The Chemistry of Hydrazides. X. The Reduction of Cyclic and Acyclic Hydrazides with Diborane

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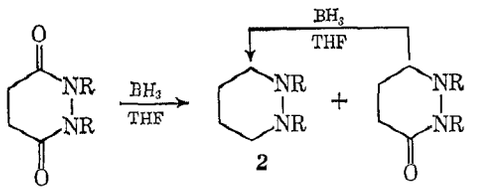
1,2-Dialkyl- and 1,2-diarylperhydropyridazine-3,6-diones (1) are reduced in high yield to the corresponding 1,2-dialkyl- and 1,2-diarylperhydropyridazines (2) on treatment with diborane at 65°. Half-reduced 1,2-dialkylperhydropyridazin-3-ones (**3a–3d**) in addition to the fully reduced compounds **2a–2d** are obtained if reactions are performed at 25°. At higher diborane concentrations (10 equiv) at 65°, compounds **1a–1f** undergo reduction of the carbonyl groups and cleavage of the N–N bond to give the corresponding N,N′-disubstituted 1,4-butanediamines. Temperatures of 129–135° are required to effect reduction of 1,2-diacylhydrazines to the corresponding 1,2-dialkylhydrazines with diborane. On the other hand, the reduction of 1,2-diacyl-1,2-dialkylhydrazines to the corresponding tetraalkylhydrazines requires only a temperature of 65°.

1,2-Disubstituted Perhydropyridazine-3,6-diones.—Recently we presented a new synthesis of 1,2-dialkyl- and 1,2-diarylperhydropyridazine-3,6-diones.[1]

We are now reporting on the reduction of these systems to the corresponding perhydropyridazines (eq 1).



(1)

1

a, R = $(CH_2)_2CH_3$
b, R = $CH(CH_3)_2$
c, R = $CH(CH_3)C_2H_5$
d, R = $(CH_2)_3CH_3$

2

3

e, R = C_6H_5
f, R = $C_6H_4CH_3$-*o*
g, R = H

A survey of the literature revealed that Stetter and Spangenberger[2] reduced 1,2-succinylpyrazolidine and 1,2-succinylpiperidazine to the corresponding cyclic hydrazines in good yield with lithium aluminum hydride. By using the same reagent, E. Hedaya, *et al.*,[3] converted 1,4,6,9-tetraketo[1,2-*a*]pyridazine into perhydropyridazo[1,2-*a*]pyridazine in 10% yield.

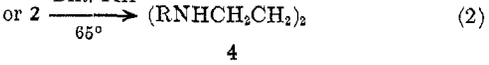
The reduction of 1,2-dialkylperhydropyridazine-3,6-diones **1a–1d** and 1,2-diarylperhydropyridazine-3,6-diones **1e** and **1f** at 65° with a slight excess of borane (5 equiv) in tetrahydrofuran (THF) followed by acidic or basic hydrolysis of the reaction mixture gave the corresponding perhydropyridazines **2a–2f** in high yield.

When reactions were carried out at 25° while employing 5 equiv of borane, the reductions of compounds **1a–1d** were incomplete, because in addition to **2a–2d** there were also obtained the corresponding half-reduced 1,2-dialkylperhydropyridazin-3-ones, **3a–3d** (eq 1).

On the other hand, only compounds **2e** and **2f** were obtained when **1e** and **1f** were treated with borane under similar conditions.

The structure of **3** was indicated by physical data and by the fact that **3b** was readily converted into **2b** in 79% yield on treatment with borane in THF at 25°.

When compounds **1a–1f** were treated with a large excess of borane (10 equiv) in refluxing THF, not only



(2)

4

reduction of both carbonyl groups, but also cleavage of the N–N bond occurred with the formation of N-N′-disubstituted 1,4-diaminobutanes, **4a–4f** (eq 2). It is very likely that the formation of **4** occurred *via* **2**, for **2b** was converted in 65% yield into **4b** under similar reaction conditions.

The reduction of the parent compound perhydropyridazine-3,6-dione (**1g**) with 12 equiv of borane at 65° gave perhydropyridazine (**2g**) in 52% yield as the only compound. No product resulting from the cleavage of the N–N bond was obtained.

1,2-Diacylhydrazines.—The successful reduction of compounds **1** to **3** with diborane prompted us to investigate the reaction with 1,2-diacylhydrazines. If successful, it would provide a convenient one-step preparation of 1,2-dialkylhydrazines.

Hinman[4] reported that 1,2-diacetylhydrazine was reduced with lithium aluminum hydride to 1,2-diethylhydrazine in 26% yield, but that under similar reaction conditions 1,2-dibenzoylhydrazine (**4**) was recovered unchanged.

In this study it was found that reaction temperatures of 129–135° were required to achieve reduction of 1,2-dipropionylhydrazine and 1,2-dibutyrylhydrazine to the corresponding 1,2-dipropylhydrazine (**5**) and 1,2-dibutylhydrazine (**6**) in yields of 65 and 49%, respectively.

