were 9.3 min. and 13.2 min., respectively. The yields, determined by peak area measurements and adjusted on the basis of the total amount of the ketonic material, were 30.2% and 5.7% for the respective isomers. The refractive index, ultraviolet spectra, and the 2,4-dinitrophenylhydrazone derivatives of each ketone were obtained on pure samples by trapping the helium off-gas from the fractometer. Twenty successive trappings of 8-microliter samples were sufficient to obtain enough material for these determinations.

2-Isopropyl-2-cyclohexenone (30.2%), n^{20}_{D} 1.4769; λ_{max} 235 mμ, log. ε 4.20 (lit.[18b] n^{20}_{D} 1.4773; λ_{max} 235 mμ, log ε 3.82). The 2,4-dinitrophenylhydrazone derivative after two recrystallizations from chloroform–methanol was isolated as fine red needles, m.p. 186–187° (lit.[18b] 190–191°).

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 57.31; H, 5.77; N, 16.55. Found: C, 57.30; H, 5.92; N, 16.49.

2-Isopropylidenecyclohexanone (5.7%), n^{20}_{D} 1.4920; λ_{max} 254 mμ, log ε 4.02 (lit.[18b] n^{20}_{D} 1.4922; λ_{max} 254 mμ, log ε 3.80). The 2,4-dinitrophenylhydrazone derivative after two recrystallizations from chloroform–methanol was isolated as maroon needles, m.p. 181.5–182.5° (lit.[18b] m.p. 182–183°).

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 57.31; H, 5.77; N, 16.55. Found: C, 57.23; H, 5.64; N, 16.44.

7-Methyloctanamide.—Fractions 48–59 were combined and the chloroform was evaporated to yield 2.90 g. (57.2%) of 7-methyloctanamide which after a crystallization and sublimation (100° at 0.05 mm.) melted at 106.5–107.5° undepressed by admixture with an authentic sample prepared as previously described.

Reduction of the Ketonic Mixture.—A mixture of 0.50 g. of the crude ketonic mixture, isolated from the rearrangement, 0.1 g. of Raney nickel, and 10 ml. of 1,2-dichloroethane, was hydrogenated for 1.5 hr. at 60 p.s.i.g. The vessel was vented and the solution filtered and evaporated. The residue was treated with 2,4-dinitrophenyhydrazine reagent to give an orange precipitate. After two recrystallizations from chloroform–methanol, orange needles of 2-isopropylcyclohexanone 2,4-dinitrophenylhydrazone were obtained, m.p. 136.5–137°, undepressed by admixture with an authentic sample.

Cyclization of 7-Methyl-6-octenonitrile in Polyphosphoric Acid.—The unsaturated nitrile (1.00 g.) and 17 g. of polyphosphoric acid were heated at 125–130° for 10 min. The ketonic component was isolated as previously described and the mixture analyzed chromatographically to give 31.5% and 4.3% of 2-isopropyl-2-cyclohexenone and 2-isopropylidenecyclohexanone, respectively.

A General Route to Hydantoins

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A general method for preparing hydantoins directly from a variety of carbonyl derivatives is reported. In spite of the enhanced stability normally exhibited by such derivatives, the reaction appears to be equivalent to that observed with the parent carbonyl compounds. As such, it provides a useful extension to the general route to α-amino acids from carbonyl compounds *via* a hydantoin intermediate.

Hydantoins, because of their pronounced stability and availability from a variety of carbonyl compounds, find general utility as precursors of α-amino acids.[2,3] One limitation imposed on their use in this capacity stems from the fact that the carbonyl compound is not always readily accessible. Such is the case in the synthesis of tryptophan from 5-(3′-indolylmethyl)hydantoin, the parent 3-indoleacetaldehyde being difficult to prepare and handle because of its limited stability.[4,5]

Recently reported work on the synthesis of tryptophan[6] has demonstrated the feasibility of preparing 5-(3′-indolylmethyl)hydantoin from 3-indoleacetaldehyde semicarbazone, a stable and readily accessible derivative of 3-indoleacetaldehyde.[5] The demonstration of this reaction has prompted the examination of various other carbonyl derivatives as precursors of the corresponding hydantoins. It can now be reported that hydantoin formation has been observed with a sufficient variety of these derivatives to indicate the general nature of the reaction. Since carbonyl derivatives are inherently more stable than the parent carbonyl compounds, it is felt this provides a useful extension to the general method of preparing α-amino acids from carbonyl compounds *via* a hydantoin intermediate.

