moved by rotary evaporator, and the residue was recrystallized with 50% ethanol to give 420 mg (91%) of product that has the same R_f values and uv spectra as **10**.

Registry No.—**1**, 39007-51-7; **2**, 50663-83-7; **3**, 50663-82-6; **4**, 54277-40-6; **5**, 54277-41-7; **6**, 54277-42-8; **7**, 54277-43-9; **8**, 54277-44-0; **9**, 54277-45-1; **10**, 54277-46-2; urea, 57-13-6; *N*-chlorosuccinimide, 128-09-6; hydrazine, 302-01-2; acetylacetone, 123-54-6.

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Reactions of Grignard Reagents with Nitrosamines[1a]

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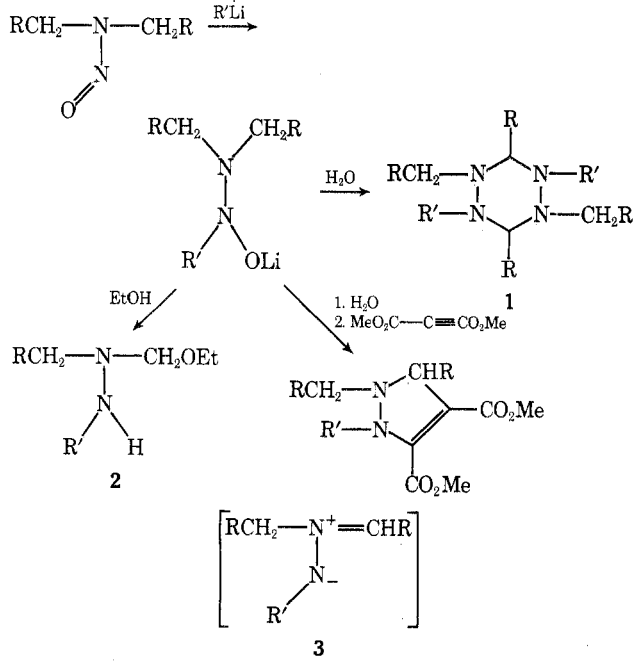
Reaction of aliphatic and alicyclic nitrosamines with excess phenyl-, cyclohexyl-, or *tert*-butylmagnesium halide gave trisubstituted hydrazines resulting from α-carbon and nitroso nitrogen alkylation. Benzylmagnesium chloride and *N*-nitrosodimethylamine gave hydrazones.

In previous reports[2,3] we described the reactions of some nitrosamines[4] with phenyl- and *tert*-butyllithium. This study (Scheme I) demonstrated that nucleophilic attack on the nitroso moiety gave *sym*-hexahydrotetrazines **1**, ethoxymethylhydrazines **2**, and other products, all presumably derived from a dipolar intermediate **3** generated after addition of either water or ethanol to the reaction mixture. The intermediate **3** was readily trapped with dimethyl acetylenedicarboxylate.

Scheme I
Reactions of Nitrosamines with Organolithium Reagents



We have extended our investigation to include reactions of Grignard reagents which serve to complement previous work and offer an expanded view of the reactions of nitrosamines with organometallics.

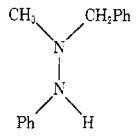
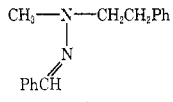
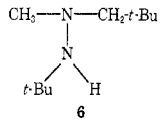
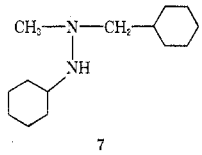
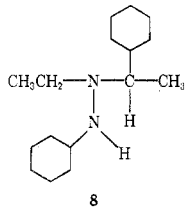
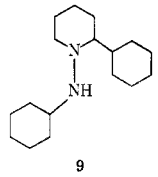
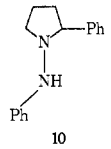
The earliest studies on the reaction of nitrosamines with Grignard reagents were reported over 60 years ago.[5,6] Wieland and Fressel[5] examined possible routes to the synthesis of hydroxyhydrazines, nitrogen homologs of hydroxylamines, by the condensation of nitrosamines with Grignard reagents. They found, however, that the reaction of ethylmagnesium iodide with diethylnitrosamine (DENA) gave the diethylhydrazone of acetaldehyde. Phenylmagnesium bromide and DENA gave 1,1-diethyl-2-phenylhydrazine and 1-ethyl-1-(α-phenylethyl)-2-phenylhydrazine. It was postulated that the latter product was formed via a diaziridine intermediate, which opened to add an additional mole of Grignard reagent to an α carbon.