In the cases of compound **4** and 1,2-dicyclohexanoylhydrazine, the reaction led to the half-reduced products, 1-benzoyl-2-benzylhydrazine (**7**) and 1-cyclohexanoyl-2-cyclohexylmethylhydrazine (**8**), respectively. Subsequent treatment of **8** with diborane gave the fully reduced 1,2-dicyclohexylmethylhydrazine (**9**) and some cyclohexylmethylamine. Compound **7** also underwent reduction but gave rise to a mixture which could not be separated.

1,2-Diacyl-1,2-dialkylhydrazines.—As in the case of **1**, reduction of 1,2-diacyl-1,2-dialkylhydrazines with diborane occurred already at 65° and led to tetraalkylhydrazines in good yield. Small amounts of half-reduced compounds were also obtained. For instance, in the reduction of 1,2-dipropionyl-1,2-dimethylhydrazine, there was obtained, in addition to 82% 1,2-dipropyl-1,2-dimethylhydrazine (**10**), 14% 1-propionyl-2-propyl-1,2-dimethylhydrazine (**11**). 1,2-Dibenzoyl-

(1) H. Feuer, E. P. Rosenquist, and F. Brown, Jr., *Israel J. Chem.*, **6**, 587 (1968).

(2) H. Stetter and H. Spangenberger, *Chem. Ber.*, **91**, 1982 (1958).

(3) E. Hedaya, R. L. Hinman, V. Schomaker, S. Theodoropulos, and L. M. Kyle, *J. Amer. Chem. Soc.*, **89**, 4875 (1967).

(4) R. L. Hinman, *ibid.*, **78**, 1645 (1956).

1,2-dimethylhydrazine (**12**) gave 60% 1,2-dibenzyl-1,2-dimethylhydrazine (**13**) and 28% N-methylbenzylamine, the latter apparently arising from cleavage of the N—N bond. It is of interest that in the reduction of **12** with lithium aluminum hydride cleavage of the N—C=O rather than the N—N bond occurred for, in addition to **13**, there were isolated 1-benzoyl-1,2-dimethylhydrazine and benzyl alcohol.[4]

Experimental Section

Apparatus.—All diborane reductions were performed in a three-neck flask equipped with a magnetic stirrer, thermometer, reflux condenser, and septum stopple or gas dispersion tube, depending on the method of introducing diborane. Hydrogen evolution was measured by attaching a series of burets through a Dry Ice trap to the outlet of the condenser.

Reagents.—Diborane was generated as described by Brown[5] and solutions of borane in THF were prepared and standardized.

1,2-Disubstituted perhydropyridazine-3,6-diones were prepared by the procedure of Feuer, *et al.*[1] 1,2-Diacyl- and 1,2-diaroylhydrazines were prepared by methods described in the literature. Tetrahydrofuran (THF) was purified by the method of Feuer and Savides.[6] Dimethyl ether of diethylene glycol (Diglyme) was purified by vacuum distillation from $LiAlH_4$.

Equipment.—Infrared spectra were taken with a Perkin-Elmer recording spectrophotometer, Models 21 and 421. Nuclear magnetic resonance spectra were determined on a Varian Model A-60 analytical nmr spectrometer using tetramethylsilane as an internal standard. Gas chromatographic analyses were performed on Aerographs A-700 and A-903 using SF-96 on Chromosorb W columns.

1,2-Diisopropylperhydropyridazine. A. From 1,2-Diisopropylperhydropyridazine-3,6-dione (1b).—The following experiment is typical of the procedure employed for preparing 1,2-dialkylperhydropyridazines. To 3.96 g (20.0 mmol) of 1,2-diisopropylperhydropyridazine-3,6-dione in 100 ml of THF at 0° was introduced by means of a syringe 8.3 ml of 12 *N* borane in THF (99.6 mmol of hydride) at such a rate that the temperature did not exceed 5°. The mixture was stirred at 0–5° for 1 hr, allowed to attain room temperature, and refluxed for 24 hr. This operation yielded 5.04 mmol of hydrogen at STP. Recooling the reaction mixture to 0–5°, adding dropwise 20 ml of 20% potassium hydroxide, and refluxing for 1 hr gave an additional 13.21 mmol of hydrogen at STP. Thus a total of 81.4 mmol of hydride was consumed (theory requires 80.0 mmol of hydride).

Extracting the reaction mixture with ether, drying the extract ($MgSO_4$), removing ether, and distilling the residue *in vacuo* gave 2.90 g (85%) of **1,2-diisopropylperhydropyridazine (2b)**: bp 33° (0.2 mm); $n^{20}D$ 1.4581; ir (neat) 2976 cm^{-1} (C–H); nmr (CCl_4) 0.98 [d, 12, $CH(CH_3)_2$], 3.1 [m, 2, $CH(CH_3)_2$], 2.8 (m, 4, $NCH_2CH_2CH_2CH_2N$), and 1.45 ppm (m, 4, $NCH_2CH_2CH_2CH_2N$).

Anal. Calcd for $C_{10}H_{22}N_2$: C, 70.53; H, 13.02; N, 16.45. Found: C, 70.28; H, 12.80; N, 16.30.

When the reaction was carried out at 25° for 24 hr, from 1.98 g (10.0 mmol) of **1b** and 4.4 ml of 12 *N* borane in THF (52.8 mmol of hydride) there was obtained 1.28 g of liquid, bp 28–68° (0.1 mm). Glpc analysis at 180° and 90 ml/min He indicated the presence of two compounds in addition to starting material (6%).