Types of carbonyl derivatives found to be operable include semicarbazones, thiosemicarbazones, oximes, azines, phenylhydrazones, imidazolidines, and azomethines. Indications are that these derivatives respond in an equivalent manner whether they are derived from an aldehyde or ketone. The reaction conditions used parallel closely those normally employed to prepare a hydantoin from a free carbonyl compound, namely—treatment of the particular carbonyl derivative with an excess of hydrogen cyanide and ammonium carbonate. A reasonable rate of reaction was observed in most cases operating under oxygen-free conditions at 100° under autogenous pressure. The addition of sodium bisulfite (two to two hundred molar per cent based on the carbonyl derivative) frequently improved the yield of hydantoin but was not es-

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[1] Present address: Weyerhaeuser Timber Company, 413 Stoneway, Seattle 13, Washington.

[2] E. Ware, *Chem. Rev.*, **46**, 403 (1950).

[3] H. T. Bucherer and W. Steiner, *J. prakt. Chem.*, **140**, 291 (1934).

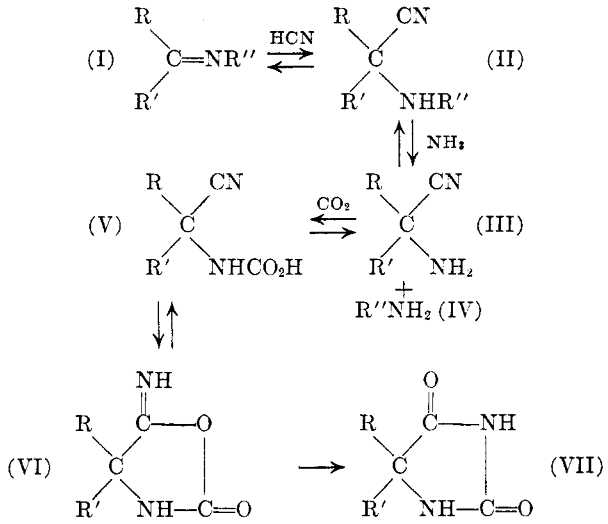
[4] J. B. Brown, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 3172 (1952).

[5] H. Plieninger and G. Werst, *Ber.*, **88**, 1956 (1955); **89**, 2783 (1956).

[6] J. N. Coker, W. L. Kohlhase, M. Fields, A. O. Rogers, and M. A. Stevens, *J. Org. Chem.*, **27**, 850 (1962).

sential. Of all the carbonyl derivatives examined, only α-acetoxypropionitrile (tried in a single experiment without sodium bisulfite) failed to yield a hydantoin product.

While the yield of hydantoin obtained with the various types of carbonyl derivatives was somewhat variable, the extent to which the reaction took place appears to be unrelated to the hydrolytic stability of the starting material. For example, 3-indoleacetaldehyde semicarbazone is reported to be incapable of undergoing to any appreciable extent hydrolysis to 3-indoleacetaldehyde.[5] Nevertheless this compound was converted into 5-(3′-indolylmethyl)hydantoin in 66% yield. On the other hand, a comparable yield (59%) was obtained with 3-indoleacetaldehyde oxime, a compound which should be appreciably easier to hydrolyze. Thus it would appear that the reaction does not involve the free carbonyl compound as such as an intermediate. The following mechanism for the reaction is therefore proposed.



