Pyrolysis of 1-Methyl-2-phenylpiperidine-1-acylimides

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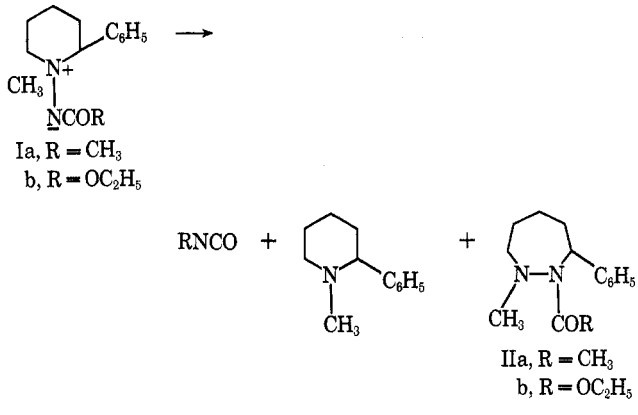
1-Methyl-2-phenylpiperidine-1-acetylimide upon pyrolysis formed methyl isocyanate, 1-methyl-2-phenylpiperidine, and 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine. The corresponding carbethoximide gave ethyl carbamate and 1-methyl-2-carbethoxy-3-phenylhexahydro-1,2-diazepine. The structures of the diazepines were demonstrated by spectra and an independent synthesis from ethyl 4-benzoylbutyrate.

The successful rearrangement of 1-methyl-2-phenylpyrrolidine-1-acetylimide to 1-methyl-2-acetyl-3-phenylhexahydropyridazine[3] suggested a study of the rearrangement of the related piperidine derivatives as a possible method for preparing hexahydrodiazepines.

In this work the rearrangement of 1-methyl-2-phenylpiperidine-1-acetylimide (Ia) and 1-methyl-2-phenylpiperidine-1-carbethoxyimide (Ib) is described. The aminimides were prepared from 2-phenylpiperidine by reactions described earlier.[4] The yield of aminimide



Ia was comparable to that obtained from 2-phenylpyrrolidine[3] but the yield of the carbethoxy analog (Ib) was low; alkylation of 1-carbethoxyamino-2-phenylpiperidine with methyl iodide gave low yields of the corresponding hydrazinium salt.

The alternate method[5] for preparing aminimides using the base-catalyzed condensation of 1-amino-1-methyl-2-phenylpiperidinium iodide and ethyl carbonate gave a 28% yield of Ib based on the iodide.

The structure of Ia was supported by a band at 1560–1580 cm^{-1} in the infrared, the nmr spectrum, and the formation of 1-acetamino-1-methyl-2-phenylpiperidinium iodide upon treatment with hydriodic acid in acetonitrile.

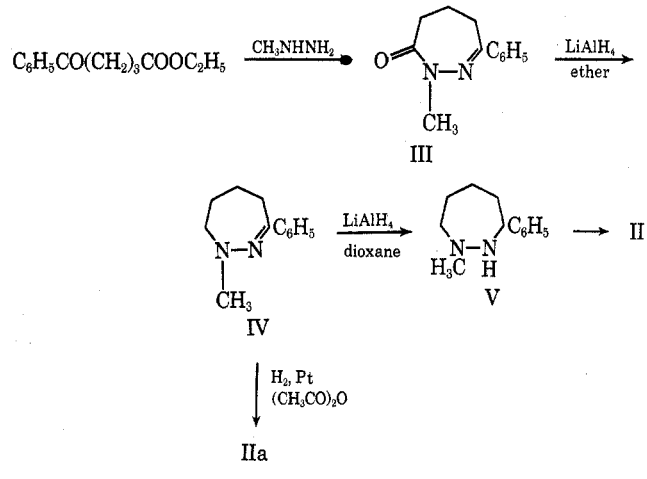
The carbethoxyaminimide (Ib) as expected showed a band at longer wavelength, 1630 cm^{-1}, in the infrared. Further evidence for the structure was the nmr spectrum and the facile hydrolysis with hydriodic acid in water to 1-methyl-1-amino-2-phenylpiperidinium iodide.