Formation of Trisubstituted α-Carbon Substituted Hydrazines. In the present study dimethylnitrosamine (DMNA), diethylnitrosamine (DENA), *N*-nitrosopiperidine (PipNO), and *N*-nitrosopyrrolidine (PyrNO) were treated with cyclohexyl-, *tert*-butyl-, phenyl-, and benzylmagnesium halides. All reactions were run in ether solvent at 0° in an inert atmosphere with reaction times of 1–3 hr.

The addition of an excess of organomagnesium reagent to the nitrosamine gave, after work-up, a trisubstituted hydrazine which had incorporated 2 mol of Grignard reagent, one at a nitroso nitrogen and one at an α carbon of the aliphatic nitrosamine (Table I). Structure assignments were based on NMR and ir analyses. For example, the NMR spectrum of hydrazine **4** displayed singlets at 2.20 (3 H, *N*-methyl) and 3.55 ppm (2 H, *N*-benzyl), an exchangeable proton (NH) at 4.10 ppm, and aromatic multiplets between 6.5 and 7.3 ppm. The ir spectrum displayed an NH stretch at 3.07 μ.

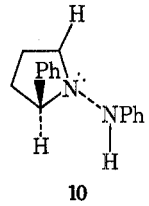
The NMR spectrum of 1-ethyl-1-(α-cyclohexylethyl)-2-cyclohexylhydrazine (**8**) from the reaction between DENA

Table I
α-Carbon Substituted Hydrazines and Hydrazones from the Reaction of Aliphatic Nitrosamines with Grignard Reagents

Nitrosamine	Grignard reagent	α-C alkylated hydrazine	Bp, °C (mm)	Mp of HCl salt, °C	Isolated yield, %
DMNA	PhMgBr	 4	135–136 (1.7)	177.5–180.5	30
DMNA	$PhCH_2MgCl$	 5		45–45.5 (free base)	Undetermined
DMNA	*t*-BuMgBr	 6	30–32 (1.6)		50
DMNA	$C_6H_{11}MgBr$	 7	113–115 (1.8)	199–201	48 (75–80 GC)
DENA	$C_6H_{11}MgBr$	 8	122–124 (0.35)	159–160	47
PipNA	$C_6H_{11}MgBr$	 9	124–127 (0.3)	216–217.5	52
PyrNA	PhMgBr	 10	129–132 (0.6)	67–68 (free base)	51

and cyclohexyl bromide showed a doublet at 0.79 ppm due to the β-methyl group. The integrity of the *N*-ethyl group was indicated by a three-proton triplet at 0.94 ppm (CH_2CH_3). An exchangeable one-proton singlet at 1.96 ppm (NH) and ir absorption at 3.1 μ demonstrated that the hydrazine was trisubstituted.