R	R′	=NR″	% Yield of Hydantoin (VII)
3-Indolyl	H	$=NNHCONH_2$	66
3-Indolyl	H	$=NOH$	59[a]
3-Indolyl	H	$-(NC_6H_4CH)_2CH_2N(C_6H_4)-$	75[a]
1-Acetyl-3-indolyl	H	$=NNHCONH_2$	64
1-Acetyl-3-indolyl	H	$=NOH$	5[a]
1-Acetyl-3-indolyl	H	$=NNHC_6H_5$	61[a]
1-Acetyl-3-indolyl	H	$-N(C_6H_4)CH_2CH_2N(C_6H_4)-$	24[a]
n-C_3H_7	H	$=NNHCONH_2$	47
n-C_3H_7	H	$=NOH$	29
n-C_3H_7	H	$=NNHC_6H_5$	34[a]
C_6H_5	H	$=NNHCONH_2$	28[a]
C_6H_5	H	$=NN=CHC_6H_5$	54[a]
C_6H_5	H	$=NC_6H_5$	81[a]
C_6H_5	H	$=NCH_3$	56[a]
$-CH_2CH_2CH_2CH_2-$		$=NNHCSNH_2$	43[a]
$-CH_2CH_2CH_2CH_2-$		$=NOH$	..[a]
i-C_4H_9	CH_3	$=NN=C(CH_3)i$-C_4H_9	61[a]

[a] Formed in the presence of sodium bisulfite.

In the initial step hydrogen cyanide adds to the azomethine bond to produce a substituted aminonitrile (II). Reaction of the latter with ammonia regenerates the carbonyl reagent (IV) yielding the corresponding aminonitrile (III) which then reacts with carbon dioxide to form a cyanocarbamic acid (V). This is followed by ring closure to yield the hydantoin (VII). All reactions prior to the one involving formation of the hydantoin ring should be reversible. The driving force of the reaction sequence would be the irreversible transformation of intermediate VI into the stable hydantoin product (VII). The presence of sodium bisulfite most likely facilitates the initial reaction in this sequence—namely, the addition of hydrogen cyanide to the carbonyl derivative (I).[7]

The work of Plieninger and Werst[5] has provided the basis for preparing the derivatives of 3-indoleacetaldehyde and 1-acetyl-3-indoleacetaldehyde considered in this investigation. The semicarbazone and 1,3-diphenylimidazolidine derivatives were obtained by hydrogenation of either 3-indoleacetonitrile or 1-acetyl-3-indoleacetonitrile in the presence of the appropriate carbonyl reagent. The other 3-indoleacetaldehyde derivatives were prepared from the free aldehydes, the procedures used being described in the Experimental. As for the other carbonyl derivatives examined in this investigation, these are known compounds and were derived from the respective carbonyl compounds by conventional procedures.

Experimental[8]

Derivatives of 3-Indoleacetaldehyde. 1. 3-Indoleacetaldehyde Oxime.—Hydroxylamine hydrochloride (0.14 g., 0.002 mole) and sodium hydroxide (0.08 g., 0.002 mole) were dissolved in 5 ml. of distilled water. 3-Indoleacetaldehyde in 10 ml. of absolute ethanol was added and the mixture heated for 0.5 hr. on a steam bath. Removal of the solvent *in vacuo* left a brown residue which after trituration with water consisted largely of 3-indoleacetaldehyde oxime. The crude product (0.30 g., 0.00172 mole; 86% based on the 0.70 g. 1,3-diphenyl-2-(3′-indolylmethyl)imidazolidine used to prepare the free aldehyde) melted at 124–130°. Recrystallization of the product from hot aqueous ethanol raised its melting point to 140–142°.

Anal. Calcd. for $C_{10}H_{10}ON_2$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.30; H, 5.81; N, 16.21.

2. **3-Indoleacetaldehyde Phenylhydrazone.**—Phenylhydrazine (0.32 g., 0.003 mole) was dissolved in 5 ml. of abolute ethanol and 1.5 ml. of water was added. The resulting solution was mixed with 5 ml. of ethanol containing 3-indoleacetaldehyde and the mixture allowed to stand for several days. Cooling yielded 3-indoleacetaldehyde phenylhydrazone [0.51 g., 0.00204 mole, 68% based on the 0.0030 mole of 1,3-diphenyl-2-(3′-indoylmethyl)imidazolidine used to prepare the free aldehyde]. After recrystallization from aqueous methanol, the crystalline product melted at 112–113°.