Pyrolysis of the aminimide (Ia) at 150–200° under reduced pressure gave a 15.5% yield of 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa). The major products in this reaction were methyl isocyanate and 1-methyl-2-phenylpiperidine.

(1) To whom inquiries should be addressed.
(2) Abstracted in part from the Ph.D. thesis of J. G. S., June 1969.
(3) S. Wawzonek and R. C. Gueldner, *J. Org. Chem.*, **30**, 3031 (1965).
(4) S. Wawzonek, J. Chua, E. L. Yeakey, and W. J. McKillip, *ibid.*, **28**, 2376 (1963).
(5) W. J. McKillip and R. C. Slagel, *Can. J. Chem.*, **45**, 2620 (1967).

The same reaction with the carbethoxy derivative (Ib), which cannot form an isocyanate, gave the hexahydro-1,2-diazepine derivative IIb (22.4%), ethyl carbamate, 1-methyl-2-phenylpiperidine, and tarry materials (50%).

The structures of the diazepines (II) was established by the following independent synthesis from ethyl 4-benzoylbutyrate and by the nmr spectra which were temperature dependent.



Condensation of ethyl 4-benzoylbutyrate with methylhydrazine at 200–210° gave 1-methyl-3-phenyl-Δ^2-tetrahydro-1,2-diazepin-7-one (III). The structure was supported by bands at 1680 and 1660 cm^{-1} in the infrared spectrum and by the characteristic splitting of the aromatic hydrogen peaks observed in the nmr spectrum for the benzylidene system. Reduction of this compound III with lithium aluminum hydride in ether gave 1-methyl-3-phenyl-Δ^2-tetrahydro-1,2-diazepine (IV). This compound had the same splitting for the protons of the phenyl group in the nmr spectrum as III.

Reduction of IV with lithium aluminum hydride in dioxane gave 1-methyl-3-phenylhexahydro-1,2-diazepine (V). This compound could not be obtained in a pure condition since it is easily oxidized by air to IV. A similar sensitivity to air has been reported for 3,7-diphenylhexahydro-1,2-diazepine.[6]

The hexahydrodiazepine V when treated with acetic anhydride gave 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa). This product was also obtained by the catalytic reduction of IV in acetic anhydride and was identical with the product obtained by pyrolysis. The acetyldiazepine (IIa) was resistant to basic hydrolysis and was obtained unchanged after refluxing in glycerol with potassium hydroxide at 200° for 9 hr.

(6) C. G. Overberger and J. G. Lombardino, *J. Amer. Chem. Soc.*, **80**, 2317 (1958).

The hexahydrodiazepine (V) when treated with ethyl chloroformate in the presence of triethylamine gave the carbethoxy derivative IIb which was identical with the product obtained by the pyrolysis of Ib.

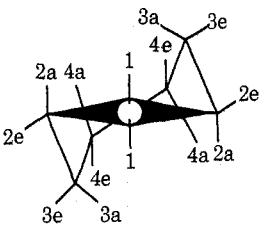
Diazepine IIa in deuteriochloroform showed at −48° three singlets of unequal size at δ 2.08, 2.12, and 2.20 for the CH_3CO protons and three singlets of unequal size at δ 2.71, 2.93, and 2.95 for the NCH_3 protons. On raising the temperature to 0° the methyl singlet for CH_3CO at δ 2.20 disappeared and the NCH_3 singlets appeared at δ 2.70, 2.86, and 2.92. At 35° the two acetyl methyl singlets were at δ 2.04 and 2.13 and the three *N*-methyl singlets were at δ 2.68, 2.81, and 2.90. Raising the temperature to 68° coalesced these peaks to one singlet for each group.

The nmr behavior in carbon tetrachloride was quite similar and gave singlets for these groups at 71°.

The carbethoxy compound IIb showed two singlets at δ 2.67 and 2.78 for the NCH_3 protons between −40 and +15° in deuteriochloroform. At temperatures of +23.5–29° a broad singlet was observed at δ 2.73 with a shoulder at δ 2.71. This combination coalesced to a singlet at 33°. The nmr behavior in carbon tetrachloride was approximately the same.

