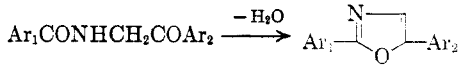
The difference in the extinction coefficients of 2-(*p*-dimethylaminophenyl)-5-phenyloxazole and 5-(*p*-dimethylaminophenyl)-2-phenyloxazole could account for the difference in relative pulse heights of the two. It is thought that an increase in the extinction coefficient with the consequent diminution of the life-time of the excited state would allow fluorescence to occur before internal quenching could interfere.[9] In the case of the two isomeric dialkylamino substituted oxazoles, it can be seen that the compound with the higher pulse height is indeed the one with the larger extinction coefficient. In all cases, the extinction coefficient of the aminated oxazole is higher than that of the analogous nonaminated oxazole. Any expected improvement from this cause is offset by other, detrimental effects, as is evident in the lowered pulse heights.

It seems, in conclusion, that a molecule with an extended resonance system but with strong internal quenching or too short an emission wave length can be helped by dialkylamino substitution; however, such substitution does not improve a good scintillator.

EXPERIMENTAL

All compounds listed in Table II were synthesized according to the following general scheme:

$$Ar_1COCl + Ar_2COCH_2NH_2.HCl \xrightarrow{C_6H_5N} Ar_1CONHCH_2COAr_2$$



The general procedure of Hayes, Rogers, and Ott[15] was used to obtain the intermediate ketoamides from the acid chlorides and the *p*-dimethylaminophenacylammonium chloride.[16]

The cyclization of the ketoamides, with 98% phosphoric acid in acetic anhydride, to form the oxazoles was performed in the same manner as that given for the pyridylphenyl oxazoles in a previous paper.[17]

Details concerning the methods for obtaining the pulse heights[18] and the fluorescence[8] and the ultraviolet absorption spectra[8] may be found in previous publications. The infrared absorption spectra are in the Sadtler Standard Spectra.[19]

Los Alamos, N. M.

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(15) F. N. Hayes, B. S. Rogers, and D. G. Ott, *J. Am. Chem. Soc.*, **77**, 1850 (1955).

(16) Product of Pilot Chemicals, Inc., Watertown, Mass.

(17) D. G. Ott, F. N. Hayes, and V. N. Kerr, *J. Am. Chem. Soc.*, **78**, 1941 (1956).

(18) F. N. Hayes, D. G. Ott, V. N. Kerr, and B. S. Rogers, *Nucleonics*, **13**, No. 12, 38 (1955).

(19) Samuel P. Sadtler and Son, Inc., Philadelphia, Pa.

[Contribution from the Indian Association for the Cultivation of Science]

Synthesis of Condensed Cyclic Systems. I.[1] New Synthesis of 7-Methylbicyclo[3.3.0]octan-3-one and 8-Methylbicyclo[4.3.0]nonan-4-one

KALYANMAY SEN and USHA RANJAN GHATAK[1a]

Received April 7, 1959

7-Methylbicyclo[3.3.0]octan-3-one (II) was obtained in good yield by application of an analogous method which had been reported for 8-methylbicyclo[4.3.0]nonan-4-one. (I). This modification, however, failed with the latter compound. A new simple method for its synthesis is described.

In the course of the synthesis of degradation products of antirachitic vitamins, Bagchi and Banerjee reported the synthesis 8-methylbicyclo-[4.3.0]nonane-4-one (I).[2] The present experiments were undertaken to improve the previously developed method.

Synthesis of 7-methylbicyclo[3.3.0]octan-3-one (II) was attempted first, using simplifications of the analogous reported procedure for I. Excellent result were obtained. Fewer steps were required and a higher yield was achieved than had been reported for 8-methylbicyclo[4.3.0]nonan-4-one.

The condensation of 2-methyl-2-carbethoxylcyclopentanone with ethyl cyanoacetate according to the method of Cope *et al.*,[3] was studied by Bagchi and Banerjee.[2] In the present investigation when the condensation was carried out according to the modification of Cragoe *et al.*,[4] the condensation product (III) was obtained in a reproducible yield exceeding 90%. The unsaturated cyano ester (III) was condensed with ethyl chloroacetate according

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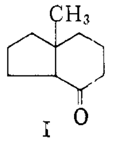
[1] A preliminary note embodying a part of the experimental results appeared in *Science and Culture (India)*, **21**, 545 (1956) and *Proc. 45th Session Indian Science Congress*, (1958), p. 129. Taken from the thesis of K. Sen submitted for the degree of Doctor of Philosophy (Science) of the University of Calcutta, April, 1957.

