

5-Hydroxy-1,3,4,5-tetrahydrobenz[cd]indole Isopropyl-Ether (XVII).—To a solution of 50 mg. of aluminum in 10 ml. of absolute isopropyl alcohol was added 171 mg. (0.001 mole) of the ketone (VIII) and the mixture maintained at reflux temperature for four hours. The isopropyl alcohol was distilled under diminished pressure and the residue extracted with ether and 10% sodium hydroxide solution. The residue from the washed and dried ether solution was recrystallized from a mixture of ethanol and water; yield 138 mg. (64%); m. p. 131–132°. The compound did not react with *p*-nitrobenzoyl chloride or with phenyl isocyanate.

Anal. Calcd. for $C_{14}H_{17}NO$: C, 78.11; H, 7.96. Found: C, 78.11; H, 7.91.

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pany, Indianapolis, Indiana. The author is indebted to Louis S. Harris for assistance in certain of the experiments.

Summary

A synthesis of 4-substituted indoles has been developed. 4-Cyanoindole has been converted through the Mannich base to β -(4-carboxy-3-indole)-propionic acid, and cyclization of the dicarboxylic acid has afforded a new synthesis of the tricyclic 1,3,4,5-tetrahydrobenz[cd]indole ring system.

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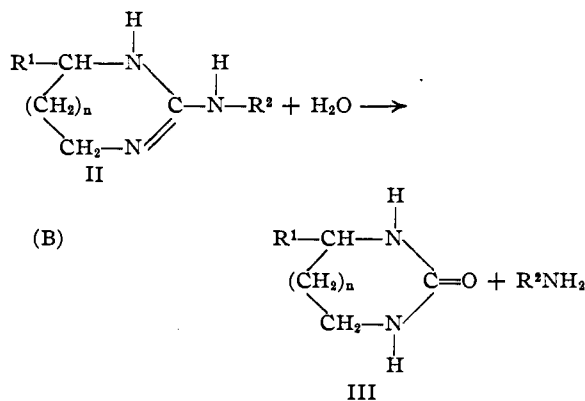
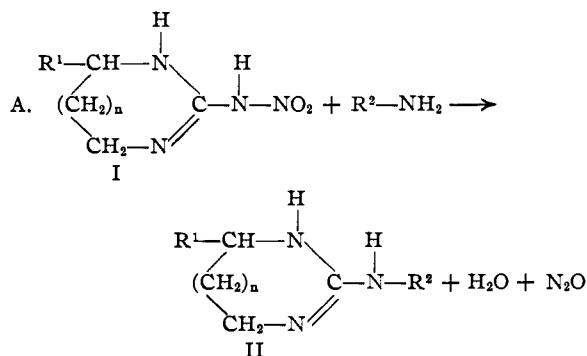
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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, QUEEN'S UNIVERSITY, AND THE RESEARCH AND BIOLOGICAL LABORATORIES, AYERST, MCKENNA AND HARRISON, LTD., MONTREAL]

The Reaction of Primary Amines with 2-Nitramino- Δ^2 -1,3-diazacycloalkenes

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When 2-nitramino- Δ^2 -1,3-diazacycloalkenes¹ I are heated in the presence of primary amines a rapid evolution of gas occurs and the nitramino group is replaced by a substituted amino group. This reaction is analogous to the one described by Davis and Elderfield² in the preparation of *sym*-dibutylguanidine from *N*-butyl-*N*¹-nitroguanidine and butylamine in the presence of water. On the other hand, *N*-methyl-*N*¹-nitroguanidine and *N*-ethyl-*N*¹-nitroguanidine on heating with aqueous methylamine and aqueous ethylamine respectively gave the corresponding alkylureas. This would be expected because of the large volumes of water used by these authors. A. W. Hofmann³ found that *sym*-triethylguanidine monohydrate on distillation decomposed into ethylamine and *sym*-diethylurea. Therefore, in order to eliminate the formation of cyclic ureas the 2-nitramino- Δ^2 -1,3-diazacycloalkenes I were heated with the anhydrous amines (reaction A). Water, however, is produced during this reaction in sufficient quantities to effect hydrolysis of part of the product II by reaction B.