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(7) E. Knoevenagel and E. Merklin, *Ber.*, **37**, 4087 (1904).

(8) All melting points are uncorrected. The preparation of 5-(3′-indolylmethyl)hydantoin from 3-indoleacetaldehyde semicarbazone and from 1-acetyl-3-indoleacetaldehyde semicarbazone, in yields of 66% and 64%, respectively, has already been reported.[6]

Anal. Calcd. for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.85. Found: C, 77.13; H, 6.16; N, 17.32.

Derivatives of 1-Acetyl-3-indoleacetaldehyde. 1. 1-Acetyl-3-indoleacetaldehyde Oxime.—Hydroxylamine hydrochloride (0.70 g., 0.010 mole) and freshly fused sodium acetate (1.0 g., 0.012 mole) were refluxed in 15 ml. of dry methanol for 0.25 hr. The mixture was cooled and filtered to remove the precipitated sodium chloride. The filtrate was then added to a solution of 1-acetyl-3-indoleacetaldehyde (2.0 g., 0.010 mole) in 15 ml. of dry methanol and the resulting mixture heated at gentle reflux for 0.25 hr. After the volume of the mixture had been reduced *in vacuo* to 4–5 ml. and allowed to stand at 0–5° for several hours, 1-acetyl-3-indoleacetaldehyde oxime precipitated as pale yellow crystals (1.5 g., 0.007 mole, 70%). After a single recrystallization from methanol, the product melted at 137–138°.

Anal. Calcd. for $C_{12}H_{12}O_2N$: C, 66.67; H, 5.56; N, 12.96. Found: C, 66.96; H, 5.82; N, 12.83.

2. 1-Acetyl-3-indoleacetaldehyde Phenylhydrazone.—1-Acetyl-3-indoleacetaldehyde (0.10 g., 0.005 mole), phenylhydrazine hydrochloride (0.10 g., 0.0007 mole), and sodium acetate trihydrate (0.15 g., 0.0011 mole) in 15 ml. of methanol were refluxed for 0.25 hr. The hot solution was filtered to remove the precipitated sodium chloride and then concentrated *in vacuo* to a volume of 6–8 ml. Cooling produced 1-acetyl-3-indoleacetaldehyde phenylhydrazone as pale yellow needles in a yield of 0.15 g. (0.005 mole, 100%). After a single recrystallization from methanol the product melted at 122–124°.

Anal. Calcd. for $C_{18}H_{17}ON_3$: C, 74.23; H, 5.84; N, 14.43. Found: C, 74.21; H, 5.75; N, 14.52.

Preparation of 5-(3′-Indolylmethyl)hydantoin. 1. From 3-Indoleacetaldehyde Oxime.—A mixture of 3-indoleacetaldehyde oxime (1.20 g., 0.0069 mole), sodium bisulfite (0.18 g., 0.0017 mole), ammonium carbonate (4.33 g., 0.027 mole), hydrogen cyanide (0.75 g., 0.027 mole), 25 ml. of methanol, and 25 ml. of water was heated at 100° under autogenous pressure for 3.5 hr. in a Hastelloy B-lined tube. The product mixture was taken to dryness *in vacuo* and extracted with two 10-ml. portions of water, leaving a white residue. Extraction of the latter with 12.5 ml. of boiling water followed by cooling the extract yielded crude 5-(3′-indolylmethyl)hydantoin (0.93 g., 59%; m.p. 205–215°). Recrystallization of the hydantoin, once from water and once from methanol, gave white crystals melting at 219–221°.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.88; H, 4.83; N, 18.33. Found: C, 62.89; H, 4.89; N, 18.19.

