-2-pentanol. It yielded an amide, m. p. and mixed m. p. 115–116°, and an anilide, m. p. and mixed m. p. 92–93°.

---

[12] Meister, *et al.*, *Ber.*, **16**, 449 (1883).

[13] Bartlett, Swain and Woodward, THIS JOURNAL, **63**, 3229 (1947).

The Dehydration of 4,4-Dimethyl-3-ethyl-2-Pentanol.—The dehydration of 4,4-dimethyl-3-ethyl-2-pentanol was effected by means of β-naphthalenesulfonic acid[14] in the following manner: A mixture of 86.5 g. (0.6 mole) of 4,4-dimethyl-3-ethyl-2-pentanol and 0.1 g. of β-naphthalenesulfonic acid (Eastman Kodak Company) was heated under the 25-plate column until a rapid reflux set in. After the removal of the foreshots (1.2 g.), an olefin-water mixture amounting to 77.2 g. distilled over at 128–129°, leaving a residue of 8.3 g. The olefinic material was dried over anhydrous sodium sulfate and redistilled. The dried product yielded 71.9 g. of unsaturated material, b. p. 129–132° (765 mm.), n^{25}D 1.4274.

Ozonolysis of the Dehydration Product.—The ozonolysis of the unsaturated material obtained above was carried out using a 60 cycle, 1-phase U. S. Ozone Company ozonizer. The ozonolysis of 71.9 g. of hydrocarbon was carried out using the procedure of Church, Whitmore and McGrew.[15] The oil layer was separated and allowed to stand over anhydrous sodium sulfate. The water layer gave a negative Tollens test for formaldehyde. The dried oily material, n^{25}D 1.4132, with a pronounced ketonic odor, was fractionated through a 25 × 0.8 cm. Whitmore–Lux column packed with $^3/_{64}$ inch glass helices and equivalent to 15 theoretical plates.

Identification of the Products of the Ozonolysis.—A small amount of material (0.8 g.) was obtained from the acetone–Dry Ice trap following the decomposition of the ozonide. It was identified as acetaldehyde by means of its 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 147°, and its semicarbazone, m. p. and mixed m. p. 162°. Fractionation of the ketonic oil above yielded the following substances: 3.7 g. of acetone, 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 126, semicarbazone, m. p and mixed m. p. 162°; 10.8 g. of ethyl isopropyl ketone, 2,4-dinitrophenylhydrazone, m. p. and mixed 145°, semicarbazone, m. p. and mixed m. p. 135–136°; and 40.0 g. of undehydrated 4,4-dimethyl-3-ethyl-2-pentanol, identified by its 3,5-dinitrobenzoate, m. p. and mixed m. p. 115–116°.

Summary

The dehydration of 4,4-dimethyl-3-ethyl-2-pentanol with β-naphthalenesulfonic acid yields 4,4-dimethyl-3-ethyl-2-pentene, the normal product, and 2,4-dimethyl-3-ethyl-2-pentene, the product of an intramolecular rearrangement, in the ratio of 3:4. The formation of the latter product is considered evidence that the 1,3-rearrangement of methyl groups may take place in the dehydration of highly-branched alcohols.

A synthesis of 4,4-dimethyl-3-ethyl-2-pentanol is presented, as well as the conditions for the optimum yield (56%) of methyl neopentyl ketone by the oxidation of diisobutylene.

4,4-Dimethyl-3-ethyl-2-pentanol, 4,4-dimethyl-3-ethylidene-2-pentanone, and ethyl-*t*-butylacetic acid have not been previously reported and their synthesis, properties, and the melting points of some of their derivatives are given.

NEWARK, DELAWARE RECEIVED OCTOBER 31, 1949

---

[14] See Whitmore and Laughlin, THIS JOURNAL, **55**, 3732 (1933).

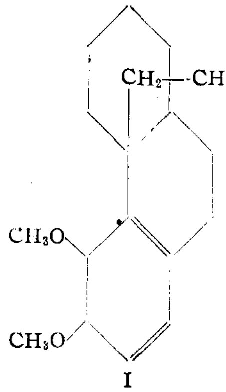
[15] Church, Whitmore and McGrew, *ibid.*, **56**, 176 (1934).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SMITH COLLEGE]

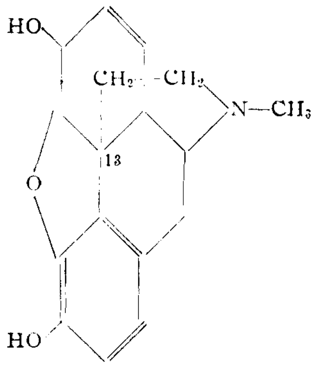
Syntheses in the Direction of Morphine. II.[1] Some Intermediates and Model Compounds

BY MILTON D. SOFFER, ROBERTA A. STEWART,[2a] J. CHARLES CAVAGNOL,[2b] HILDA E. GELLERSON AND ELIZABETH ANN BOWLER

Attention has been directed for some time[3] toward certain degradation products of morphine (*e. g.*, I[4]) whose synthesis by unambiguous methods would provide direct evidence concerning the main element of structure, in the Gulland and Robinson[5] formula (II), for which rigid experimental support has not yet been reported in the literature, *i.e.*, the attachment of the ethanamine chain to C_{13}. Many accomplishments in this direction, and toward morphine itself and re-



I



II

---

[1] Soffer, Cavagnol and Gellerson, THIS JOURNAL, **71**, 3857 (1949).

[2] Present addresses: (a) Department of Chemistry, Wellesley College; (b) Department of Chemistry, University of Kentucky.

[3] Fieser and Holmes, THIS JOURNAL, **60**, 2548 (1938); **58**, 2319 (1936).

[4] Cahn, *J. Chem. Soc.*, 2565 (1926).

[5] *Mem. Proc. Manchester Lit. Phil. Soc.*, **69**, 79 (1925).