These data indicate that three conformations exist for the acetyl compound IIa and two for the carbethoxy compound IIb at ordinary temperatures. Since C-3 is an asymmetric carbon, eight different optically active conformers are possible or four different *dl* modifications. Only three of these possibilities contribute to the nmr spectrum for the acetyl derivative IIa.

Assuming that the diazepine ring system will not differ greatly from cycloheptane, a twisted chair form[7] would be the preferred arrangement over other alternatives. In such an arrangement the relative steric hindrance encountered by substituents is qualitatively 2e, 3e, 4e < 1 < 4a < 2a, 3a.[7] This formulation would predict the following conformations.



VI, trans-2,3; trans-3,4; 2e, 3e, 4e
VII, cis-1,2; trans-2,3; 1, 2e, 3e
VIII, trans-2,3; cis-3,4; 2e, 3e, 4a
IX, cis-2,3; cis-3,4; 2e, 3a, 4e

The least sterically hindered configuration would be VI since all three substituents are in an equatorial position. Among the remaining three structures IX would be the most sterically hindered form and would not exist since the acetyl group is axial and causes more crowding than when the methyl is in the 1 (VII) and the phenyl is in the 4a (VIII) positions.

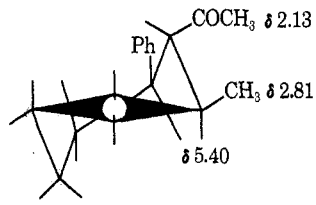
The relative strength of the singlets at δ 2.68, 2.81, and 2.90 at room temperature is approximately 1.2:1.8:1 and is relatively constant up to 49°. At this temperature broadening of the singlet at δ 2.9 occurs without a change in its intensity. At 62° the singlets at δ 2.81 and 2.90 coalesce into a singlet at δ 2.80 which is twice as large in area as the singlet at δ 2.71.

(7) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961).

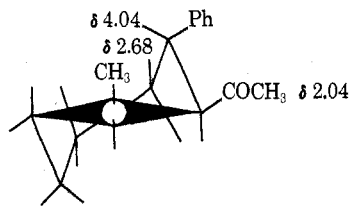
On the basis of Dreiding models the singlets at δ 2.68, 2.81, and 2.90 are assigned to conformation VII, VI, and VIII, respectively. The shielding of the methyl group by the acetyl is slightly larger when these groups are equatorial than when the methyl is in the 1 position of the twisted chair conformer VII.

The singlets for the acetyl methyls, which overlap with the broad multiplet for the 4,5,6-methylene hydrogens, have approximately the same intensities (1:1.1). The smaller singlet at δ 2.13 would correspond to conformer VI and the larger one at δ 2.04 would include both VII and VIII; the shielding would be slightly greater when the three groups are equatorial.

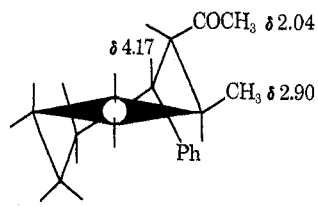
The benzylic proton appears at 35° as three poorly defined multiplets centered at δ 4.17, 4.40, and 5.40 with approximate relative intensities of 1:1:1.8, respectively. The multiplet at δ 5.40 in agreement with the assignments for the NCH_3 would correspond to conformer VI. The marked downfield shift for the axial



IV



VII



VIII

hydrogen is similar to that shown in substituted oxazoles.[8] The multiplet at δ 4.40 is ascribed to conformer VII which also has an axial hydrogen. The reason for the smaller downfield shift observed may be less long-range shielding by the electron pair on the NCH_3.

The carbethoxy group is less bulky than the acetyl group and the barrier to inversion is lower. This compound IIb would therefore exist as the conformer VI with a small amount of conformer VII at lower temperatures.

The yield of 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa) obtained by the pyrolysis of Ia was similar to that (16.4%) obtained for the pyridazine.[3] This behavior indicates that the rearrangement of heterocyclic aminimides incorporating a benzyl group in the ring is more general than when alkyl groups are involved.[9]

(8) F. G. Riddell and J. M. Lehn, *J. Chem. Soc. B*, 1224 (1968).
(9) W. S. Wadsworth, Jr., and W. Bruxwoort, *Chem. Commun.*, 542 (1968).

