82°. The following signals were variously used for analysis of the mixtures (δ, parts per million, from TMS external standard): CH_2CH_3 triplets, 1.0–1.5; $MeNHNHCOCH_3$, 1.93; $EtOCOCH_3$, 2.00; total $COCH_3$, 1.8–2.3; $CH_3NHNHAc$, 2.56; CH_3NHNH_2, 2.56 in neutral medium, 2.59 with water present, and 2.83 with HOAc present; $CH_3NAcNHAc + CH_3NAcNH_2$, 3.0–3.3; CH_3CH_2OH quartet, 3.4–3.9; CH_3CH_2OAc quartet, 3.9–4.4; and NH and OH, further downfield. The initial compositions (molar ratios, averages based on nmr analyses) were as follows: (1) $MeNHNH_2/EtOAc$, 1.0/1.3; (2) $MeNHNH_2/EtOAc/EtOH$, 1.0/1.3/0.5; (3) $MeNHNH_2/EtOAc/H_2O$, 1.0/1.4/0.7; and (4) $MeNHNH_2/EtOAc/HOAc$, 1.0/0.85/0.6. The percentages of methylhydrazine reacted at various times are shown in Figure 1.

Equilibrations of 1 and 2.—About 0.4-ml samples of mixtures of the two isomers were placed in nmr sample tubes and a few drops of glacial acetic acid were added. In some runs at 87°, ethanol was added to approximate the conditions of acetylation of methylhydrazine with ethyl acetate. The air was displaced by nitrogen, the tubes were tightly capped, and the contents were mixed by thorough shaking. The tubes were either kept at room temperature (27°) or in a constant-temperature bath at 87°, comprised of ~400 ml of water contained in a 500-ml erlenmeyer flask resting on a thermostated hot plate and loosely stoppered to retard evaporation of the water.

They were examined from time to time by nmr. The amounts of acetic acid and alcohol were estimated from the nmr spectra. The acetic acid was 10–20 mol % and the alcohol 80 mol % of the total hydrazine content. In one sample at room temperature, the ratio, **1**/**2**, changed from 16 to 0.37 in the course of 154 days, while in another the ratio went from 0.32 to 0.41 in the same period, to give an average equilibrium ratio of 0.39 ± 0.02. Runs at 87° required ~100 hr for equilibration and gave an average equilibrium ratio of 0.49 ± 0.01, with or without alcohol. (See Figure 2.)

Registry No.—**1**, 3530-13-0; **2**, 29817-35-4; methylhydrazine, 60-34-4; acetic anhydride, 108-24-7; ethyl acetate, 141-78-6.

Synthesis of 1-Alkyl-2-methylhydrazines by Way of Hydrazones of 1-Acetyl-1-methylhydrazine

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1-Acetyl-1-methylhydrazine was converted to acetylmethylhydrazones by reaction with the aldehydes and ketones: formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, benzaldehyde, acetone, and 2-butanone. Boiling points, densities, and nmr spectra of these hydrazones are reported. By reduction with sodium borohydride in ethanol, followed by hydrolysis with dilute hydrochloric acid, each hydrazone, except benzaldehyde acetylmethylhydrazone, was converted to the corresponding 1-alkyl-2-methylhydrazine. Boiling points and nmr spectra of the following are reported: 1-ethyl-2-methyl-, 1-methyl-2-propyl-, 1-isopropyl-2-methyl-, 1-butyl-2-methyl-, 1-isobutyl-2-methyl-, and 1-*sec*-butyl-2-methylhydrazine and 1-acetyl-1-methyl-2-ethylhydrazine.