One compound (retention time 8 min) was identified as **2b** (75%), $n^{20}D$ 1.4583.

The second product (retention time 16 min) was **1,2-diisopropylperhydropyridazin-3-one (3b, 8%)**: $n^{21}D$ 1.4754; ir (neat) 2976 (CH) and 1660 cm^{-1} (C=O); nmr (CCl_4) 1.1 [d, 6, $CH_2NCH(C_3)H_2$], 1.2 [d, 6, $O{=}CNCH(CH_3)_2$], 1.5 (m, 2, $NCH_2CH_2CH_2C{=}O$), and 4.0 ppm [m, 2, $CH(CH_3)_2$].

Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.17; H, 10.94; N, 15.20. Found: C, 65.10; H, 11.06; N, 15.38.

B. From 1,2-Diisopropylperhydropyridazin-3-one (3b).—The procedure was similar to that employed in part A. From 0.18 g (0.98 mmol) of **3b** in 10 ml of THF and 1.0 ml of 4.4 *N* borane in THF (4.4 mmol of hydride), there was obtained 0.13 g (79%) of **2b**, bp 33° (0.2 mm), $n^{20}D$ 1.4584. **1,2-Dipropylperhydropyridazine (2a, 82%)** was prepared as above: bp 33° (0.2 mm); $n^{20}D$ 1.4578; nmr (CCl_4) 0.88 [t, 6, $(CH_2)_2CH_3$], 1.42 (m, 4, $CH_2CH_2CH_3$), 2.6 (t, 4, $CH_2CH_2CH_3$), 1.5 [m, 4, $NCH_2(CH_2)_2CH_2N$], and 2.8 ppm [m, 4, $NCH_2(CH_2)_2CH_2N$].

Anal. Calcd for $C_{10}H_{22}N_2$: C, 70.50; H, 12.94; N, 16.47. Found: C, 70.45; H, 12.99; N, 16.56.

1,2-Dipropylperhydropyridazin-3-one (3a, 8%) was prepared as above: bp 60–65° (0.2 mm); $n^{20}D$ 1.4713; nmr (CCl_4) 1.0 [t, 6, $(CH_2)_2CH_3$], 1.45 (m, 4, $CH_2CH_2CH_3$), 1.5 (m, 2, $NCH_2CH_2CH_2C{=}O$), 2.3 (t, 2, $CH_2C{=}O$), and 3.0 ppm (t, 6, NCH_2).

Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.17; H, 10.94; N, 15.20. Found: C, 65.13; H, 11.03; N, 14.92.

1,2-Di(*sec*-butyl)perhydropyridazine (2c, 81%) was prepared as above: bp 44–46° (0.15 mm); $n^{20}D$ 1.4671; nmr (CCl_4) 0.82 (t, 6, CH_2CH_3), 1.0 (d, 6, $CHCH_3$), 1.42 (m, 4, CH_2CH_3), 1.5 [m, 4, $NCH_2(CH_2)_2CH_2N$], 2.8 [t, 4, $NCH_2(CH_2)_2CH_2N$], and 3.0 ppm [m, 2, $CH(CH_3)C_2H_5$].

Anal. Calcd for $C_{12}H_{26}N_2$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.51; H, 13.03; N, 14.01.

1,2-Di(*sec*-butyl)perhydropyridazin-3-one (3c, 15%) was prepared as above: $n^{20}D$ 1.4808; nmr (CCl_4) 0.89 (t, 6, CH_2CH_3), 1.05 (d, 3, $CHCH_3$), 1.18 (d, 3, $O{=}CNCHCH_3$), 1.5 [m, 4, $CH(CH_3)CH_2CH_3$], 1.6 (m, 2, $NCH_2CH_2CH_2C{=}O$), 2.2 (m, 2, $CH_2C{=}O$), 3.05 (t, 4, NCH_2), 3.1 (m, 1, CH), and 3.75 ppm (m, 1, CH).

Anal. Calcd for $C_{12}H_{24}N_2O$: C, 67.88; H, 11.39; N, 13.19. Found: C, 67.36; H, 11.32; N, 13.05.

1,2-Dibutylperhydropyridazine (2d, 74%) was prepared as above: bp 41–44° (0.2 mm); $n^{20}D$ 1.4620; nmr (CCl_4) 0.90 (t, 6, CH_3), 1.4 (m, 12, CH_2), 2.6 [t, 4, $NCH_2(CH_2)_2CH_3$], and 2.7 ppm [t, 4, $NCH_2(CH_2)_2CH_2N$].

Anal. Calcd for $C_{12}H_{26}N_2$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.64; H, 13.39; N, 13.89.

1,2-Dibutylperhydropyridazin-3-one (3d, 15%) was prepared as above: $n^{20}D$ 1.4734; nmr (CCl_4) 0.93 (t, 6, CH_3), 1.4 (m, 10, CH_2), 2.2 (m, 2, $CH_2C{=}O$), and 3.0 ppm (m, 6, NCH_2).