2. From 1,3-Diphenyl-2(3′-indolylmethyl)imidazolidine.—A Hastelloy B-lined shaker tube was charged with 1,3-diphenyl-2(3′-indolylmethyl)imidazolidine (2.12 g., 0.006 mole[5]), sodium bisulfite (1.25 g., 0.012 mole), ammonium carbonate (3.77 g., 0.033 mole), hydrogen cyanide (0.65 g., 0.024 mole), 30 ml. of water, and 20 ml. of methanol. The resulting mixture, after heating for 3.5 hr. at 100° under autogenous pressure, was evaporated to dryness *in vacuo*. Salts were removed from the residue by extraction with 25 ml. of cold water and organic by-products by extraction with 35 ml. of benzene. The residue consisted of crude hydantoin (1.03 g., 75%; m.p. 212–218°). After recrystallization from methanol, then water, the product melted at 219–222°.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.88; H, 4.83; N, 18.33. Found: C, 62.95; H, 4.87; N, 18.49.

3. From 1-Acetyl-3-indoleacetaldehyde Oxime.—1-Acetyl-3-indoleacetaldehyde oxime (1.0 g., 0.0046 mole), ammonium carbonate (4.0 g., 0.042 mole), hydrogen cyanide (2.0 g., 0.074 mole), sodium bisulfite (0.1 g., 0.001 mole), 30 ml. of water, and 30 ml. of methanol were placed in a Hastelloy B-lined tube and heated at 100° for 4 hr. under autogenous pressure. The resulting mixture was taken to dryness *in vacuo*, yielding an oily residue. The latter, after extraction initially with hot water, then with hot methanol, consisted of the crude hydantoin. One recrystallization from methanol yielded a product (0.05 g., 5%; m.p. 221–222°) which did not depress the melting point of an authentic sample of 5-(3′-indolylmethyl)hydantoin.

4. From 1,3-Diphenyl-2-(1′-acetyl-3′-indolylmethyl)-imidazolidine.—1,3-Diphenyl-2-(1′-acetyl-3′-indolylmethyl) imidazolidine (3.0 g., 0.0076 mole), ammonium carbonate (6.0 g., 0.063 mole), hydrogen cyanide (2.0 g., 0.074 mole), sodium bisulfite (0.1 g., 0.001 mole), 30 ml. of methanol, and 30 ml. of water reacted using the conditions described above. The resulting product mixture was taken to dryness *in vacuo*. The residue after extraction with three 5-ml. portions of ether was obtained as a pale yellow solid (0.0018 g., 24%) which after a single recrystallization from methanol melted at 215–218°. The recrystallized product did not depress appreciably the melting point of an authentic sample of 5-(3′-indolylmethyl)hydantoin.

5. From 1-Acetyl-3-indoleacetaldehyde Phenylhydrazone.—The reaction was carried out in the manner described in the previous sections using 1-acetyl-3-indoleacetaldehyde phenylhydrazone (0.99 g., 0.004 mole), ammonium carbonate (2.50 g., 0.022 mole), sodium bisulfite (0.82 g., 0.008 mole), hydrogen cyanide (0.43 g., 0.016 mole), 35 ml. of water, and 15 ml. of methanol. Evaporation of the product mixture to dryness yielded a partially crystallized mass. The latter upon extraction with 60 ml. of hot water yielded crude hydantoin (0.55 g., 61%; m.p. 212–220°). Recrystallization of this product, first from water, then from methanol, and finally from water, yielded a material melting at 220–222°.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.88; H, 4.83; N, 18.33. Found: C, 62.85; H, 4.72; N, 18.30.

5-*n*-Propylhydantoin. 1. From *n*-Butyraldehyde Semicarbazone.—A Carius tube was charged with *n*-butylraldehyde semicarbazone (4.5 g., 0.035 mole), ammonium carbonate (5.5 g., 0.056 mole), hydrogen cyanide (1.5 g., 0.056 mole), and 35 ml. of water. The tube was sealed and heated for 4 hr. at 100°. Upon discharging from the tube, the reaction mixture was cooled to induce crystallization of the product. The latter was then removed by filtration and air-dried. It amounted to 2.3 g. (47%). After a single recrystallization from water the product melted at 133–135° and did not depress appreciably the melting point of 134–135° exhibited by an authentic sample of 5-*n*-propylhydantoin.