It has been shown that the acetylation of methylhydrazine with acetic anhydride can be controlled so as to give chiefly 1-acetyl-1-methylhydrazine (**1**), accompanied by small amounts of its isomer, 1-acetyl-2-methylhydrazine (**2**), and 1,2-diacetyl-1-methylhydrazine; and **1** of 96% purity was obtained in 76% yield.[1] In this paper is described the use of **1** for the synthesis of some 1-alkyl-2-methylhydrazines as shown in eq 1.

$$\underset{\mathbf{1}}{MeNAcNH_2} + R_1R_2C{=}O \longrightarrow MeNAcN{=}CR_1R_2 \xrightarrow{NaBH_4}$$

$$MeNAcNHCHR_1R_2 \xrightarrow[2.\ NaOH]{1.\ H_2O,\ HCl} MeNHNHCHR_1R_2 \quad (1)$$

The hydrazines obtained in good yield were 1,2-dimethyl-,[2] 1-ethyl-2-methyl-,[3] 1-isopropyl-2-methyl-,[3,4] 1-methyl-2-propyl-,[4b] 1-butyl-2-methyl-,[5] 1-isobutyl-2-methyl-, and 1-*sec*-butyl-2-methylhydrazine. The method failed in the case of 1-benzyl-2-methylhydrazine.[5a,6] Those for which references are given had been synthesized before by one method or another. The route from **1**, eq 1, provides an alternative method which seems preferable in many cases.

Each of the 1-alkyl-2-methylhydrazines made here might have been made by lithium aluminum hydride reduction of an appropriate formylhydrazone, $HCONHN{=}CR_1R_2$, for example.[4b] Lithium aluminum hydride reduction of hydrazides, however, is frequently accompanied by cleavage at the acyl–nitrogen bond.[7] In the present case, this would have led to 1-alkyl-2-methylhydrazine accompanied by a monoalkylhydrazine having nearly the same boiling point. This possibility may account for the failure of the earlier workers to obtain good analytical results for dialkylhydrazines made that way and for the low yields of azoalkanes obtained from them by mercuric oxide oxidation. The new route described here is free of this complication and gave dialkylhydrazines for which acceptable analyses were obtained.

Experimental Section

Materials and Instruments.—These were as described in previous publications from this laboratory.[1,8] Liquid densities were obtained with a U-shaped pyknometer having a volume of ~3.3 cm³.

Preparation of Acetylmethylhydrazones. A. From Aldehydes.—Forty-six grams (0.50 mol) of 96% 1-acetyl-1-methylhydrazine[1] (containing 2% each of **2** and 1,2-diacetyl-1-methylhydrazine) was placed in a 250-ml erlenmeyer flask cooled in an ice bath, and 0.55 mol of freshly distilled aldehyde was introduced beneath the surface by means of a Pasteur pipet with swirling and cooling so as to maintain the temperature below 25°. Formaldehyde was used as a 37% aqueous solution, and acetaldehyde as a 58% aqueous solution. In these two cases, 15 g of sodium

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TABLE I

ACETYLMETHYLHYDRAZONES, $MeNAcN{=}CR_1R_2$[a]