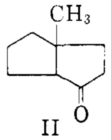
[1a] To whom all communications should be made. Present Address: Department of Chemistry, University of Maine, Orono, Me.

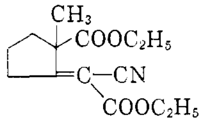
[2] P. Bagchi and D. K. Banerjee, *J. Indian Chem. Soc.*, **23**, 397 (1946).

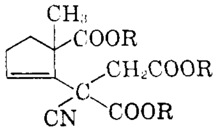
[3] A. C. Cope, C. M. Hofmann, C. Wyckoff, and F. Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

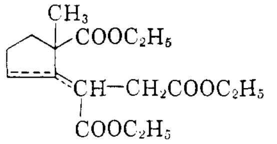
[4] E. J. Cragoe, C. M. Robb, and J. M. Sprague, *J. Org. Chem.*, **15**, 381 (1950).

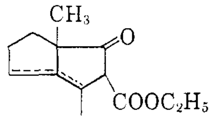

I

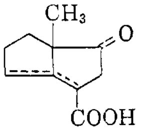

II

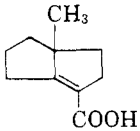

III

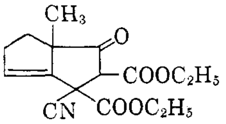

IV a. $R = -CH(CH_3)_2$
b. $R = -C_2H_5$


V


VI


VII


VIII


IX

to Cope *et al.*,[5] in ethanol as well as in isopropyl alcohol. In the latter case ester exchange simultaneously took place, the triisopropyl ester (IVa) being obtained. The cyanoester (IVb) was hydrolyzed by boiling with concentrated hydrochloric acid and the crude hydrolysate was directly esterified with ethanol and concentrated sulfuric acid. The product of esterification was separated into two fractions through distillation. The lower boiling fraction gave analytical figures required for the triester (V). The higher boiling product proved to be a γ-lactonic ester from elementary analysis and infrared examination. Chatterjee and Bhattacharyya[6] also mention the formation of a γ-lactonic acid in connection with the hydrolysis of diethyl α-cyano-α-(6-methyl-6-carbethoxy cyclohexenyl) succinate.

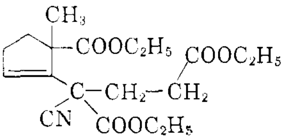
The triester (V) on Dieckman cyclization followed by direct hydrolysis of the β-keto ester (VI) gave a keto acid (VII) m.p. 122°, in which the exact position of the double bond has not been assigned with certainty as the product may be a mixture of bond isomers. When (VII) was subjected to Huang-Minlon reduction, not only was the keto group reduced, but also the double bond was brought into conjugation with the carboxyl as was proved by the easy conversion of (VIII) to the ketone (II) through the Schmidt reaction.[7]

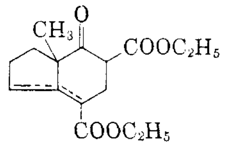
A further simplification of the above scheme was achieved by cyclization of (IV) followed by direct hydrolysis of the intermediate β-keto ester (IX), when the keto acid (VII) m.p. 122° was obtained in 36% overall yield.

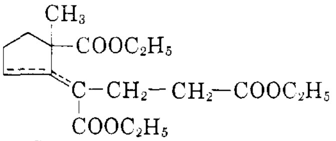
The steps involved in the present scheme are smooth and the yields in different steps on the whole workable. The present procedure thus appeared to be an improvement over that of Bagchi and Banerjee.[2]

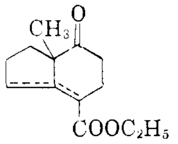
In view of the encouraging results obtained in the synthesis of the ketone (II), we decided to extend the above procedure to the synthesis of 8-methylbicyclo[4.3.0]nonan-4-one (I).