The pyrolysis of the carbethoxyimide Ib which cannot form an isocyanate gave a slightly better yield of the diazepine IIb. This reaction is complicated by the formation of carbethoxynitrene which can abstract hydrogen from the starting material Ib and the product IIb and form ethyl carbamate.

Experimental Section

Melting points are corrected and boiling points are not. Infrared spectra were determined with a Perkin-Elmer spectrophotometer. Nmr spectra were determined using a Varian A-60 spectrometer. Gas chromatography was performed on F & M Models 500, 720, and 5750. Mass spectra were obtained on a Hitachi RMUGE mass spectrometer.

1-Acetamino-2-phenylpiperidine.—1-Amino-2-phenylpiperidine (10 g)[10] in benzene (40 ml) was treated with acetic anhydride (5.8 g) in benzene (20 ml), and the resulting solution was stirred for 12 hr at room temperature. The benzene solution after washing with sodium bicarbonate solution and water gave an oil which was recrystallized from ether, yield 10.8 g, mp 52–57°. This melting point did not change upon further recrystallization from ether: ir (KBr) 2.93, 3.10, 3.27, 6.00 μ; nmr ($CDCl_3$) δ 1.5 (m, CH_3 and 3,4,5 methylenes), 3.1 (m, C_6H_5CH, NH, and NCH_2), 7.25 (s, C_6H_5).

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.56; H, 8.26; N, 12.84. Found: C, 71.50; H, 8.50; N, 12.64.

1-Acetamino-1-methyl-2-phenylpiperidinium Iodide.—A solution of 1-acetamino-2-phenylpiperidine (30 g) in methyl iodide (100 ml) was refluxed for 4 days. Removal of the excess methyl iodide gave a brown syrup which was recrystallized from a mixture of acetonitrile and ether, yield 26.4 g. The filtrate upon further refluxing with methyl iodide (55 ml) for 5 days gave an additional 5.6 g of product. Recrystallization from an acetonitrile–ether mixture gave a melting point of 151–152° dec; ir (Nujol) 3.13, 3.35, 5.92 μ; nmr ($CDCl_3$) δ 2.04 (m, 4,5,6 methylenes), 2.2 (s, CH_3CO), 3.70 (s, NCH_3), 4.28 (m, NCH_3), 6.10 (m, C_6H_5CH), 7.50 (m, C_6H_5), 10.24 (m, NH).

Anal. Calcd for $C_{14}H_{21}N_2OI$: C, 46.68; H, 5.83; N, 7.78. Found: C, 46.76; H, 5.88; N, 7.99.

1-Methyl-2-phenylpiperidine-1-acetimide (Ia).—A solution of the methiodide (58.8 g) in water (50 ml) was titrated with 10% sodium hydroxide using phenolphthalein as an indicator. Removal of the water and extraction of the residue with chloroform (100 ml) gave an oil (37 g) which solidified on standing. Recrystallization from ethyl acetate gave a pale yellow solid: mp 150.5–152° dec; ir (Nujol) 6.31, 6.39 μ; nmr ($CDCl_3$) δ 1.78 (s, CH_3CO), 1.94 (m, 3,4,5 CH_2), 2.92 (s, NCH_3), 3.50 (m, NCH_2), 6.12 (m, C_6H_5CH), 7.42 (m, C_6H_5).

Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.38; H, 8.68; N, 12.06. Found: C, 72.20; H, 8.51; N, 11.95.

Pyrolysis of 1-Methyl-2-phenylpiperidine-1-acetimide.—The aminimide Ia (20 g) when distilled at 150–200° under reduced pressure gave three products. Methyl isocyanate was collected at −45° and converted with aniline into *N*-methyl-*N'*-phenylurea (3.1 g), mp 150–151.5°. A mixture with an authentic sample[11] melted at the same point.