Anal. Calcd for $C_{12}H_{24}N_2O$: C, 67.88; H, 11.30; N, 13.19. Found: C, 67.64; H, 11.51; N, 13.24.

Perhydropyridazine (2g, 52%) was prepared as above: bp 52° (18 mm); $n^{20}D$ 1.4858 [lit.[7,8] bp 54° (12 mm); $n^{17}D$ 1.4862]; ir (neat) 3300 (NH) and 2924 cm^{-1} (CH); nmr (CCl_4) 1.58 [m, 4, $NCH_2(CH_2)_2CH_2N$], 2.89 (m, 4, NCH_2), and 3.2 ppm (m, 2, NH).

1,2-Di(*o*-tolyl)perhydropyridazine (2f, 70%) was prepared as above: mp 61–62°; nmr (CCl_4) 1.77 [t, 4, $NCH_2(CH_2)_2CH_2N$], 2.35 (s, 6, CH_3), 3.2 (m, 4, NCH_2), and 7.0 ppm (m, 8, aromatic H).

Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.33; N, 10.52. Found: C, 81.12; H, 8.13; N, 10.44.

N,N′-Diisopropyl-1,4-diaminobutane. A. From 1,2-Diisopropylperhydropyridazine-3,6-dione.—The following experiment is typical of the procedure employed for preparing N,N′-disubstituted 1,4-diaminobutanes. To 3.96 g (20.0 mmol) of 1,2-diisopropylperhydropyridazine-3,6-dione in 100 ml of THF at 0° was added 32.5 ml of 6.4 *N* borane in THF (208 mmol of hydride). The reaction mixture was stirred at 0–5° for 1 hr and then refluxed for 24 hr. Adding dropwise 30 ml of 10% hydrochloric acid[9] to the reaction mixture at 0–5°, removing THF by distillation, refluxing the aqueous residue for 1 hr, basifying with solid sodium hydroxide, extracting the emulsion with ether, drying the extract ($MgSO_4$), removing ether, and distilling the residue gave 2.66 g (77%) of **N,N′-diisopropyl-1,4-diaminobutane**: bp 45° (0.03 mm) (lit.[10] bp 208.5–218°); $n^{20}D$ 1.4418; ir (neat) 3285 (NH) and 2975 cm^{-1} (CH); nmr (CCl_4) 0.63 (s, 2, NH), and 0.96 ppm [d, 12, $CH(CH_3)_2$].

The dipicrate salt, mp 189–190° (lit.[11] mp 189.5–190°), was prepared by the usual method.[12]

(5) H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **81**, 6428 (1959).

(6) H. Feuer and C. Savides, *ibid.*, **81**, 5826 (1959).

(7) P. Baranger and J. Levisalles, *Bull. Soc. Chim. Fr.*, 704 (1957).

(8) K. Alder, H. Niklas, R. Aumüller, and B. Olsen, *Justus Liebigs Ann. Chem.*, **585**, 81 (1954).

(9) Only acidic hydrolysis led to pure product. When the hydrolysis was performed in basic medium, the reaction product was contaminated with boron-containing material.

(10) R. G. Shepherd and R. G. Wilkinson, *J. Med. Pharm. Chem.*, **5**, 823 (1962).

(11) A. A. Ryabinin and E. M. Il'ina, *J. Appl. Chem. USSR*, **26**, 369 (1953).

(12) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, John Wiley & Sons, Inc., New York, N. Y., 1960, p 222.

B. From 1,2-Diisopropylperhydropyridazine.—The procedure was similar to that employed in part A. From 3.40 g (20.0 mmol) of 1,2-diisopropylperhydropyridazine, 60 ml of THF, and 10 ml of 12.1 *N* borane in THF (121 mmol of hydride), there was obtained 2.23 g (65%) of **N,N'-diisopropyl-1,4-diaminobutane**, bp 45° (0.3 mm), $n^{20}D$ 1.4418, and 0.77 g (23%) of starting material.

By following procedure A, from 1.03 g (3.50 mmol) of 1,2-di(*o*-tolyl)perhydropyridazine-3,6-dione, 30 ml of THF, and 3.1 ml of 11.4 *N* borane in THF (35.5 mmol of hydride), there was obtained 0.79 g (84%) of **N,N'-di(*o*-tolyl)-1,4-diaminobutane**: mp 45°; ir (neat) 3420 (NH) and 2925 cm^{-1} (CH); nmr ($CDCl_3$) 1.2 (s, 2, NH), 1.7 (m, 4, $NCH_2CH_2CH_2CH_2N$), 2.1 (s, 6, CH_3), 3.1 (m, 4, $NCH_2CH_2CH_2CH_2N$), and 6.8 ppm (m, 8, aromatic H).

The dihydrochloride salt, mp 223°, was prepared by the usual method.[12]

Anal. Calcd for $C_{18}H_{26}N_2Cl_2$: C, 63.34; H, 7.62; N, 8.21; Cl, 20.82. Found: C, 63.08; H, 7.64; N, 8.28; Cl, 20.71.