R_1 (Registry no.)	R_2	Bp,[b] °C (Torr)	Density, 25°, g/cm³	Nmr spectrum (in CCl_4 with TMS), δ, ppm
H (35906-04-8)	H	78 (30)	1.0197	6.66 and 6.34 (d, 2, J = 11 Hz, $N{=}CH_2$), 3.13 (s, 3, CH_3N), 2.22 (s, 3, CH_3CO)
H (35906-05-9)	Me[c]	88 (18)	0.9803	6.96 (q, 1, J = 5 Hz, $N{=}CH$), 3.10 (s, 3 CH_3N), 2.19 (s, 3, CH_3CO), 1.99 (d, 3, J = 5 Hz, $=CHC\mathbf{H}_3$)
H (35906-06-0)	Et	106 (25)	0.9608	7.00 (t, 1, J = 5 Hz, $N{=}CH$), 3.11 (s, 3, CH_3N), 2.33 (m, 2, CH_2), 2.19 (s, 3, CH_3CO), 1.12 (t, 3, J = 7 Hz, $CH_2C\mathbf{H}_3$)
H (35907-07-1)	Pr[d]	83 (1.5)	0.9443	6.98 (t, 1, J = 5 Hz, $N{=}CH$), 3.12 (s, 3, CH_3N), 2.2 (m, 2, $=CHC\mathbf{H}_2$-CH_2), 2.18 (s, 3, CH_3CO), 1.6 (m, 2, $CH_2C\mathbf{H}_2CH_3$), 0.98 (t, 3, J = 7 Hz, $CH_2C\mathbf{H}_3$)
H (35906-08-2)	*i*-Pr	74 (1.7)	0.9348	6.93 (d, 1, J = 5 Hz, $N{=}CH$), 3.11 (s, 3, CH_3N), 2.5 [m, 1, $C\mathbf{H}(CH_3)_2$], 2.19 (s, 3, CH_3CO), 1.12 [d, 6, J = 7 Hz, $CH(C\mathbf{H}_3)_2$]
H (21075-81-0)	Ph	120 (2.8)	*e*	7.1–7.8 (m, 6, $C_6\mathbf{H}_5C\mathbf{H}{=}N$), 3.40 (s, 3, CH_3N), 2.33 (s, 3, CH_3CO)
Me (35906-10-6)	Me	117 (25)	*f*	3.01 (s, 3, CH_3N), 2.08 (s, 3, CH_3CO), 1.93 [s, 3, $=C(CH_3)_2$], 1.97 [s, 3, $=C(CH_3)_2$]
Me (35906-11-7)	Et[g]	128 (30)	0.9575	2.97[h] (s, 3, CH_3N), 2.37 (q, 2, J = 7 Hz, $C\mathbf{H}_2CH_3$), 2.03 and 1.90[i] (s, 3, CH_3CO), 1.83 (s, 3, $=CEtC\mathbf{H}_3$), 1.13 (t, 3, J = 7 Hz, $CH_2C\mathbf{H}_3$)

[a] *Anal.*[11] All C values were ±0.32 and H ±0.10 of theoretical, except as noted. [b] Midpoint of narrow range. [c] *Anal.* Calcd for $C_5H_{10}N_2O$: C, 52.62; H, 8.83. Found: C, 53.16; H, 8.86. [d] *Anal.* Calcd for $C_7H_{14}N_2O$: C, 59.12; H, 9.93. Found: C, 59.13; H, 10.28. [e] Solid, mp 80° (benzene–petroleum ether). [f] Not determined. [g] *Anal.* Calcd for $C_7H_{14}N_2O$: C, 59.12; H, 9.93, N, 19.70. Found: C, 57.58, 57.80; H, 9.98, 9.73; N, 19.73. [h] With small branches at 3.05 and 3.15 attributable to syn–anti isomerism. [i] Main branch; branching attributable to syn–anti isomerism.

hydroxide was added to the reaction mixture, and the hydrazone was extracted into ether prior to purification by distillation under reduced pressure. In other cases, the reaction mixture was simply distilled under reduced pressure. After a wet forerun, obtained by distillation with the aspirator, the product was collected over a narrow range, as shown in Table I. Additional product was obtained by redistillation of the forerun. Yields were quantitative, except in the case of formaldehyde (67%) and acetaldehyde (87%).

B. From Ketones.—Acetone and 2-butanone reacted only slowly with 1. Benzene (150 ml) was added, therefore, and the mixture was heated under reflux with a Dean-Stark trap[9] being used for removal of water. After 2 hr 90% of the theoretical amount of water had collected. Most of the benzene was removed by distillation at atmospheric pressure. The residue was distilled under reduced pressure for recovery of the product. Yields were quantitative.

The products are described in Table I.