Distillation at reduced pressure gave 1-methyl-2-phenylpiperidine (7.0 g), bp 62–64° (0.15 mm). The infrared spectrum was identical with that of an authentic sample.[12]

The residue (8.1 g) consisted of 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa) (3.1 g) and 1-methyl-2-phenylpiperidine (5 g). This composition was established by vpc analysis using a 0.25 in. by 10 ft SE-30 column at 235° with a flow rate of 65 ml of helium per minute. The piperidine had a retention time of 3.4 min and the diazepine 13.6 min. Separation of the two compounds was accomplished by chromatography on silica gel with benzene as a solvent. The diazepine IIa had a boiling point of 310–312° using the Siwoloboff method[13] and benzophenone as a standard; $n^{21}D$ 1.5490; ir (film) 5.98–6.02, 6.20 μ; nmr (CCl_4) (30°) δ 1.65 (m, 4,5,6 CH_2), 1.94, 2.02 (s, CH_3CO), 2.65–2.84 (3 s, NCH_3 and NCH_2), 4.30, 5.30 (m, C_6H_5CH), 7.22 (m, C_6H_5); nmr (70°) δ 1.65 (m, 4,5,6 CH_2), 1.96 (s, CH_3CO), 2.75 (s, NCH_3 and NCH_2), 7.21 (m, C_6H_5).

Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.41; H, 8.62; N, 12.07; mol wt, 232. Found: C, 72.61; H, 8.78; N, 12.35; mol wt, 232 (mass spectrum).

The hydrochloride was obtained by treating the diazepine IIa with dry hydrogen chloride in benzene: mp 111–112°; ir (Nujol) 3.35, 5.90, 6.20 μ; nmr (CCl_4) δ 1.76 (s, CH_3CO), 1.94 (m, 5,6 CH_2), 2.34 (m, 4 CH_2), 3.36 (s, NCH_3), 3.74 (m, NCH_2), 5.80 (m, C_6H_5CH) 7.20 (m, C_6H_5), 12.54 (broad singlet, NH).

Anal. Calcd for $C_{14}H_{21}N_2OCl$: C, 62.56; H, 7.87; N, 10.42. Found: C, 62.91; H, 8.03; N, 10.49.

1-Carbethoxyamino-2-phenylpiperidine.—A solution of 1-amino-2-phenylpiperidine (26.3 g) in benzene was treated dropwise simultaneously with ethyl chloroformate (23.9 g) and with triethylamine (22.2 g). The addition of the last two compounds was carried out separately and regulated so that the temperature remained between 10 and 20°. The resulting mixture was stirred an additional 2.5 hr and the triethylamine hydrochloride was filtered. Removal of the solvent gave a yellow oil (41.0 g) which was purified by chromatography on silica gel. Elution with a 1:3 ethyl acetate–benzene mixture gave 1-carbethoxyamino-2-phenylpiperidine (31.4 g) which after crystallization from hexane melted at 56–57.5°: ir (film) 2.95, 5.80 μ; nmr ($CDCl_3$) δ 1.08 (t, CH_3), 2.75 (m, 3,4,5 CH_2), 3.23 (m, NCH_2, C_6H_5CH), 3.99 (q, CH_2CH_3), 6.85 (s, NH), 7.40 (m, C_6H_5).

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.74; H, 8.06; N, 11.45. Found: C, 67.92; H, 8.17; N, 11.66.

1-Carbethoxyamino-1-methyl-2-phenylpiperidinium Iodide.—A solution of 1-carbethoxyamino-2-phenylpiperidine (23.5 g) in methyl iodide (75 ml) was refluxed for 3 days. Removal of the methyl iodide gave a solid which was recrystallized from a mixture of acetonitrile and other. The salt (8.2 g) melted at 131.5–132°. Further refluxing of the filtrate with methyl iodide for 2 weeks gave an additional 4.8 g. A second recrystallization from an acetonitrile–ether mixture gave a sample melting at 134.0–134.5°: ir (Nujol) 3.15, 5.71 μ; nmr (DMSO-d_6) δ 1.08 (t, CH_2CH_3), 1.84 (m, 3,4,5 methylenes), 4.08 (s and m, NCH_2, NCH_3, and CH_3CH_2), 5.54 (m, C_6H_5CH), 7.62 (s, C_6H_5).