$\text{R}^1 = \text{CH}_3$ or H; $\text{R}^2 = \text{alkyl}$ or aralkyl; $n = 0$ or 1

The 1,3-diazacyclopentene-2 I ($n = 0$) compounds displayed less tendency to form urea derivatives than the 1,3-diazacyclohexene-2 I ($n = 1$) compounds. On heating 2-nitramino- Δ^2 -1,3-diazacyclopentene or 2-nitramino- Δ^2 -1,3-diazacyclohexene with a primary amine until gas evolution ceased the former compound gave 4–8% 1,3-diazacyclopentanone-2 III ($n = 0$, $\text{R}^1 = \text{H}$) while the latter gave a 22% yield of 1,3-diazacyclohexanone-2 III ($n = 1$; $\text{R}^1 = \text{H}$). These yields of cyclic ureas were decreased considerably by using a large excess (2–10 mole equivalents) of the amine which was slowly distilled during the course of the reaction. This excess amine on slow distillation carried with it the water produced during the reaction. The 2-alkylamino- and 2-aralkylamino- Δ^2 -1,3-diazacycloalkenes prepared in this manner are recorded along with their properties in Table I.

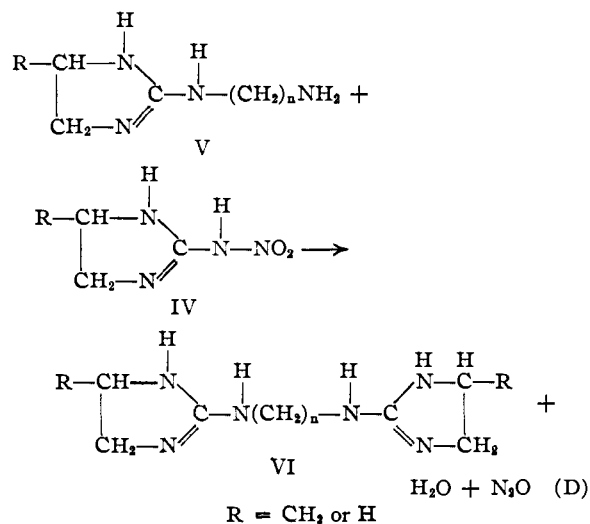
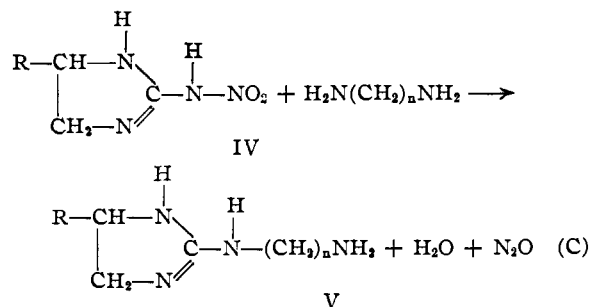
The formation of cyclic urea derivatives by the reaction of water with the 2-alkylamino- or 2-aralkylamino- Δ^2 -1,3-diazacycloalkenes II rather than with the corresponding 2-nitramino- Δ^2 -1,3-diazacycloalkenes I was verified by refluxing

(1) A. F. McKay and G. F. Wright, *THIS JOURNAL*, **70**, 430 (1948).
 (2) T. L. Davis and R. C. Elderfield, *ibid.*, **55**, 731 (1933).
 (3) A. W. Hofmann, *Jahresber. Fortschr. Chem.*, 516 (1861).

both types of compounds in water for a period of eight hours. 2-Nitramino-1,3-diazacyclohexene-2 was recovered unchanged while (4 or 6)-methyl-2-benzylamino-1,3-diazacyclohexene-2 gave a 58% yield of 4-methyl-1,3-diazacyclohexanone-2 III ($n = 1$, $R^1 = CH_3$).

During the course of these studies 1,3-diazacyclohexanone-2 and 4-methyl-1,3-diazacyclohexanone-2 were isolated and characterized. 1,3-Diazacyclohexanone-2⁴ and 4-methyl-1,3-diazacyclohexanone-2⁵ have been described previously.

When diamines, e. g., ethylenediamine, are used in place of primary amines, then two products may be obtained



The expected compounds N-2-[4(or 5)-methyl-1,3-diazacyclopentene-2]-ethylenediamine V ($R = CH_3$) and N,N¹-2-[4(or 5)-methyl-1,3-diazacyclopentene-2]-ethylenediamine VI ($R = CH_3$) were obtained when ethylenediamine and 4 (or 5)-methyl-2-nitramino-1,3-diazacyclopentene-2 IV ($R = CH_3$) were heated together. On heating 2-nitramino-1,3-diazacyclopentene-2 IV ($R = H$) in a large excess of ethylenediamine V ($R = H$) was obtained. These compounds are described in Table I.