1-Alkyl-2-methylhydrazines.—The acetylmethylhydrazone (0.50 ml) was mixed with 200 ml of 95% ethanol in a 500-ml erlenmeyer flask, and 2 g (0.55 mol) of sodium borohydride was added in small portions with swirling. The flask was capped with a one-holed rubber stopper fitted with an inverted Pasteur pipet and was heated in a hot water both at 80° for 10 hr.[10] The mixture was allowed to cool and was filtered with suction. The solid (Borax?) was extracted with three 10-ml portions of absolute ethanol and removed by filtration with suction each time. The filtrates were combined in a 500-ml erlenmeyer flask, cooled in an ice bath, and acidified by slow addition of 250 ml of 4 *M* HCl. The mixture was distilled to remove alcohol and until the vapor temperature reached 101°. The residue was allowed to cool to room temperature. It was then filtered with suction from a small amount of crystalline solid, presumably boric acid. To the resulting filtrate, contained in a 500-ml erlenmeyer flask cooled in an ice bath, 100 g of solid sodium hydroxide was added in small portions with continuous swirling to ensure complete dissolution. As the large amount of solid sodium chloride that formed made impractical the use of a separatory funnel, the mixture was poured into a 250-ml erlenmeyer flask and allowed to settle. The upper layer of crude hydrazine was drawn off with a pipet and placed in a 125-ml flask with solid sodium hydroxide for additional drying. The aqueous layer, containing much suspended sodium chloride, was returned to the 500-ml erlenmeyer flask, mixed thoroughly with 20 ml of ether, and then returned to the 250-ml flask. The ether layer was drawn off with a pipet and mixed with the crude hydrazine in the 125-ml flask. In this flask, an aqueous concentrated sodium hydroxide solution formed slowly beneath the hydrazine, and, from time to time, this was withdrawn with the pipet and returned to the aqueous layer in one of the larger flasks. After the extraction with ether already described, the aqueous layer was filtered with suction. The solid was washed well with two 20-ml portions of ether, each portion being used also to extract the aqueous filtrate and then combined with the hydrazine already isolated. After removal of as much as possible of the concentrated aqueous sodium hydroxide that had formed beneath the ether–hydrazine mixture, the mixture was left to dry overnight with sodium hydroxide.

The crude hydrazine–ether mixture was decanted carefully from the sodium hydroxide into a 125-ml Claisen flask, and ~0.5 g of calcium hydride was added. After reaction subsided, the hydrazine was distilled under reduced pressure. After removal of the ether and a small forerun, the bulk of the remaining material was collected as a single fraction and redistilled from fresh calcium hydride so as to obtain the products described in Table II.

A modification of the foregoing procedure was also used with 1,2-dimethyl-, 1-ethyl-2-methyl-, and 1-methyl-2-propylhydrazine, which form crystalline dihydrochlorides. Instead of being dried with solid sodium hydroxide, the crude hydrazine and ether extracts were injected carefully beneath the surface of 165 ml of 12 *M* HCl by means of a Pasteur pipet, with cooling by means of an ice bath. The crude dihydrochloride was purified by recrystallization from 6 *M* HCl, and also by precipitation with ether from a solution in absolute ethanol.[3,4]

Isolation of 1-Acetyl-1-methyl-2-ethylhydrazine.—In general, the acetylhydrazine resulting from sodium borohydride reduction of a hydrazone was hydrolyzed as described above without being isolated. That isolation was possible, however, was shown with the reduction product of acetaldehyde acetylmethylhydrazone. The procedure above was followed, and a 10-ml portion of the alcoholic filtrate, prior to addition of hydrochloric acid, was distilled under reduced pressure. The material that distilled up to 95° (14 Torr) was twice redistilled with rejection of small foreruns and residues. There was obtained 2 g of colorless liquid boiling at 90–95° (14 Torr). The nmr spectrum indicated the syn–anti isomerism characteristic of amides: the N-CH_3 group gave signals at δ 2.97 and 3.12 ppm (in CCl_4 with internal TMS), and the $COCH_3$ group gave two signals at δ 2.02 and 2.20 ppm; the upfield signal was the stronger in each case. A 2 H multiplet centered at ~2.8 ppm and a 3 H triplet centered at 1.03 ppm (J = 7 Hz) completed the spectrum.