N,N'-Dipropyl-1,4-butanediamine (74%) was prepared: bp 54–60° (0.27 mm); $n^{20}D$ 1.4469; ir (neat) 3280 (NH) and 2860 cm^{-1} (CH); nmr (CCl_4) 0.68 (s, 2, NH), 0.92 (t, 6, CH_3), 1.50 [m, 4, $NCH_2(CH_2)_2CH_2N$], 1.55 (m, 4, $CH_2CH_2CH_3$), 2.58 [t, 4, $NCH_2(CH_2)_2CH_2N$], and 2.60 ppm (t, 4, $CH_2CH_2CH_3$).

The dipicrate salt was prepared, mp 210–212° dec after recrystallization from 95% ethanol.

Anal. Calcd for $C_{22}H_{30}N_8O_{14}$: C, 41.90; H, 4.76; N, 17.78. Found: C, 42.03; H, 5.01; N, 17.96.

N,N'-Di(*sec*-butyl)-1,4-butanediamine (75%) was prepared: bp 54–60° (0.12 mm); $n^{20}D$ 1.4487; ir (neat) 3280 (NH) and 2975 cm^{-1} (CH); nmr (CCl_4) 0.79 (s, 2, NH), 0.95 [d, 6, CH(CH_3)], 0.99 (t, 6, CH_2CH_3), 1.4 (m, 8, CH_2), 2.57 (t, 4, NCH_2), and 2.6 ppm (m, 2, CH).

The dipicrate salt was prepared, mp 215–216° dec.

Anal. Calcd for $C_{24}H_{34}N_8O_{14}$: C, 43.77; H, 5.17; N, 17.02. Found: C, 44.02; H, 5.45; N, 16.80.

N,N'-Di(*o*-tolyl)-1,4-butanediamine (84%) was prepared: mp 45°; ir (neat) 3420 (NH) and 2925 cm^{-1} (CH); nmr ($CDCl_3$) 1.2 (s, 2, NH), 1.7 [m, 4, $(CH_2)_2$], 2.1 (s, 6, CH_3), 3.1 (m, 4, NCH_2), and 6.8 ppm (m, 8, aromatic H).

The dihydrochloride salt was prepared, mp 223° (from CH_3OH).

Anal. Calcd for $C_{18}H_{26}N_2Cl_2$: C, 63.34; H, 7.62; N, 8.21; Cl, 20.82. Found: C, 63.08; H, 7.64; N, 8.28; Cl, 20.71.

N,N'-Dibutyl-1,4-butanediamine (80%) was prepared: mp 64–66°; ir (melt) 3300 (NH) and 2975 cm^{-1} (CH); nmr (CCl_4) 0.81 (s, 2, NH), 0.93 (t, 6, CH_3), 1.4 {m, 12, $[CH_3(CH_2)_2CH_2]_2$-$NHCH_2(CH_2)_2CH_2NH$}, and 2.58 ppm (t, 8, NCH_2).

The dipicrate salt was prepared, mp 213–214° dec.

Anal. Calcd for $C_{24}H_{34}N_8O_{14}$: C, 43.77; H, 5.17; N, 17.02. Found: C, 44.02; H, 5.32; N, 17.23.

1,2-Dipropylhydrazine (**5**).—The following experiment is typical of the procedure employed for the reduction of 1,2-diacylhydrazines. To 4.32 g (30.0 mmol) of 1,2-dipropionylhydrazine in 240 ml of diglyme at 0° was added 44 ml of 6.25 *N* borane in THF (274 mmol of hydride). The reaction mixture was stirred at 0–5° for 15 min, allowed to attain room temperature, and then heated to 134° for 24 hr. Removing THF and diglyme *in vacuo*, hydrolyzing the residue with 30 ml of 10% hydrochloric acid at 0°, and then refluxing for 1 hr was followed by basifying with sodium hydroxide. Extracting the reaction mixture with ether, drying the extract ($MgSO_4$), filtering, removing ether, and distilling the residue gave 2.27 g (65%) of **1,2-dipropylhydrazine**: bp 149–151°, $n^{20}D$ 1.4297 (lit.[13] bp 149–150°; $n^{20}D$ 1.4287); ir (neat) 3320 cm^{-1} (NH); nmr (CCl_4) 0.95 (t, 6, $CH_2CH_2CH_3$), 1.6 (m, 4, $CH_2CH_2CH_3$), 3.7 (t, 4, $CH_2CH_2CH_3$), and 3.7 ppm (s, 2, NH).

1,2-Dibutylhydrazine (**6**).—From 1,2-dibutyrylhydrazine (5.16 g, 30.0 mmol), diglyme (240 ml), and 44 ml of 6.25 *N* borane in THF (274 mmol of hydride), there was obtained 2.12 g (49%) of 1,2-dibutylhydrazine: bp 190–193°; $n^{20}D$ 1.4317 (lit.[14] bp 192–194°; $n^{20}D$ 1.4346); nmr (CCl_4) 0.95 (t, 6, CH_3), 1.4 (m, 8, CH_2), 3.6 (t, 2, NCH_2), and 3.7 ppm (s, 2, NH).