In the compounds prepared by reactions A, C

(4) E. Fischer and H. Koch, *Ann.*, **232**, 224 (1886); A. P. N. Franchimont and H. Friedmann, *Rec. trav. chim.*, **26**, 218 (1907).

(5) J. Tafel and A. Weinschenk, *Ber.*, **33**, 3378 (1900).

and D, the double bond has been placed in the ring in agreement with the parent 2-nitramino- Δ^2 -1,3-diazacycloalkenes¹ and the results of the hydrolysis studies.

Acknowledgment.—The authors wish to thank Dr. A. S. Cook of Ayerst, McKenna and Harrison, Ltd., for a Grant-in-aid of this work and Miss C. Jockel of Ayerst, McKenna and Harrison Laboratories for the microanalyses.

Experimental

Preparation of 2-Alkylamino- Δ^2 -1,3-diazacyclopentenes.

—A mixture of the 2-nitramino-1,3-diazacyclopentene-2 with 1.1 to 4 mole equivalents of primary amine and xylene was heated under reflux for ten to thirty minutes. This was the time required for cessation of gas evolution which indicated that the reaction had gone to completion. The larger molar excesses of amines were used with the lower boiling amines. At the end of the reaction period the reaction mixture was distilled at atmospheric pressure until the vapor temperature reached 140°. The residue was then distilled at reduced pressure (0.1–5 mm.) to give the desired products as colorless crystalline solids or oils. The yields of 2-alkylamino- Δ^2 -1,3-diazacyclopentenes varied from 94.7–99% by theory. The picrates were formed by dissolving 0.5–1.0 g. of the 2-alkylamino- Δ^2 -1,3-diazacyclopentenes in a minimum of hot water and adding saturated picric acid solution until precipitation was complete. The crystalline picrates were recrystallized from water to a constant melting point and analyzed.

2-Benzylamino-1,3-diazacyclopentene-2.—A mixture of 74.6 g. (0.697 mole) of benzylamine and 46.5 g. (0.357 mole) of 2-nitramino-1,3-diazacyclopentene-2 was gently heated until the evolution of gas had ceased. The solution was then distilled *in vacuo* (1.0 mm.) to give a colorless oil which solidified on cooling, yield 60.7 g. (97%). The picrate of this compound was formed by dissolving 0.5 g. in a minimum amount of hot water and adding a saturated solution of picric acid. After two recrystallizations from water it melted at 150.5–151.5°.

2-(β -Phenylethylamino)-1,3-diazacyclopentene-2.—Twenty-six grams (0.20 mole) of 2-nitramino-1,3-diazacyclopentene-2 and 48.5 g. (0.40 mole) of β -phenylethylamine were heated together cautiously to effect slow distillation of the excess amine. After the completion of gas evolution, the remaining liquid was distilled at reduced pressure. The distillate was a water-white oil which solidified on cooling, yield 35.6 g. (94.2%). The picrate was formed in the usual manner, and after two recrystallizations from water melted at 186.4–186.9°.

N- α -Naphthyl-N¹-1,3-diazacyclopentene-2-ethylenediamine.—A suspension of 5.9 g. (0.045 mole) of 2-nitramino-1,3-diazacyclopentene-2 and 8.4 g. (0.045 mole) of N- α -naphthylethylenediamine in 15 cc. of xylene was heated for twenty-five minutes. On cooling the reaction mixture solidified. This solid was triturated with ether (30 cc.) then filtered, washed with fresh ether (30 cc.) and dried. The crude yield was 9.2 g. (80.6%) which melted at 151–157°. A wasteful crystallization of 2.04 g. from 15 cc. of 95% ethanol raised the melting point to 175°. A sample of this material was converted to the picrate in the usual way and after two recrystallizations from water deep-red needles which melted at 144.8–145.6° were obtained.

2-Benzylamino-1,3-diazacyclohexene-2.—Seventy-two grams (0.50 mole) of 2-nitramino-1,3-diazacyclohexene-2 was added to 172 g. (1.60 mole) of benzylamine and heated to a temperature sufficient to maintain a slow rate of distillation of the excess benzylamine. This distillation at atmospheric pressure was continued until gas evolution ceased after which the residue was distilled *in vacuo*. A crystalline distillate of the desired product mixed with propylene urea (1,3-diazacyclohexanone-2) was obtained, yield 80.3 g. The cyclic urea by-product was separated by treating the distillate with sufficient chloroform to dis-