Anal. Calcd for $C_{15}H_{23}N_2OI$: C, 46.17; H, 5.90; N, 7.21. Found: C, 46.13; H, 5.76; N, 6.96.

1-Methyl-2-phenylpiperidine-1-carbethoxyimide (Ib).—A solution of 1-methyl-1-carbethoxyamino-2-phenylpiperidinium iodide (4.24 g) in water (25 ml) was neutralized exactly with 1.186 *N* sodium hydroxide. Removal of the water and extraction of the resulting residue with chloroform gave an oil (3.3 g) which was purified by chromatography on silica gel using methanol as a solvent. The product obtained upon recrystallization from ethyl acetate melted at 104–106°: ir (Nujol) 6.10 μ; nmr ($CDCl_3$) δ 1.30 (t, CH_2CH_3), 2.10 (m, 3,4 and 5 CH_2), 3.04 (s, NCH_3), 4.15 (s and m, CO_2CH_2 and NCH_2), 6.07 (m, C_6H_5CH), 7.60 (m, C_6H_5).

Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.70; H, 8.40; N, 10.69. Found: C, 68.70; H, 8.63; N, 10.74.

1-Methyl-1-amino-2-phenylpiperidinium iodide (1.0 g) was stirred with potassium *tert*-butoxide (0.36 g) and ethyl carbonate (0.50 g) in dimethyl sulfoxide (15 ml) for 2 days at room temperature. The resulting gelatinous mixture was treated with dimethyl sulfoxide until clear and the resulting potassium iodide was filtered. Removal of the solvent gave a residue which was treated with benzene. Unchanged iodide (0.61 g) was removed by filtration and the filtrate was chromatographed on alumina using benzene, 10% ethyl acetate–benzene, and 25% ethyl acetate–benzene as solvents. The aminimide Ib (0.21 g) was obtained in three of the fractions.

Pyrolysis of 1-Methyl-2-phenylpiperidine-1-carbethoxyimide (Ib).—The aminimide Ib (2.92 g) was heated under nitrogen at 100–200°; a volatile product (0.24 g) was obtained which gave an identical ir spectrum with that of ethyl carbamate. No other volatile products were found in the Dry Ice–acetone and aniline traps attached to the system.

The residue (2.49 g) when chromatographed on silica gel using benzene, 10% ethyl acetate–benzene, 25% ethyl acetate–benzene, and 10% methanol–benzene as solvents gave 1-methyl-2-carbethoxy-3-phenylhexahydro-1,2-diazepine (IIb) (0.8 g) in the first four fractions and 1-methyl-2-phenylpiperidine (0.42 g) in fractions 7–12. The remaining eluents gave a tarry material which was not characterized further.

(10) C. G. Overberger and L. P. Herrin, *J. Org. Chem.*, **27**, 417 (1962).

(11) R. Scholl and K. Holdermann, *Justus Liebigs Ann. Chem.*, **345**, 382 (1906).

(12) R. Lukes and M. Cerney, *Collect. Czech. Chem. Commun.*, **24**, 1287 (1959).

(13) A. I. Vogel, "Elementary Practical Organic Chemistry," part I, Wiley, New York, N. Y., 1966, p 86.

The diazepine had a boiling point of 306–308° dec; $n^{21}D$ 1.5202; ir (film) 5.85 μ; nmr ($CDCl_3$) δ 1.30 (t, CH_2CH_3), 2.0 (m, 4,5,6-CH_2), 2.83 (s, NCH_3), 3.30 (m, NCH_2), 4.35 (q, OCH_2), 5.17 (broad s, C_6H_5CH), 7.60 (m, C_6H_5).

Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.70; H, 8.40; N, 10.69. Found: C, 68.70; H, 8.35; N, 10.52.