The unsaturated cyano ester (III) was condensed with ethyl β-chloro- or β-bromo-propionate to yield X. Attempts to introduce a propionic acid chain by cyanoethylation[8] in presence of Triton B or through Michael addition of methyl acrylate in the presence of sodium ethoxide in ethanol failed to yield the desired product. Hydrolysis of (X) followed by esterification with ethanol and sulfuric acid yielded two products. The lower boiling product showed analytical data required for the ester (XI). The position of the double bond is uncertain, for reasons stated previously. The other fraction, which was the major product in this case, is apparently a γ-lactonic ester, as its infrared spectrum is almost identical with the lactonic ester obtained earlier.


X


XII


XI


XIII

The triester (XI) was cyclized with sodium dust in benzene and the crude β-keto ester (XII) was directly hydrolyzed. Unlike the previous case the keto acid could not be obtained in the crystalline state and even after repeated sublimations an analytically pure sample could not be obtained. In the subsequent experiments, therefore, the crude keto acid was converted into the ethyl ester (XIII), which was obtained in the pure state.

The modification of the original procedure of Bagchi and Banerjee[2] did not prove very fruitful in the case of the synthesis of the ketone (I). A major set back was our inability to utilize the lactonic ester (obtained as the major product) for the succeeding steps.

Recently a method has been developed in this laboratory[9] for the synthesis of 10-methylbicyclo[4.4.0]decan-1-one from 10-methylbicyclo[4.4.0]decan-1,3-dione. This method was utilized with

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[5] A. C. Cope and C. M. Hofmann, *J. Am. Chem. Soc.*, **63**, 3456 (1941).

[6] R. C. Chatterjee and B. K. Bhattacharyya, *Science and Culture (India)*, **21**, 543 (1956); *J. Indian Chem. Soc.*, **34**, 515 (1957).

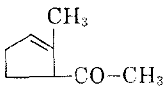
[7] H. Wolff, *Org. Reactions*, III, 307 (1947).

[8] H. A. Bruson and T. W. Riene, *J. Am. Chem. Soc.*, **70**, 214 (1948).

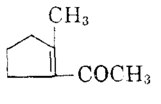
[9] U. Ghatak, N. N. Saha, and P. C. Dutta, *J. Am. Chem. Soc.*, **79**, 4487 (1957).

success for the synthesis of the ketone (I) in a satisfactory yield, and has turned out to be the simplest method for its synthesis.

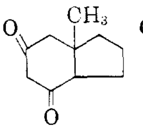
A simple method has been developed for the synthesis of 1-acetyl-2-methyl-Δ^1 (and Δ^2)-cyclopentene (XIV and XV) through the condensation of acetic anhydride with 1-methylcyclopentene in the presence of zinc chloride. It was found that the reaction temperature, purity of the zinc chloride and the time of reaction represented the most important factors in controlling the uniformity of yield and purity of the products. Under proper experimental conditions pure ketonic product (XIV and XV) was obtained in about 50–60% yield. The ketonic fraction exhibited a maximum ultraviolet absorption at 250 mμ (log ϵ 3.6). That this extinction coefficient is low compared with that of pure α,β-unsaturated ketone (XV)[10] and that the melting point of semicarbazone prepared from our ketone was raised from 208 to 221–222° on crystallization (lit. 223–224° m.p. of the semicarbazone from XV)[10] revealed that the ketonic product obtained by us consisted of a mixture of two isomeric products (XIV and XV). It is interesting to record here the difference between the acetylation of 1-methylcyclopentene and 1-methylcyclohexene. In the latter case β,γ-unsaturated ketone was found to be the only product.[11] The isomeric 1-acetyl-2-methyl-Δ^1 (and Δ^2)-cyclopentene (XIV and XV) was condensed with diethyl malonate according to Clemo and Dickenson.[12] The condensation product on subsequent alkaline hydrolysis yielded the diketone (XVI) m.p. 90–91° (lit. 91–92°)[12] as a white powder; 45% after sublimation. The diketone (XVI) was converted to the chloroketone (XVII) by treatment with phosphorus trichloride and the latter was reduced to the bicyclic ketone (I) in an excellent yield.



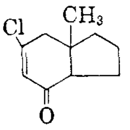
XIV



XV



XVI



XVII

The homogeneity as well as the structure of the above ketone obtained was proved from its formation of a single semicarbazone in about 93% yield, which was found to be identical with an authentic sample of semicarbazone of the ketone (I), prepared according to Bagchi and Banerjee.[2] The structure of the final product incidentally established the structure of the chloroketone as XVII.