1,2-Dicyclohexylmethylhydrazine (**9**).—From 2.38 g (10 mmol) of 1-cyclohexanoyl-2-cyclohexylmethylhydrazine (**8**) dissolved in 23 ml of diglyme and 4.2 ml of 12 *N* borane in THF at 142°, there were obtained 1.21 g (54%) of **1,2-dicyclohexylmethylhydrazine** (**9**): bp 112–114 (0.2 mm); [lit.[15] bp 112–114° (0.2 mm)]; $n^{20}D$ 1.5010; ir (neat) 3320 (NH) and 2940 cm^{-1} (CH); nmr (CCl_4) 1.1–1.6 (m, 22, C_6H_{11}), 2.76 (d, 4, CH_2), and 4.3 ppm (s, 2, NH).

Cyclohexylmethylamine (0.13 g, 6%) was also obtained: bp 28–30° (2 mm); $n^{20}D$ 1.4659 (lit.[16] bp 163.5°; $n^{15}D$ 1.4664); ir (neat) 3300 cm^{-1} (NH); nmr ($CDCl_3$) 1.2–1.6 (m, 11, ring H), 2.4 (m, 2, CH_2), and 2.45 ppm (m, 2, NH_2).

1-Cyclohexanoyl-2-cyclohexylmethylhydrazine (**8**).—The procedure was similar to that employed for the preparation of **5** except that 7.56 g (30.0 mmol) of 1,2-dicyclohexanoylhydrazine, 125 ml of diglyme, and 22.8 ml of 12 *N* borane in THF (273.6 mmol of hydride) were employed, and that the reaction temperature was 129°. After the usual work-up the ether was removed *in vacuo* and 20 ml of hexane was added to the residue. Cooling to −78° and filtering gave 3.93 g (55%) of **1-cyclohexanoyl-2-cyclohexylmethylhydrazine** (**8**): mp 97°; ir (neat) 3300 (NH), 2920 (CH), and 1630 cm^{-1} (C=O); nmr (DMSO-d_6) 0.8–1.8 (m, 22, C_6H_{11}), 1.9 (m, 1, CH_2NH), 2.45 (s, 2, CH_2NH), and 3.35 ppm (m, 1, O=C—NH).

Anal. Calcd for $C_{14}H_{26}N_2O_2$: C, 70.54; H, 10.99; N, 11.75. Found: C, 70.40; H, 11.24; N, 11.77.

Removing hexane from the filtrate and distilling gave 0.50 g (7%) of **9**.

1-Benzoyl-2-benzylhydrazine (**7**).—The procedure was similar to that described for the preparation of 1-cyclohexanoyl-2-cyclohexylmethylhydrazine (**8**), except that the reaction was carried out at 149° for 24 hr. After evaporation of the ether extract, there was obtained **1-benzoyl-2-benzylhydrazine** (69%): mp 110° (H_2O); ir (neat) 3300 (NH) and 1640 cm^{-1} (C=O); nmr ($CDCl_3$) 4.0 (m, 4, CH_2NHNHC=O), and 7.4 ppm (m, 10, aromatic H).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.05; H, 6.01; N, 12.28.

1-(*p*-Methoxybenzoyl)-2-(*p*-methoxybenzyl)hydrazine (54%) was obtained: mp 135° (50% aqueous EtOH); ir (KBr) 3220 (NH) and 1610 cm^{-1} (C=O); nmr (DMSO-d_6) 1.9 (d, 6, OCH_3), 3.4 (m, 2, $NHCH_2$), 3.9 [m, 2, $(NH)_2$], and 7.2 ppm (m, 8, aromatic H).

Anal. Calcd for $C_{16}H_{18}N_2O_3$: C, 67.11; H, 6.34; N, 9.78. Found: C, 67.05; H, 6.29; N, 9.84.

Acidification of the aqueous layer with 10% hydrochloric acid gave on filtration 34% of starting material.

1-(*p*-Chlorobenzoyl)-2-(*p*-chlorobenzyl)hydrazine (42%) was obtained: mp 138° (40% aqueous EtOH); ir (Nujol) 3280 (NH) and 1640 cm^{-1} (C=O); nmr (DMSO-d_6) 3.2 (s, 2, CH_2NH), 3.9 [m, 2, $(NH)_2$], 7.3 (s, 4, ClC_6H_4CO), and 7.6 ppm (q, 4, $ClC_6H_4CH_2$).

Anal. Calcd for $C_{14}H_{12}N_2OCl_2$: C, 56.95; H, 4.07; N, 9.49; Cl, 24.07. Found: C, 57.08; H, 4.14; N, 9.36; Cl, 23.97.

The usual work-up of the aqueous lager afforded 40% of starting material.

1,2-Dipropyl-1,2-dimethylhydrazine (**10**).—The following experiment is typical of the procedure employed for the preparation of tetrasubstituted hydrazines. To 5.16 g (30.0 mmol) of 1,2-dipropionyl-1,2-dimethylhydrazine in 200 ml of THF at 0° was added by means of a syringe 24 ml of 6.25 *N* borane in THF (150 mmol of hydride). The reaction mixture was stirred at 0–5° for 15 min, allowed to attain room temperature, and then refluxed for 24 hr. The reaction mixture was recooled to 0°, hydrolyzed by adding dropwise 30 ml of 10% hydrochloric acid, and then refluxed for 1 hr. Basifying with solid sodium hydroxide, extracting with ether, drying the extract ($MgSO_4$), removing ether, and distilling the residue gave two fractions.