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(9) E. W. Dean and D. D. Stark, *Ind. Eng. Chem.*, **12**, 486 (1920).

(10) Reactions were monitored by means of nmr spectroscopy, and heating was continued until the spectrum remained unchanged by 2 hr of heating. Runs with smaller amounts of sodium borohydride (0.25 mol/mol of hydrazone is theoretical) did not go to completion.

TABLE II

1-ALKYL-2-METHYLHYDRAZINES, $MeNHNHCHR_1R_2$[a]

R_1	R_2	(Registry no.)	Yield,[b] %	Bp,[c] °C (Torr)	Nmr spectrum (in CCl_4 with TMS),[d] δ, ppm
H	H[e]	(540-73-8)	82[f]	81 (755)	2.70 (s, 2, NH), 2.48 (s, 6, $\mathbf{CH_3}$NH)
H	Me[e]	(18247-19-3) (18247-20-6)[h]	65[g]	93 (758)	2.90 (s, 2, NH), 2.74 (q, 2, J = 7 Hz, $\mathbf{CH_2}$NH), 1.02 (t, 3, J = 7 Hz, $CH_2\mathbf{CH_3}$)
H	Et	(3711-30-6)	42	65 (110)	2.87 (s, 2, NH), 2.65 (t, 2, J = 7 Hz, $\mathbf{CH_2}$NH), 1.4 (m, 2, $\mathbf{CH_2}CH_3$), 1.07 (t, 3, J = 7 Hz, $CH_2\mathbf{CH_3}$)
H	Pr	(35906-16-2)	60	80 (80)	2.89 (s, 2, NH), 2.69 (t, 2, J = 7 Hz, $NH\mathbf{CH_2}$), 1.4 (m, 4, $CH_2\mathbf{CH_2}CH_3$), 0.93 (t, 3, J = 6 Hz, $CH_2\mathbf{CH_3}$)
H	*i*-Pr	(35906-17-3)	56	84 (140)	3.06 (s, 2, NHO), 2.52 (d, 2, J = 7 Hz, $NH\mathbf{CH_2}$), 1.7 [m, 1, $\mathbf{CH}(CH_3)_2$], 0.90 [d, 6, J = 6 Hz, $CH(\mathbf{CH_3})_2$]
Me	Me	(1615-82-3)	38[i]	69 (140)	3.10 (s, 2, NH), 2.92 [m, 1, $NHC\mathbf{H}(CH_3)_2$], 0.97 [d, 6, J = 6 Hz, $CH(\mathbf{CH_3})_2$]
Me	Et[j]	(35906-19-5)	61	83 (140)	2.81 (s, 2, NH), 2.63 (m, 1, C$\mathbf{H}$EtMe), 1.28 (m, 2, CHMe-$\mathbf{CH_2}CH_3$), 0.97 (t, 3, $CH_2\mathbf{CH_3}$), 0.95 (d, 3, J = 6 Hz, CHEt-$\mathbf{CH_3}$)

[a] *Anal.* All C values were ±0.24 and H ±0.28 of theoretical, except as noted. [b] From $MeNAcN{=}CR_1R_2$. [c] Midpoint of narrow range. [d] All compounds gave a 3 H singlet for $NHCH_3$ at δ 2.48 ± 0.01 ppm. [e] Known compounds were not analyzed or were identified as the known dihydrochloride. [f] As the dihydrochloride. [g] As the dihydrochloride, mp 141–143° in an open capillary and 163–167° in a sealed capillary (lit.[3] mp 139–140°). [h] Dihydrochloride. [i] Autoxidizes rapidly to MeN=NPr-*i*. [j] *Anal.* Calcd for $C_5H_{14}N_2$: C, 58.80; H, 13.80. Found: C, 58.16; H, 13.56.