EXPERIMENTAL[13]

Ethyl 2-methyl-2-carbethoxycyclopentylidenecyanoacetate (III). A mixture of 2-methyl-2-carbethoxycyclopentanone (22 g.), ethyl cyanoacetate (17.5 g.), glacial acetic acid (5.2 ml.) and benzene (25.8 ml.) was refluxed on an oil bath in a flask fitted with a water separator for 15 hrs., during which ammonium acetate (3.9 g.) was added in three equal portions. The dark red reaction mixture was washed with water (10 times). The benzene was removed and the residual oil was distilled. Product boiled at 170–172°/5 mm. (30.8 g.; 90%), $n_D^{34.5}$ 1.4800.

Diisopropyl α-cyano-α-(5-methyl-5-carbisopropoxycyclopentenyl)succinate (IVa). Ethyl 2-methyl-2-carbethoxycyclopentylidenecyanoacetate (28.5 g.) was added to ice cold sodium isopropylate (prepared from isopropyl alcohol, 115 ml., and sodium, 2.6 g.). To the complex was added ethyl chloroacetate (15.2 g.), whereby the contents turned wine red. The mixture was refluxed for 32 hr. (neutral). After removal of the isopropyl alcohol under suction, water was added and the precipitated oil was extracted with benzene. The solution was washed and evaporated and the residual oil distilled. The product boiled at 188–190°/2 mm. (27.4 g.; 65%).

Anal. Calcd. for $C_{21}H_{31}O_6N$: C, 64.1; H, 7.8. Found: C, 63.9; H, 7.7.

Diethyl α-cyano-α-(5-methyl-5-carbethoxycyclopentenyl)-succinate (IVb). Ethyl 2-methyl-2-carbethoxycyclopentylidenecyanoacetate (28 g.) was added under nitrogen atmosphere to a suspension of sodium ethoxide (from 2.6 g. sodium and 115 ml. ethanol) cooled in ice. After some time ethyl chloroacetate (15.2 g.) was added and the mixture refluxed till neutral to litmus (17–19 hr.). Water was then added and the oil extracted with benzene. The benzene extract was washed with water, and benzene removed. The residual oil distilled at 175–176°/0.6 mm. (24.9 g.; 67%).

Anal. Calcd. for $C_{18}H_{25}O_6N$: C, 61.5; H, 7.1. Found: C, 61.1; H, 7.4.

Hydrolysis of the ester (IVb). The ester (IVb) (45 g.) was refluxed with concentrated hydrochloric acid (150 ml.) for 30 hr. The hydrolysate was then evaporated to dryness and the residue extracted with ether. The ether extract was dried, the ether evaporated and the residue esterified by refluxing with ethanol (225 ml.) and concentrated sulfuric acid (25 ml.). The reaction product was then worked up in the usual way. The residual oil gave two fractions on distillation. Fraction I, b.p. 167–70°/5 mm. (17.6 g.; 42%) was found to analyze correctly for diethyl 2-methyl-2-carbethoxycyclopentylidenesuccinate.

Anal. Calcd. for $C_{17}H_{26}O_6$: C, 62.6; H, 8.0. Found: C, 62.4; H, 7.7.

Fraction II, b.p. 185–194°/4 mm. This was found to be the lactonic ester. Infrared spectrum (film on KBr pellet) $\nu_{\max}$ 1775 cm.$^{-1}$ (lactone), $\nu_{\max}$ 1726 cm.$^{-1}$ (ester).

Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.4; H, 7.3. Found: C, 60.1; H, 7.5.

7-Methylbicyclo[3.3.0]oct-$\Delta^{3:8 \text{ or } 4:8}$-ene-1-one-3-carboxylic acid (VII). (a) *From ester* (V). Ester (V, 13.5 g.) was refluxed with sodium dust (1.2 g.) in thiophene free benzene (50 ml.) under nitrogen atmosphere for 3 hr. The reaction mixture was then decomposed with dilute hydrochloric acid and the benzene layer was washed with water. The oil obtained by evaporation of benzene was hydrolyzed by refluxing with hydrochloric acid (150 ml., 1:10) for 36 hr. The product was then extracted with ether and the ether layer extracted with sodium carbonate solution (5%). The alkaline layer was acidified and the precipitated oil extracted with ether. Sublimation of the residue gave an oil which solidified. It was recrystallized from benzene, m.p. 122° (3.5 g.; 47%).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.6; H, 6.6. Found: C, 66.4; H, 6.3.