2. From *n*-Butyraldehyde Oxime.—Using the above procedure, *n*-butyraldehyde oxime (3.04 g., 0.035 mole), ammonium carbonate (5.5 g., 0.055 mole), hydrogen cyanide (1.5 g., 0.056 mole), in 10 ml. of water, and 10 ml. of methanol yielded 5-*n*-propylhydantoin (1.4 g., 0.010 mole, 29%) which after one recrystallization from water melted at 134–136°.

Anal. Calcd. for $C_6H_{10}O_2N_2$: C, 50.70; H, 7.04; N, 19.42. Found: C, 50.92; H, 7.24; N, 19.66.

3. From *n*-Butyraldehyde Phenylhydrazone.—Reaction of *n*-butyraldehyde phenylhydrazone (11.4 g., 0.070 mole) with ammonium carbonate (11.0 g., 0.110 mole), sodium bisulfite (1.0 g., 0.010 mole), and hydrogen cyanide (3.0 g., 0.110 mole) in 40 ml. of water and 40 ml. of methanol for 6 hr. at 100° gave 5-*n*-propylhydantoin (3.4 g., 0.024 mole, 34%). The product after one recrystallization from water melted at 135–137°. It did not depress the melting point of an authentic sample of 5-*n*-propylhydantoin.

5-Phenylhydantoin.[9] 1. From Benzaldehyde Semicarbazone.—Reaction of benzaldehyde semicarbazone (6.5 g., 0.040 mole), ammonium carbonate (5.5 g., 0.55 mole), hydrogen cyanide (0.7 g., 0.026 mole), and sodium bisulfite (20.0 g., 0.20 mole) in 80 ml. of methanol and 1 ml. of water at 100° for 4 hr. yielded 5-phenylhydantoin (2.0 g., 0.011 mole, 28%). After one recrystallization from ethanol the compound melted at 183–185°.

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(9) Difficulty was encountered in separating 5-phenylhydantoin from its monohydrate; this is believed to be responsible for the observed carbon-nitrogen values being higher than those expected for the monohydrate.

Anal. Calcd. for $C_9H_8N_2O_2.H_2O$: C, 55.66; H, 5.19; N, 14.43. Found: C, 56.21; H, 4.74; N, 14.82.

2. **From Dibenzalazine.**—5-Phenylhydantoin has been prepared in 54% yield by treating dibenzalazine under the above conditions. The compound melted at 180–182° and did not depress appreciably the melting point of an authentic sample of 5-phenylhydantoin.

3. **From N-Benzylidine Aniline.**—A mixture of N-benzylidine aniline (12.7 g., 0.070 mole), ammonium carbonate (11.0 g., 0.110 mole), sodium bisulfite (1.0 g., 0.010 mole), hydrogen cyanide (3.0 g., 0.110 mole), 40 ml. of methanol, and 40 ml. of water was heated at 100° for 4 hr. under autogenous pressure. 5-Phenylhydantoin was isolated in 81% (10.0 g., 0.057 mole). After one recrystallization from ethanol, the compound melted at 181–183° and did not depress the melting point of an authentic sample of 5-phenylhydantoin.

4. **From N-Benzylidinemethylamine.**—A mixture of N-benzylidinemethylamine (8.4 g., 0.017 mole), sodium bisulfite (1.0 g., 0.010 mole), hydrogen cyanide (3.0 g., 0.110 mole), 40 ml. of methanol, and 40 ml. of water reacted as above. The product (7.0 g., 0.040 mole; 56%) after recrystallization from ethanol melted at 182–184°. It did not depress the melting point of an authentic sample of 5-phenylhydantoin.