Anal.[11] Calcd for $C_5H_{12}N_2O$: C, 51.73; H, 10.41; Found: C, 51.95; H, 10.22.

Attempted Catalytic Hydrogenation of Hydrazones.—Several attempts were made to reduce some of the hydrazones in Table I by catalytic hydrogenation at 5–6 atm in 1 *M* solution in absolute alcohol. The catalysts used were 10% palladium on charcoal, platinum oxide, 5% rhodium on alumina, and freshly prepared Raney nickel (W-2). The catalysts were effective for the hydrogenation of cinnamic acid to hydrocinnamic acid, but no hydrogen absorption took place with the hydrazones.

Lithium Aluminum Hydride Reduction of 2.—This was investigated as a route to 1 ethyl-2-methylhydrazine. A 1-l. three-necked flask was fitted with a motor-driven Teflon stirrer, dropping funnel, and reflux condenser protected from atmospheric moisture. Provision was made for escape of vapors from the top of the condenser into a hood. The flask was charged with 100 g (130 ml, 0.50 mol) of a 19% solution of lithium aluminum hydride in ether[12] and cooled thoroughly in an ice bath. A solution of 36 g (0.41 mol) of **2**, melting point about 40°,[1] in 150 ml of ether was added dropwise with stirring in the course of 2 hr. The mixture was heated at reflux for 2 hr and then cooled again in an ice bath. About 150 ml of 50% aqueous potassium hydroxide was added very slowly with stirring and cooling. The mixture was then distilled from the same flask, with stirring, until a vapor temperature of 105° was reached. The entire distillate, consisting of two layers, was added slowly to 150 ml of concentrated hydrochloric acid with stirring and cooling in an ice bath. The ice-cold mixture was filtered with suction and gave 34 g of moist solid melting at 100–110° with decomposition. Examination by nmr spectroscopy in D_2O as solvent indicated this solid was about 90% methylhydrazine sesquihydrochloride sesquihydrate (lit.[13] mp 118°) and only ~10% 1-ethyl-2-methylhydrazine dihydrochloride. No effort was made to isolate the latter from it.

The filtrate was allowed to evaporate at room temperature to a volume of 50 ml and was then chilled thoroughly in ice. Filtration then yielded 1.3 g of solid which was purified by dissolving it in 10 ml of 95% ethanol, with slight heating, and reprecipitation by addition of 50 ml of ether.[3] There was obtained 0.9 g (1.5%) of solid melting at 152–153° in an open capillary and 160–164° in a sealed capillary. The reported melting point of 1-ethyl-2-methylhydrazine dihydrochloride is 139–140°.[3] The nmr spectrum, in D_2O with TMS external, indicated this was ~95% 1-ethyl-2-methylhydrazine dihydrochloride [δ 1.3 (t, 3, J = 7 Hz), 3.8 (q, 2, J = 7 Hz), and 2.9 ppm (s, 3)] and 5% methylhydrazine sesquihydrochloride sesquihydrate [δ 3.0 ppm (s)].

Registry No.—**2**, 29817-35-4; 1-acetyl-2-methyl-2-ethylhydrazine, 35906-20-8.

Acknowledgments.—Miss Gloria Bass and Miss Jane Yuan performed some exploratory experiments in which **1**, produced by acetylation of methylhydrazine with acetic anhydride in pyridine, was converted to hydrazones without being isolated. As the yields and purities of the 1-alkyl-2-methylhydrazines so obtained were inferior to those obtained with isolated **1**, the results are not presented in detail. The work was supported in part by National Science Foundation Institutional Grant GU 3550 awarded to The City College.

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[11] All analyses were by Schwartzkopf Microanalytical Laboratory, Woodside, N. Y.

[12] Obtained from Foote Mineral Co., Exton, Pa.

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