(b) *From ester* (IVb). Ester (IV, 17.5 g.) was refluxed under nitrogen with sodium dust (2.4 g.) in benzene (50

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[10] R. B. Turner and D. M. Voitle, *J. Am. Chem. Soc.*, **73**, 1403 (1951).

[11] N. C. Deno and H. Chafetz, *J. Am. Chem. Soc.*, **74**, 3940 (1952).

[12] G. R. Clemo and H. G. Dickenson, *J. Chem. Soc.*, 735 (1935).

[13] All melting points and boiling points are uncorrected.

ml.) for 3 hr. The product was decomposed with dilute hydrochloric acid. The benzene layer was separated and the oil obtained on evaporation of the benzene was hydrolyzed by refluxing with hydrochloric acid (20 ml.), water (50 ml.) and glacial acetic acid (130 ml.) for 30 hr. The acids were then removed under reduced pressure and the product worked up as in the previous case. It had an m.p. of 122° and showed no depression when mixed with the product described before.

7-Methylbicyclo[3.3.0]oct-$\Delta^{3:8}$-ene-3-carboxylic acid (VIII). Acid (VII, 4 g.) was heated with hydrazine hydrate (6.5 ml.; 100%) and caustic potash (4.4 g.) in diethylene glycol (33 ml.) for 4 hr. After cooling the reaction mixture was diluted and then acidified. The precipitated oil was then repeatedly extracted with ether. On removal of ether an oil was obtained which distilled at 135–136°/1.5 mm. (1.1 g.; 30%).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.2; H, 8.4. Found: C, 71.8; H, 8.4.

7-Methylbicyclo[3.3.0]octan-3-one (II). Acid (VIII, 1.5 g.) in benzene was treated with hydrazoic acid (13 ml.; 5.5%). The mixture was then cooled and treated with concentrated sulfuric acid (5 ml.) with stirring. Then the temperature was maintained at 40–45° for 2 to 2.5 hr. Water was next added and the mixture refluxed on a water-bath for 1.5 hr. The benzene layer was separated, washed with water and benzene removed. The residual oil was distilled; b.p. 85–90°/5 mm. (0.38 g.; 31%).

Anal. Calcd. for $C_9H_{14}O$: C, 78.2; H, 10.1. Found: C, 77.8; H, 10.1.

The 2,4-dinitrophenylhydrazone was prepared and crystallized from ethanol-ethyl acetate; m.p. 177–178°.

Anal. Calcd. for $C_{15}H_{18}O_4N_4$: N, 17.6. Found: N, 17.6.

Diethyl α-cyano-α-(5-methyl-5-carbethoxycyclopentenyl) glutarate (X). To an ice-cold solution of sodium ethanol (prepared from 3.6 g. sodium and 75 ml. ethanol) was added ethyl 2-methyl-2-carbethoxycyclopentylidenecyanoacetate (39 g.) in an atmosphere of nitrogen. After 5 min. ethyl β-chloropropionate (21 g.) was added to the dark solution whereby intense heat developed. Within a very short time sodium chloride precipitated out. The mixture was refluxed in a nitrogen atmosphere for 16 hr. until neutral to litmus. After addition of water the separated oil was extracted with benzene and the solution was thoroughly washed with water. After removal of the solvent the ester distilled at 195–200°/0.6 mm. (42.9 g.; 80%).

Anal. Calcd. for $C_{19}H_{27}O_6N$: C, 62.4; H, 7.4. Found: C, 61.9; H, 7.7.

Diethyl 2-methyl-2-carbethoxycyclopentylideneglutarate (XI). Cyanoester (X, 20 g.) and concentrated hydrochloric acid (100 ml.) were refluxed for 30 hr. The reaction mixture was evaporated to dryness and the residue was mixed with 20% ethanolic sulfuric acid (150 ml.) and refluxed for 20 hr. The product was treated with excess water and the separated oil collected in ether. The ethereal solution was washed with water and sodium bicarbonate solution, dried over sodium sulfate, and distilled. Two distinct fractions were obtained.

Fraction I, 167°/0.4 mm. (21.5%) was found to be diethyl 2-methyl-2-carbethoxycyclopentylideneglutarate (XI).