1-Amino-1-methyl-2-phenylpiperidinium Iodide.—A solution of 1-amino-2-phenylpiperidine (10 g) and methyl iodide (10 ml) in acetonitrile (25 ml) was refluxed for 12 hr and cooled. The resulting solid (3.25 g) upon recrystallization from methanol gave white granules melting at 167–168.5°: ir (Nujol) 3.01, 3.11, and 6.12 μ; nmr (DMSO-d_6) δ 1.80 (m, 3,4,5-CH_2), 2.95 (s, NCH_3), 3.72 (m, NCH_2), 4.70 (m, C_6H_5CH), 5.71 (m, NH_2), 7.38 (m, C_6H_5).

Anal. Calcd for $C_{12}H_{19}N_2I$: C, 45.30; H, 5.97; N, 8.81. Found: C, 45.09; H, 5.79; N, 8.65.

1-Methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepin-7-one (III).—A solution of ethyl 4-benzoylbutyrate (45.2 g)[14] and methylhydrazine (10 g) in benzene (90 ml) was heated in a 500-ml Parr bomb at 200–210° for 70 hr. The resulting brown oil after removal of the solvent was chromatographed on silica gel using benzene, 15% ethyl acetate–benzene, and ethyl acetate as solvents and gave ethyl 4-benzoylbutyrate (4.2 g), 1-methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepin-7-one (16.1 g), and *N*-methyl-4-benzoylbutyramide (6.0 g). (This compound was formed from methylamine present as an impurity in methylhydrazine.) Recrystallization of the diazepinone III from hexane gave a white solid melting at 69–69.5°: ir (Nujol) 5.97, 6.05 μ; nmr ($CDCl_3$) δ 2.35 (m, CH_2CH_2CO), 2.81 (t, 4-CH_2), 3.31 (s, NCH_3), 7.40 (m, meta and para aromatic H), 7.78 (m, ortho aromatic H).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.97; N, 13.84. Found: C, 70.94; H, 7.00; N, 13.95.

N-Methyl-4-benzoylbutyramide was recrystallized from benzene and melted at 93–94°: ir (Nujol) 2.93, 5.94, 6.04 μ; nmr ($CDCl_3$) 2.20 (m, CH_2CH_2CO), 2.79 (d, CH_3N), 3.02 (t, $C_6H_5COCH_2$), 6.80 (broad s, NH), 7.40 (m, meta and para aromatic H), 7.90 μ (m, ortho aromatic H).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.13; H, 7.22; N, 6.87.

1-Methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepine (IV).—To a refluxing solution of lithium aluminum hydride (8.0 g) in ether (400 ml), a solution of 1-methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepine-7-one (III) (12.4 g) in benzene (100 ml) was added dropwise and the resulting solution was refluxed for 20 hr. Decomposition of the excess lithium aluminum hydride was followed by removal of the ether and gave an oil (11 g). Distillation at 80–82° (0.13 mm) gave a pale yellow liquid (9.2 g) which showed two minor impurities on a tlc silica gel plate using 1:1 ethyl acetate–benzene as an eluent. Purification was accomplished by chromatography on a silica gel column using 1:5 ethyl acetate–benzene as the solvent: $n^{21}D$ 1.5202; ir (film) 6.23, 6.30 μ; nmr (neat) δ 1.45 (m, 5,6 CH_2), 2.53 (m, 4,7 CH_2), 2.79 (s, NCH_3), 7.05 (m, meta and para aromatic H), 7.48 (m, ortho aromatic H).

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.60; H, 8.51; N, 14.89. Found: C, 77.00; H, 8.51; N, 15.18.

The picrate was prepared by refluxing the diazepine with picric acid in methanol for 15 min and melted at 128–129.5°.

Anal. Calcd for $C_{18}H_{19}N_5O_7$: C, 51.80; H, 4.59; N, 16.78. Found: C, 51.74; H, 4.83; N, 16.26.