TABLE I

| Compound | Yield, % | °C. ^b | B. p. Mm. |
|---|-------------------|--------------------|-----------|
| 2-Butylamino-1,3-diazacyclopentene-2 | 97.5 | 140 | 0.5 |
| 2-Isobutylamino-1,3-diazacyclopentene-2 | 96.0 | 144 | 0.5 |
| 2-Amylamino-1,3-diazacyclopentene-2 | 96.0 | 158 | 0.1 |
| N- α -Naphthyl-N ¹ -1,3-diazacyclopentene-2-ethylenediamine | 80.6 | N. D. ^f | .. |
| 2- β -Phenylethylamino-1,3-diazacyclopentene-2 | 94.2 | 215 | 1.0 |
| 2-Benzylamino-1,3-diazacyclopentene-2 | 97.0 | 195 | 1.0 |
| 4(or 5)-Methyl-2-butylamino-1,3-diazacyclopentene-2 | 94.7 | 175 | 1.0 |
| 4(or 5)-Methyl-2-isobutylamino-1,3-diazacyclopentene-2 | 99.0 | 133 | 0.09 |
| 4(or 5)-Methyl-2-amylamino-1,3-diazacyclopentene-2 | 98.0 | | .. |
| 2-Benzylamino-1,3-diazacyclohexene-2 | 77.5 | 165-172 | 0.1 |
| 2- β -Phenylethylamino-1,3-diazacyclohexene-2 | 76.6 | | ... |
| 4(or 6)-Methyl-2-(3-diethylaminopropylamino)-1,3-diazacyclohexene-2 | 78.2 | 180 | 1.0 |
| 4(or 6)-Methyl-2-benzylamino-1,3-diazacyclohexene-2 | 92.0 | 172-175 | 0.1 |
| 4(or 6)-Methyl-2- β -phenylethylamino-1,3-diazacyclohexene-2 | 76.0 | 180 | .1 |
| 4(or 6)-Methyl-2- β -hydroxyethylamino-1,3-diazacyclohexene-2 | 98.0 | 180 | .1 |
| N-2-(1,3-Diazacyclopentene-2)-ethylenediamine | 78.1 | 183-191 | .7 |
| N-2-(4(or 5)-Methyl-1,3-diazacyclopentene-2)-ethylenediamine | 72.0 ^a | 184-187 | .05 |
| N,N ¹ -2-(4(or 5)-Methyl-1,3-diazacyclopentene-2)-ethylenediamine | 17.0 ^a | 250-260 | .2 |

^a Both compounds obtained in the same reaction, total yield 89.0%. ^b These boiling points are high because the pressure in the distillation apparatus was found to be higher than that recorded by the manometer. ^c All melting points uncorrected. ^d Dipicrates. ^e This picrate crystallized in two forms melting at 143-149° and 159-159.5°. ^f N. D. Not distilled.

solve the 2-benzylamino-1,3-diazacyclohexene-2. The chloroform-insoluble cyclic urea was then removed by filtration, washed with fresh chloroform (20 cc.), and dried, yield 7.0 g. (14%). This crude 1,3-diazacyclohexanone-2 melted at 260°. Two recrystallizations from 95% ethanol raised the melting point to 265-266°.

Anal. Calcd. for C₈H₈N₂O: C, 48.0; H, 8.00; N, 28.0. Found: C, 47.9; H, 8.02; N, 27.9.

The picrate was prepared by dissolving 0.6 g. of the cyclic urea in 15 cc. of water and adding 200 cc. of a saturated aqueous picric acid solution. The crystalline picrate (m. p. 188-189°) after two recrystallizations from water melted at 190-191°.

Anal. Calcd. for C₁₆H₁₁N₅O₅: C, 36.4; H, 3.34; N, 21.26. Found: C, 36.4; H, 3.30; N, 21.32.

Another aliquot of the cyclic urea on nitration by the method described by McKay and Wright⁶ gave an 86.0% yield of 1,3-dinitro-1,3-diazacyclohexanone-2 (m. p. 120-121°). This latter product did not depress the melting point of an authentic sample of 1,3-dinitro-1,3-diazacyclohexanone-2 (m. p. 121-122°).

The chloroform filtrate from the cyclic urea on evaporation gave 73.3 g. (77.5%) of 2-benzylamino-1,3-diazacyclohexene-2. Its picrate, made in the usual manner, was found to exist in two forms. Both are needles and can be crystallized from water, although this procedure sometimes converts one form into the other. The more common form melts at 147-148°, while the other melts at 159-159.5°. Both forms gave analytical values in agreement with the theoretical for the monopicate of 2-benzylamino-1,3-diazacyclohexene-2.