Anal. Calcd. for $C_{18}H_{28}O_6$: C, 63.5; H, 8.2. Found: C, 62.8; H, 7.9.

Fraction II, 185–190°/0.4 mm. (38%) was found to be lactonic ester. Infrared spectra (film on KBr pellet), ν_{max} 1775 cm.$^{-1}$ (ν lactone), ν_{max} 1726 cm.$^{-1}$ (ester).

Anal. Calcd. for $C_{16}H_{24}O_6$: C, 61.5; H, 7.6. Found: C, 61.4; H, 7.6.

Ethyl 8-methylbicyclo[4.3.0]non-$\Delta^{3:9 \text{ or } 4:9}$-ene-7-one-4-carboxylate (XIII). The ester (XI, 32 g.) was refluxed for 3 hr. with (4.8 g.) sodium dust in a nitrogen atmosphere using benzene (200 ml.) as solvent. The resulting deep red solution was decomposed with 1:1 hydrochloric acid. The benzene solution was washed with water and evaporated. The crude keto ester which gave a distinct ferric chloride test was hydrolyzed by refluxing with 6% hydrochloric acid (150 ml.) for 20 hr. The hydrolyzed product was collected as usual and esterified with 5% ethanolic sulfuric acid (100 ml.). The product was taken up in ether. The extract was washed with sodium bicarbonate, dried and distilled. The product, ketoester (XIII), boiled at 115°/5 mm. (33%).

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.2; H, 8.1. Found: C, 70.4; H, 8.2.

The 2,4-dinitrophenylhydrazone, m.p. 140°, could not be crystallized.

1-Acetoxy-2-methylcyclopentenes (XIV *and* XV). To an ice-cold (0°) stirred mixture of 1-methylcyclopentene (10 g.)[14] and acetic anhydride (60 ml.), powdered and freshly fused zinc chloride (25 g.) was added in small portions (during about 1 hr.) so that the temperature remained below 10°. Stirring was continued for another 15 min. The dark reaction mass was decomposed with iced water and extracted with ether (50 × 3 ml.). The extract was washed with cold sodium hydroxide solution (5%) until alkaline, with water and finally dried over calcium chloride. Distillation yielded a colorless sweet smelling liquid, b.p. 58–65°/8 mm. (18.5 g.; 61%) λ_{max}^{alc} 250 mμ, log ε 3.6.

Semicarbazone, m.p. 208° (crude) on three crystallizations from ethanol melted at 221–222°.

6-Chloro-8-methylbicyclo[4.3.0]non-5-ene-4-one (XVII). The diketone (XVI) was prepared in about 45%, yield by the condensation of the ketone (XIV and XV mixture) with diethyl malonate and subsequent alkaline hydrolysis according to the method of Clemo *et al.*[12]

The diketone (XVI, 10.2 g.) in dry chloroform (25 ml.) was refluxed on a water-bath for 3 hr. with phosphorous trichloride (2.5 ml.). The solvent was distilled off under reduced pressure. The residue was cooled and treated with an excess of ice-cold water. The ethereal extract was washed with cold sodium hydroxide solution (2%). Product distilled at 115–116°/6 mm. as a colorless liquid (6 g.; 53%).

Anal. Calcd. for $C_{10}H_{13}OCl$: C, 65.0; H, 7.0. Found: C, 64.8; H, 7.3.

8-Methylbicyclo[4.3.0]nonan-4-one (I). The enol-chloride (5.8 g.) in ethanol (20 ml.) was hydrogenated with palladium-carbon (200 mg.; 10%) at room temperature. The hydrogenated product was worked up. The ketone, b.p. 90–91°/6 mm. was a colorless, sweet-smelling liquid (3.9 g.; 81.5%).

Semicarbazone was obtained in 93% yield, m.p. 185–186°; crystallized from ethanol m.p. 186–187°. The melting point was undepressed when mixed with an authentic sample.

Anal. Calcd. for $C_{11}H_{19}ON_3$: C, 63.1; H, 9.09; N, 20.09. Found: C, 62.9; H, 9.0; N, 20.1.

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[14] Prepared in 60% yield from crude 1-methylcyclopentanol, obtained through the condensation of methylmagnesium iodide and cyclopentanone and subsequent dehydration by distillation in presence of a trace of iodine.