Reduction of 1-Methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepine (V). A.—The unsaturated diazepine IV (2.65 g) in dioxane (25 ml) was added dropwise to lithium aluminum hydride (2.5 g) in dioxane (100 ml) and the resulting solution was refluxed for 24 hr. Destruction of the lithium aluminum hydride followed by removal of the solvent gave a pale yellow oil (2.45 g). Analysis by vpc on a 1/8 in. × 6 ft silicon rubber W98 column programmed at 100–250° at a rate of 10° per minute showed that the major component (retention time 11.2 min) (>95%) was 1-methyl-3-phenylhexahydro-1,2-diazepine (V). The minor component was starting material and had a retention time of 12.2 min. The saturated diazepine air oxidized so rapidly that it was not characterized by elemental analysis but used immediately: ir (film) 3.00, 3.35, 6.20 μ; nmr (CCl_4) δ 1.59 (m, 4,5,6-CH_2), 2.38 (s, NCH_3), 2.67 (m, NCH_2, NH), 3.75 (m, C_6H_5CH), 7.18 (m, C_6H_5).

A sample of the hexahydro-1,2-diazepine V (0.75 g) in benzene (20 ml) was stirred with acetic anhydride (2 ml) for 13 hr at room temperature and 10 min at 100°. Neutralization of the resulting solution was followed by removal of the solvent and gave a viscous oil (0.6 g). Analysis of vpc on a silicone rubber W98 column 1/8 in. × 6 ft programmed at 100–250° at a rate of 10° per minute indicated that the oil consisted of 92% 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa) and 8% of the tetrahydro derivative IV. Chromatography on silica gel using benzene and 1:10 ethyl acetate–benzene as solvents gave a sample of the hexahydro derivative which had identical ir and nmr spectra with those of the product obtained from the rearrangement of the piperidine derivative Ia.

A sample of the impure hexahydro-1,2-diazepine V (4.9 g) in benzene (50 ml) was added to a mixture of ethyl chloroformate (20 ml) and triethylamine (15 ml) and the resulting mixture was stirred at room temperature for 11 hr and at 100° for 3 hr. Filtration of the insoluble triethylamine hydrochloride was followed by removal of the solvent and excess reagent. The resulting brown oil (5.2 g) was chromatographed on silica gel using benzene and 1:3 ethyl acetate–benzene as solvents. The benzene eluents gave 1-methyl-2-carbethoxy-3-phenylhexahydro-1,2-diazepine (3.3 g). The ir and nmr spectra were identical with those of the product IIb obtained by pyrolysis.

B.—A solution of 1-methyl-3-phenyl-Δ²-tetrahydro-1,2-diazepine (18 g) in a mixture of acetic acid (21 ml), acetic anhydride (100 ml), and benzene (80 ml) was reduced catalytically at 30–50 psi of hydrogen in the presence of 1.3 g of platinum oxide. After the consumption of 0.1 mol of hydrogen, the solution was filtered out and the solvent was removed under reduced pressure. The resulting oil was dissolved in ether and washed with sodium bicarbonate solution and water. Removal of the ether gave a yellow oil (18.1 g) which was chromatographed on silica gel using benzene and 1:10 ethyl acetate–benzene as solvents. The products consisted of starting material IV (1 g) and 1-methyl-2-acetyl-3-phenylhexahydro-1,2-diazepine (IIa) (11.5 g).

The acetylhexahydrodiazepine was resistant to basic hydrolysis. The hydrochloride (0.49 g) was heated with 10 ml of 20% potassium hydroxide in glycerol for 9 hr at 200°. Dilution with water and extraction with ether gave the acetylhexahydrodiazepine IIa (0.31 g).

Registry No.—Ia, 29953-87-5; Ib, 29953-88-6; IIa, 29953-89-7; IIa HCl, 30102-40-0; IIb, 29953-90-0; III, 29953-91-1; IV, 29953-92-2; IV picrate, 29953-93-3; V, 29953-94-4; 1-acetamino-2-phenylpiperidine, 29953-95-5; 1-acetamino-1-methyl-2-phenylpiperidinium iodide, 29953-96-6; 1-carbethoxyamino-2-phenylpiperidine, 29953-97-7; 1-carbethoxyamino-1-methyl-2-phenylpiperidinium iodide, 29953-98-8; 1-amino-1-methyl-2-phenylpiperidinium iodide, 29953-99-9; *N*-methyl-4-benzoylbutyramide, 29954-00-5.

(14) M. Yu Lure, I. S. Trubnikov, N. P. Susherina, and R. Ya Levina, *Zh. Obshch. Khim.*, **28**, 1351 (1958).