4(or 6)-Methyl-2-benzylamino-1,3-diazacyclohexene-2.—A large excess (36.9 g., 0.34 mole) of benzylamine was added to 6.5 g. (0.041 mole) of 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 in a Claisen flask having a six-cm. Vigreux column side-arm. The excess amine was then distilled at a rate sufficient to maintain the vapor temperature at 160° until the reaction was complete. This required thirty minutes. The residue was then distilled at reduced pressure. The distillate was a clear, viscous, light-yellow oil, yield 7.7 g. (92.5%). The monopicate prepared in the usual way melted at 128.7-129° after two recrystallizations from water.

(6) A. F. McKay and G. F. Wright, *THIS JOURNAL*, **70**, 3990 (1948).

2-(β -Phenylethylamino)-1,3-diazacyclohexene-2.—To 35 g. (0.289 mole) of boiling β -phenylethylamine, in the reaction flask of a distillation apparatus, was added 34.6 g. (0.240 mole) of 2-nitramino-1,3-diazacyclohexene-2 suspended in 73.1 g. (0.604 mole) of β -phenylethylamine. The sludge was added slowly, enough time being allowed between portions for the frothing from the previous addition to subside. After the addition was complete, the reaction mixture was slowly distilled until no further gassing could be observed. The residue was then distilled under reduced pressure. The main fraction contained some sublimed cyclic urea derivative. Separation of the 1,3-diazacyclohexanone-2 from the 2-(β -phenylethylamino)-1,3-diazacyclohexene-2 was effected by solution of the latter compound in xylene (3.25 cc./g.) and filtering off the insoluble cyclic urea. It melted at 263° alone and on admixture with an authentic sample of 1,3-diazacyclohexanone-2 (m. p. 265°), yield 2.7 g. (11.2%). After removal of the xylene from the filtrate 37.4 g. (76.8%) of 2-(β -phenylethylamino)-1,3-diazacyclohexene-2 was obtained. The picrate of this compound after six recrystallizations from water melted at 197-198°.

4(or 6)-Methyl-2-(β -phenylethylamino)-1,3-diazacyclohexene-2.—The distillation procedure was used in treating 30.9 g. (0.195 mole) of 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 with 48.5 g. (0.40 mole) of β -phenylethylamine. The slow distillation was continued for twenty-five minutes until gassing stopped. To the cooled (20°) reaction mixture ether (50 cc.) was added, and the insoluble 4-methyl-1,3-diazacyclohexanone-2 was filtered off and washed with ether (10 cc.). The white crystals which melted at 200.5-205°, were obtained in 18.46% yield (4.1 g.). The cyclic urea after two sublimations *in vacuo* (11 mm.) melted at 203.5-205°. A sample of the final sublimate was taken for analysis.

Anal. Calcd. for C₈H₁₀N₂O: C, 52.6; H, 8.77; N, 24.5. Found: C, 52.4; H, 8.92; N, 25.0.

After evaporation of the ether from the filtrate, it was distilled under reduced pressure. A viscous yellow oil was obtained, yield 32.2 g. (76%). The picrate was recrystallized four times from water and finally melted at 175.5-176.5°.

4(or 6)-Methyl-2-(3-diethylaminopropylamino)-1,3-diazacyclohexene-2.—A mixture of 23.7 g. (0.15 mole) of 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 and 52.1 g. (0.40 mole) of 3-diethylaminopropylamine was

TABLE I (Continued)