One fraction was **1,2-dipropyl-1,2-dimethylhydrazine** (**10**, 3.53 g, 82%): bp 64–65° (40 mm); $n^{20}D$ 1.4267; ir (neat) 2951 cm^{-1} (CH); nmr (CCl_4) 0.89 (t, 6, $NCH_2CH_2CH_3$), 1.46 (m, 4, $NCH_2CH_2CH_3$), 2.39 (t, 4, $NCH_2CH_2CH_3$), and 2.21 ppm (s, 6, NCH_3).

Anal. Calcd for $C_8H_{20}N_2$: C, 66.60; H, 13.98; N, 19.42. Found: C, 66.60; H, 13.94; N, 19.62.

The other fraction was **1-propionyl-2-propyl-1,2-dimethylhydrazine** (**11**, 0.68 g, 14%): bp 92–94° (40 mm); $n^{20}D$ 1.4505; ir (neat) 2951 (CH) and 1653 cm^{-1} (C=O); nmr (CCl_4) 0.96 (t, 3, $NCH_2CH_2CH_3$), 1.03 (t, 3, CH_3CH_2C=O), 1.45 (m, 2,

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$NCH_2CH_2CH_3$), 2.55 (s, 3, NCH_3), 2.82 (s, 3, NCH_3), 2.42 (t, 2, $NCH_2CH_2CH_3$), and 2.58 ppm (q, 2, $CH_3CH_2C{=}O$).

Anal. Calcd for $C_8H_{18}N_2O$: C, 60.72; H, 11.47; N, 17.70. Found: C, 60.86; H, 11.50; N, 17.90.

1,2-Dipropyl-1,2-diethylhydrazine.—By following the usual procedure, there was obtained **1,2-dipropyl-1,2-diethylhydrazine** (82%): bp 74–76° (10 mm); $n^{20}D$ 1.4322; nmr (CCl_4) 0.88 [t, 6, $N(CH_2)_2CH_3$], 1.0 (t, 6, NCH_2CH_3), 1.38 (m, 4, $NCH_2CH_2CH_3$), 2.43 (t, 4, $NCH_2CH_2CH_3$), and 2.40 ppm (q, 4, NCH_2CH_3).

Anal. Calcd for $C_{10}H_{24}N_2$: C, 69.70; H, 14.04; N, 16.26. Found: C, 69.81; H, 14.26; N, 16.30.

When the reaction mixture was refluxed during the reduction only for 2 hr instead of 24 hr, there was also obtained **1-propionyl-2-propyl-1,2-diethylhydrazine** (10%): bp 58° (0.31 mm); $n^{20}D$ 1.4533; ir (neat) 2990 (CH) and 1653 cm^{-1} (C=O); nmr (CCl_4) 0.90 [t, 3, $N(CH_2)_2CH_3$], 1.0 (t, 3, $O{=}CNCH_2CH_3$), 1.05 (t, 3, $O{=}CCH_2CH_3$), 1.38 (m, 2, $NCH_2CH_2CH_3$), 2.40 (q, 2, NCH_2CH_3), 2.50 (t, 2, $NCH_2CH_2CH_3$), 2.70 (q, 2, $OCCH_2CH_3$), and 3.23 ppm (q, 2, $OCNCH_2CH_3$).

Anal. Calcd for $C_{10}H_{22}N_2O$: C, 64.47; H, 11.90; N, 15.04. Found: C, 64.45; H, 12.12; N, 15.07.

1,2-Diethyl-1,2-dimethylhydrazine.—By following the typical procedure, there was obtained from 4.32 g (30 mmol) of 1,2-diacetyl-1,2-dimethylhydrazine 2.61 g (75%) of 1,2-diethyl-1,2-dimethylhydrazine: bp 92–94°; $n^{20}D$ 1.4091 [lit.[4] bp 93–94° (752 mm); $n^{27}D$ 1.4121]; ir (neat) 2950 and 2800 cm^{-1} (CH); nmr (CCl_4) 1.02 (t, 6, CH_2CH_3), 2.22 (s, 6, NCH_3), and 2.48 ppm (q, 4, CH_2CH_3).

When the reduction mixture was refluxed for only 2 hr instead of 24 hr, the major product was identified by glpc analysis as the half-reduced 1-acetyl-2-ethyl-1,2-dimethylhydrazine (46% yield): $n^{20}D$ 1.4423; ir (neat) 2960, 2850 (CH), and 1665 cm^{-1} (CO); nmr (CCl_4) 1.01 (t, 3, CH_3CH_2), 2.03 (s, 3, CH_3CO), 2.55 (s, 3, NCH_3), 2.7 (q, 2, CH_2CH_3), and 2.78 ppm (s, 3, H_3CNCO).

Anal. Calcd for $C_6H_{14}N_2O$: C, 55.35; H, 10.84; N, 21.52. Found: C, 55.27; H, 10.91; N, 21.26.