1,3-Diazaspiro[4.4]nonane-2,4-dione. 1. From Cyclopentanone Thiosemicarbazone.—A mixture of cyclopentanone thiosemicarbazone (10.0 g., 0.063 mole), ammonium carbonate (11.0 g., 0.110 mole), hydrogen cyanide (1.5 g., 0.056 mole), sodium bisulfite (3.0 g., 0.030 mole), 50 ml. of water, and 50 ml. of ethanol was heated 4 hr. at 120° under autogenous pressure. Cooling the resulting product mixture yielded thiosemicarbazide (2.6 g., 0.028 mole; m.p. 181–182°) which was regenerated in the reaction. The filtrate was taken to dryness *in vacuo* and the crystalline mass obtained extracted with 100 ml. of chloroform. The residue was then extracted with 30 ml. of ethanol. The latter extract was concentrated to about 10 ml. and cooled to yield the product (4.1 g., 0.027 mole, 43%) as a crystalline mass. It melted at 208–210°.

Anal. Calcd. for $C_7H_{10}O_2N_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.37; H, 6.42; N, 18.16.

2. **From Cyclopentanone Oxime.**—The above procedure was used to convert cyclopentanone oxime to 1,3-diazaspiro-[4.4]nonane-2,4-dione. The product melted at 208–210°.

Anal. Calcd. for $C_7H_{10}O_2N_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.37; H, 6.48; N, 18.19.

5-Methyl-5-*i*-butylhydantoin from Methyl *i*-Butyl Ketone Azine.—Reaction of methyl *i*-butyl ketone azine (6.8 g., 0.035 mole), ammonium carbonate (11.0 g., 0.110 mole), sodium bisulfite (1.0 g., 0.010 mole), and hydrogen cyanide (3.0 g., 0.110 mole) in 40 ml. of methanol and 40 ml. of water yielded 5-methyl-5-*i*-butylhydantoin (7.3 g., 0.043 mole, 61%). The product melted at 146–147°.

Anal. Calcd. for $C_8H_{14}O_2N_2$: C, 56.47; H, 8.24; N, 16.47. Found: C, 56.62; H, 8.57; N, 16.63.

In the absence of sodium bisulfite, 5-methyl-5-*i*-butylhydantoin was obtained in only 28% yield.

Arnidiol and Faradiol

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Evidence is presented that the hydroxyl functions of arnidiol and faradiol are located at positions 3 and 12 of the taraxastane skeleton.

Arnidiol and faradiol are pentacyclic triterpenoid diols which frequently occur together and are separable only with considerable difficulty. They were first isolated from the blossoms of *Arnica montana L.* and *Tussilago Farfara* and characterized by Klobb[1]; more extensive work by Dieterle and co-workers[2] indicated that they were isomers of empirical formula, $C_{30}H_{50}O_2$, containing two hydroxyl groups and an ethylenic bond. An extensive survey of the occurrence of these diols was made by Zimmermann,[3] who confirmed the assigned empirical formulas and succeeded in isolating pure arnidiol and faradiol.

Chromic acid oxidation[4] of the unsaturated diols yielded the diketones, arnidione and faradione which differ; the saturated diols, dihydroarnidiol and dihydrofaradiol, obtained by catalytic hydrogenation, also differ. Dihydroarnidione and dihydrofaradione, however, have been shown to be identical by Jeger and Lardelli,[5] thus establishing that arnidiol and faradiol differ in the location of the ethylenic bond and the configuration of at least one hydroxyl group. Since arnidione, on Wolff-Kishner reduction, gave taraxastene (I) and faradione gave ψ-taraxastene (II),[4] the constitutions of which were later elucidated,[6] the parent pentacyclic taraxastane skeleton of the naturally occurring diols was established. The reported acid isomerization of arnidione (*x,y*-diketotaraxast-20(30)-ene) to faradione (*x,y*-diketotaraxast-20-ene) clearly paralleled the conversion of I to II. The mixture of arnidiol and faradiol used in this investigation was obtained either from marigold flowers (*Calendula officinalis*) as previously described[7] or from arnica flowers (see Experi-

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