| Picrate (m. p., °C.) ^a | Formula | Analyses, % | | | | | |
|-----------------------------------|--|-------------|------|------|-------|------|------|
| | | Calcd. | | | Found | | |
| | | C | H | N | C | H | N |
| 173-174 | C ₁₃ H ₁₈ N ₆ O ₇ | 42.1 | 4.90 | 22.7 | 41.9 | 4.71 | 22.5 |
| 181-182 | C ₁₃ H ₁₈ N ₆ O ₇ | 42.1 | 4.90 | 22.7 | 42.3 | 4.87 | 22.8 |
| 154-155.5 | C ₁₄ H ₂₀ N ₆ O ₇ | 43.7 | 5.24 | 21.8 | 43.8 | 4.96 | 21.8 |
| 145.5 | C ₂₁ H ₂₁ N ₇ O ₇ | 52.1 | 4.38 | 20.3 | 52.2 | 4.35 | 20.3 |
| 186.4-186.9 | C ₁₇ H ₁₈ N ₆ O ₇ | 48.8 | 4.34 | 20.1 | 48.9 | 4.40 | 20.1 |
| 150.5-151.5 | C ₁₆ H ₁₆ N ₆ O ₇ | 47.5 | 3.99 | 20.8 | 47.3 | 4.07 | 21.0 |
| 136-137 | C ₁₄ H ₂₀ N ₆ O ₇ | 43.7 | 5.24 | 21.8 | 43.6 | 5.14 | 21.8 |
| 137-138 | C ₁₄ H ₂₀ N ₆ O ₇ | 43.7 | 5.24 | 21.8 | 44.1 | 5.46 | 21.7 |
| 142-143 | C ₁₅ H ₂₂ N ₆ O ₇ | 45.2 | 5.56 | 21.1 | 45.0 | 5.53 | 21.0 |
| 159-159.5 ^c | C ₁₇ H ₁₈ N ₆ O ₇ | 48.8 | 4.34 | 20.1 | 48.9 | 4.45 | 20.4 |
| 198.5-199.5 | C ₁₈ H ₂₀ N ₆ O ₇ | 50.0 | 4.66 | 19.4 | 50.1 | 4.84 | 19.8 |
| 141-142 | C ₂₄ H ₃₂ N ₁₀ O ₁₄ ^d | 42.1 | 4.70 | 20.5 | 42.0 | 4.80 | 20.9 |
| 128.7-129 | C ₁₈ H ₂₀ N ₆ O ₇ | 50.0 | 4.67 | 19.4 | 50.0 | 4.66 | 19.6 |
| 175.5-176.5 | C ₁₉ H ₂₂ N ₆ O ₇ | 51.1 | 4.97 | 18.8 | 51.0 | 4.97 | 19.0 |
| 135.4-136 | C ₁₃ H ₁₈ N ₆ O ₈ | 40.4 | 4.20 | 21.7 | 40.9 | 4.40 | 21.8 |
| 199-200 | C ₁₇ H ₁₈ N ₁₀ O ₁₄ ^d | 23.9 | 2.91 | 34.8 | 24.0 | 3.01 | 35.0 |
| 200-201 | C ₁₈ H ₂₀ N ₁₀ O ₁₄ ^d | 36.0 | 3.33 | 23.3 | 36.0 | 3.20 | 23.6 |
| 228-229 | C ₂₂ H ₂₆ N ₁₂ O ₁₄ ^d | 38.7 | 3.84 | 24.6 | 38.7 | 3.76 | 24.7 |

heated to distillation temperature and a slow rate of distillation was maintained until the reaction had gone to completion. The remaining excess of 3-diethylamino-propylamine was distilled over and the cooled (20°) residue was triturated with ether (30 cc.). The insoluble cyclic urea by-product was removed by filtration and washed with ether (10 cc.), yield 3.2 g. (18.7%). It melted at 202-205° alone and on admixture with an authentic sample of 4-methyl-1,3-diazacyclohexanone-2 (m. p. 203.5-205°).

The ether was evaporated from the ethereal filtrate and the residue distilled under reduced pressure. A viscous oil was obtained yield 27.2 g. (78%). A portion of this oil (0.5 g.) was dissolved in 95% ethanol and treated with a saturated aqueous solution of picric acid. The crystalline dipicrate thus obtained melted at 141-142° after three recrystallizations from water.

4(or 6)-Methyl-2-(β -hydroxyethylamino)-1,3-diazacyclohexene-2.—The distillation technique was applied in the reaction of 7.9 g. (0.050 mole) of 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 with 18.3 g. (0.30 mole) of ethanolamine. The temperature of the distilling vapors was not allowed to drop below 150°. The reaction proceeded very rapidly, about four minutes being required for completion. The residual oil was distilled *in vacuo*. The distillate had a slight haziness due to the presence of a small amount (0.1 g.) of the cyclic urea by-product. The yield was 7.7 g. or 98.2%. The monopicrate prepared in the usual way melted at 135.4-136° after one recrystallization from water.

N-2-(1,3-Diazacyclopentene-2)-ethylenediamine.—Thirty grams (0.50 mole) of ethylenediamine (98-100%) was placed in a beaker and heated to 80-90°. This temperature was maintained during the portionwise addition of 6.5 g. (0.05 mole) of 2-nitramino-1,3-diazacyclopentene-2 which required twenty minutes. The reaction mixture was heated for a further five minutes and then transferred to a Claisen distilling flask and distilled *in vacuo*. After the excess ethylenediamine had distilled, a white crystalline distillate was obtained, yield 5 g. (78.1%). A portion (0.7 g.) of this product was dissolved in 15 cc. of warm water and 200 cc. of a saturated aqueous picric acid solution was added. The crystalline picrate (3.1 g.) melted at 179-181°. This melting point was raised to 199-200° by three recrystallizations from water (100 cc./g.).