Tetraethylhydrazine and 1-Acetyl-1,2,2-triethylhydrazine.—From 1,2-diacetyl-1,2-diethylhydrazine, there were obtained **tetraethylhydrazine** (70%), bp 56–58° (46 mm) [lit.[17] bp 52–53° (42 mm)], $n^{20}D$ 1.4215, and **1-acetyl-1,2,2-triethylhydrazine** (8%): bp 34–36° (0.33 mm); $n^{20}D$ 1.4498; ir (neat) 2950 (CH) and 1653 cm^{-1} (CO); nmr (CCl_4) 1.02 [t, 6, $N(CH_2CH_3)_2$], 1.17 (t, 3, $O{=}CNCH_2CH_3$), 2.0 (s, 3, $CH_3C{=}O$), 2.72 [q, 4, $N(CH_2CH_3)_2$], and 3.20 ppm (q, 2, $O{=}CNCH_2CH_3$).

Anal. Calcd for $C_8H_{18}N_2O$: C, 60.72; H, 11.47; N, 17.70. Found: C, 60.48; H, 11.61; N, 17.86.

1,2-Dibenzyl-1,2-dimethylhydrazine (**13**).—From 1,2-dibenzoyl-1,2-dimethylhydrazine was obtained **13** (60%): bp 110–112° (0.1 mm); $n^{20}D$ 1.5566 [lit.[4] bp 118–120° (0.15 mm), $n^{20}D$ 1.5538]; nmr (CCl_4) 2.3 [s, 6, $N(CH_3)_2$], 3.7 [s, 4, $N(CH_2)_2$], and 7.3 ppm (s, 10, aromatic H). **N-Methylbenzylamine** (28%) was also obtained: bp 50–52° (3 mm); $n^{20}D$ 1.5242; ir (neat) 3350 cm^{-1} (NH); nmr (CCl_4) 1.9 (s, 1, NH), 2.3 (s, 3, NCH_3), 3.7 (s, 2, NCH_2), and 7.3 ppm (s, 5, aromatic H).

Registry No.—Diborane, 19287-45-7; **2a**, 23359-97-9; **2b**, 23346-48-7; **2c**, 23346-49-8; **2d**, 23346-50-1; **2f**, 23346-51-2; **2g**, 505-19-1; **3a**, 23346-53-4; **3b**, 23346-54-5; **3c**, 23346-55-6; **3d**, 23346-56-7; **4a**, 23346-57-8; **4a** dipicrate, 23346-58-9; **4c**, 23346-59-0; **4c** dipicrate, 23359-98-0; **4d**, 19435-69-9; **4d** dipicrate, 23346-61-4; **4f**, 23346-62-5; **4f** dihydrochloride, 23346-63-6; **7**, 1215-52-7; **8**, 23337-87-3; **10**, 23337-88-4; **11**, 23337-89-5; 1-(*p*-methoxybenzoyl)-2-(*p*-methoxybenzyl)hydrazine, 23359-99-1; 1-(*p*-chlorobenzoyl)-2-(*p*-chlorobenzyl)hydrazine, 23337-90-8; 1,2-dipropyl-1,2-diethylhydrazine, 23337-91-9; 1-propionyl-2-propyl-1,2-diethylhydrazine, 23337-92-0; 1,2-diethyl-1,2-dimethylhydrazine, 23337-93-1; 1-acetyl-1,2,2-triethylhydrazine, 23389-69-7.

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Hydroxamic Acids and N-Hydroxyimides Related to Pyridine, Pyrazine, and Quinoxaline

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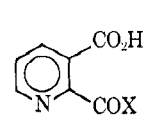
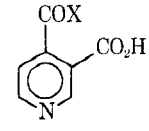
The *o*-carboxyhydroxamic acids **1b**, **2b**, **8a**, and **9a** were prepared and subjected to Lossen rearrangement. In an inert medium, the isocyanate intermediate from **1b** gives the cyclic anhydride **3**, which reacts readily with water or methanol. In the presence of methanol, *o*-amino esters were obtained in all cases, indicating that cyclization of the isocyanate is more rapid than its reaction with methanol. Rearrangement of N-(benzoyloxy)-quinolinimide **12b** and N-(benzoyloxy)cinchomeronimide **14b** gave amino acids **4a** and **15**, respectively.

In this study we have extended our earlier findings[2] on the Lossen rearrangement of *o*-carboxyhydroxamic salts. The 3-carboxyhydroxamic acids **1b** and **2b** were obtained from the corresponding methyl esters **1a** and **2a** by reaction with hydroxylamine. The esters were obtained by treatment of quinolinic and cinchomeronic anhydrides, respectively, with methanol. We were unable to isolate the isomeric methyl 2-carboxynicotinate from brief heating of quinolinic anhydride in methanol,[3] but both isomeric benzyl esters were obtained with benzyl alcohol.

The benzoyl hydroxamates **1c** and **2c** were prepared from the acids with benzoyl chloride, and were converted into the monosodium salts for rearrangement. On heating in toluene the salts gave mixtures of the cyclic anhydrides **3**[4] and **6** and the amino acids **4a** and **7a**. The aminonicotinic acid presumably arose from traces of water; a sample of the salt of **1c** that had been stored for a week gave only **4a** (76%). The rearrange-



1a, X = OCH_3
b, X = NHOH
c, X = $NHOCOC_6H_5$



2a, X = OCH_3
b, X = NHOH
c, X = $NHOCOC_6H_5$

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