N-2-(4(or 5)-Methyl-1,3-diazacyclopentene-2)-ethylenediamine and N,N¹-2-(4(or 5)-Methyl-1,3-diazacyclopentene-2)-ethylenediamine.—Forty grams (0.278 mole) of 4(or 5)-methyl-2-nitramino-1,3-diazacyclopentene-2 was added portionwise to 200 g. (3.33 mole) of ethylenediamine (98-100%) over a period of forty-five minutes. During the reaction period the temperature was held at 80-90°. After the addition of the 2-nitramino compound, the reaction mixture was heated for a further fifteen minutes until all signs of gas evolution disappeared. The unreacted ethylenediamine was removed by distilling the reaction mixture at atmospheric pressure until the vapor temperature reached 116°. The residue was then distilled *in vacuo* to give a main fraction consisting of a light-yellow oil (b. p. (0.05 mm.) 184-187°). This proved to be the mono-substituted ethylenediamine, yield 28.4 g. (71.9%). A second fraction (b. p. (0.2 mm.) 250-260°) was distilled over as an orange liquid which crystallized on cooling, yield 5.3 g. (17.0%). A sample (1 g.) of this latter fraction was dissolved in 15 cc. of water and treated with 200 cc. of a saturated aqueous picric acid solution. The crystalline picrate melted at 213-215°, yield 1.7 g. A constant melting point of 228-229° was obtained after four recrystallizations from water (700 cc./g.). The analytical values of this compound were in good agreement with the calculated for the dipicrate of N,N¹-2-(4(or 5)-methyl-1,3-diazacyclopentene-2)-ethylenediamine.

An aliquot of the yellow oil (b. p. (0.05 mm.) 184-187°) gave a crystalline dipicrate which first melted at 190-192°. Six recrystallizations from water (60 cc./g.) raised the melting point to 200-201°.

Hydrolysis of 4(or 6)-Methyl-2-benzylamino-1,3-diazacyclohexene-2.—A solution of 9.2 g. (0.045 mole) of 4(or 6)-methyl-2-benzylamino-1,3-diazacyclohexene-2 in 30 cc. of 37% aqueous ethanol was refluxed for eight hours. After removal of the water and ethanol *in vacuo*, the residue was distilled. The main fraction consisted of unchanged starting material and 4-methyl-1,3-diazacyclohexanone-2. These compounds were separated by dissolving in 100 cc. of hot absolute ethanol, adding 20 cc. of absolute ether and cooling to -20°. The white precipitate of the cyclic urea was recovered by filtration, washed with ether and dried. This product was obtained in 58% yield and melted at 178-200°. One recrystallization from ethanol-ether followed by a sublimation *in vacuo* gave crystals melting at 200-204° alone and on admixture with an authentic sample of 4-methyl-1,3-diazacyclohexanone-2.

Effect of Refluxing 4(or 6)-Methyl-2-nitramino-1,3-diazacyclohexene-2 with Water.—Seven grams (0.044 mole) of 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 in 25 cc. of water was refluxed continuously for ten hours. It was then concentrated to 15 cc. and cooled to room temperature. The white crystals melted at 146-147.5°

alone and on admixture with the original 4(or 6)-methyl-2-nitramino-1,3-diazacyclohexene-2 (m. p. 147-148°). The recovery of original material was 6.2 g. (88% by weight).

Summary

A new method of preparation of 2-alkylamino-

and 2-arylalkylaminoimidazolines and -tetrahydropyrimidines is described. The formation of cyclic ureas, e. g., 1,3-diazacyclohexanone-2, as by-products in this reaction is discussed.

KINGSTON, ONTARIO

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Acylation of Certain α -Alkoxy and α -Aryloxy Ketones and Esters¹

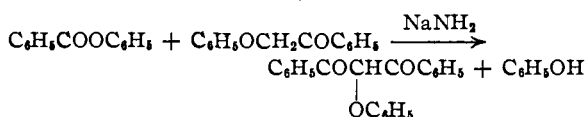
BY JON MUNCH-PETERSEN² AND CHARLES R. HAUSER

Although many acylations of ketones³ and esters⁴ have been described in the literature, relatively few successful acylations of α -alkoxy and α -aryloxy ketones and esters have been reported previously. The present paper describes some new contributions to this field. Various condensing agents have been employed.

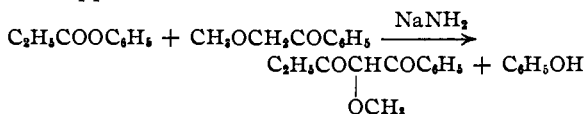
Acylation of α -Alkoxy and α -Aryloxy Ketones.—Apparently the only acylations of this type effected previously are those reported by Malkin and Robinson⁵ who acylated α -methoxy and α -4-dimethoxyacetophenone with ethyl formate using sodium ethoxide. The copper salts of the resulting β -ketoaldehydes (named as enols) were obtained in yields of 16 and 81%, respectively.⁶

We have found that, in contrast to acetophenone, α -methoxyacetophenone fails to be acylated with ethyl acetate, ethyl propionate, or ethyl benzoate, and α -phenoxyacetophenone fails to be acylated with ethyl acetate, employing sodium amide under the usual conditions.^{3a} Similarly α -methoxyacetophenone fails to be acylated with ethyl acetate employing potassium triphenylmethide⁷ in refluxing ether. In each of these cases, the methoxy or phenoxy ketone was largely recovered. However, both of these ketones may be acylated with phenyl benzoate or phenyl propionate by means of sodium amide. The benzoylations of α -methoxyacetophenone and α -

phenoxyacetophenone have been effected in yields of 26 and 59%, respectively.



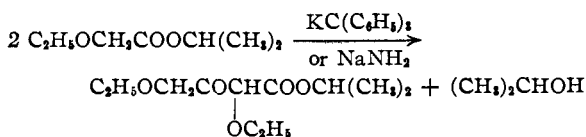
The benzoylation of α -methoxyacetophenone has also been effected with benzoyl chloride but the yield was only 11%. The propionylations of α -methoxyacetophenone and α -phenoxyacetophenone have been effected in yields of 25 and 50%, respectively; however, the latter yield is only for the copper salt.



Since some starting materials were recovered in these cases, the yields of acylation products could probably be improved.

The acylation of α -methoxyacetophenone with acetic anhydride has been effected in 10% yield by means of boron trifluoride.

Acylation of α -Alkoxy and α -Aryloxy Esters.—The self-condensation of ethyl ethoxyacetate was first reported by Conrad⁸ who used sodium, but no yield was given. Similarly, Pratt and Robinson⁹ effected the self-condensation of methyl and ethyl methoxyacetate in yields of 40-50% using sodium. Darzens and Meyer¹⁰ reported a 75% yield in the self-condensation of ethyl ethoxyacetate using sodium ethoxide. We have self-condensed isopropyl ethoxyacetate in 69% yield using potassium triphenylmethide and in 35% yield using sodium amide



The lower yield with the sodium amide may be accounted for on the basis that this reagent reacts

(8) Conrad, *Ber.*, **11**, 58 (1878).

(9) Pratt and Robinson, *J. Chem. Soc.*, 168 (1925).

(10) Darzens and Meyer, *Compt. rend.*, **198**, 478 (1934).

(1) Paper XLI on "Condensations"; paper XL, *THIS JOURNAL*, **69**, 2649 (1947).

(2) On leave of absence from the Department of Organic Chemistry, The Technical University of Denmark, Sølvgade 83, Copenhagen, Denmark.

(3) See especially (a) Adams and Hauser, *THIS JOURNAL*, **66**, 1220 (1944); (b) Levine, Conroy, Adams and Hauser, *ibid.*, **67**, 1510 (1945); (c) Hauser and Adams, *ibid.*, **66**, 345 (1944); (d) Adams and Hauser, *ibid.*, **67**, 284 (1945).

(4) See especially Hauser and Hudson, "Organic Reactions," Roger Adams, Editor-in-Chief, John Wiley and Sons, Inc., New York, N. Y., Vol. I, pp. 266-302.

(5) Malkin and Robinson, *J. Chem. Soc.*, **127**, 1190 (1925).

(6) We have verified this result with α -methoxyacetophenone, but the yield of the free β -ketoaldehyde was only 8%; most of the methoxy ketone was recovered. It should be pointed out that this reaction was carried out at 0° and that, when attempts were made to effect the formylation of the sodium derivative of α -methoxyacetophenone (prepared with sodium amide or potassium triphenylmethide) in refluxing ether, only the methoxy ketone was recovered.

(7) Levine, Baumgarten and Hauser, *THIS JOURNAL*, **66**, 1230 (1944).