The NMR spectrum of hydrazine **10**, derived from PyrNO and phenylmagnesium bromide, exhibited some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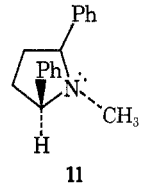
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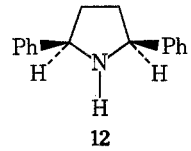
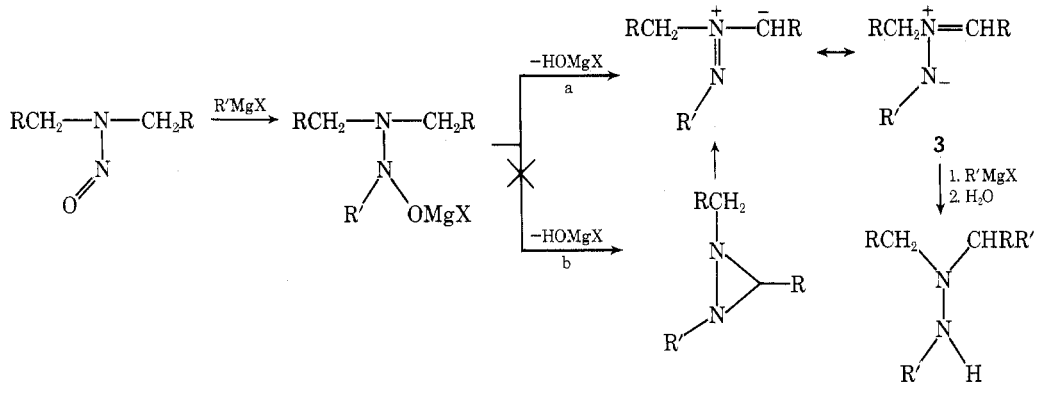

12

unusual chemical shifts for α protons. The α-methylene proton signals (CCl_4) were at 3.6 and 2.3 ppm, well separated from each other when compared to the signals from the methylene protons of pyrrolidine[11] and 2-phenylpyrrolidine, which appear at approximately the same position, 2.78–2.90 ppm. In addition, the benzylic methine proton signal was apparently shifted upfield, 3.6 ppm (cf. 2-phenylpyrrolidone and *cis*-2,5-diphenylpyrrolidine, 3.92 and 4.25 ppm, respectively in $CDCl_3$[11]) and overlapped with that of one of the α-methylene protons. An NMR spectrum of **10** in trifluoroacetic acid showed the α-methylene signals at approximately the same field, 3.9 ppm. The signal due to the benzylic methine proton was separate and shifted downfield to 4.9 ppm. This suggested that the lone pair(s) of electrons on nitrogen might be the source of this effect.

It has been demonstrated that electron lone pairs in six-membered rings are responsible for shielding adjacent protons.[7-10] The effect, however, has only recently been observed in five-membered rings, specifically, *N*-alkyl-α,α′-disubstituted pyrrolidines, by Breuer and Melumad.[11] They conclude that α protons of pyrrolidines are shielded when situated trans to an electron pair and cis to an *N*-methyl group. Therefore, *N*-methyl-*cis*-2,5-diphenylpyrrolidine (**11**), which should exist mainly in the transoid form, reflects this shielding effect in its benzylic chemical shift (3.34 ppm) when compared to *cis*-2,5-diphenylpyrrolidine (**12**) (4.25 ppm), which probably exists as a 1:1 mixture of invertomers.[11]

Scheme II
Reactions of Nitrosamines with Grignard Reagents



Although hydrazine **10** does not fall directly into the substitution pattern described by Breuer and Melumad, it becomes apparent, after examination of its NMR spectrum, that similar lone-pair effects predominate. Therefore, the preferred conformation of **10** can be assigned on the basis of nitrogen lone-pair shielding and as presented below. This result is not unexpected when nonbonded interactions are examined; however, this observation expands nitrogen lone-pair effects in establishing the stereochemistry of N-substituted pyrrolidines.

Mechanism Studies. The α-C substitution of Grignard reagents was observed for both cyclic and acyclic aliphatic nitrosamines. The structure of the products from the reaction between nitrosamines and Grignard reagents strongly suggests that an intermediate has been generated which permits nucleophilic attack on an activated α carbon.[12]

Two reaction paths are outlined in Scheme II which might account for observed products. Path b, which incorporates Wieland's diaziridine intermediate,[5] was the most easily accessible to experimental scrutiny.

Diaziridines have been proposed to undergo ring opening under thermal, acidic, and photochemical conditions to give dipolar species[13-17] which could react with nucleophiles such as Grignard reagents. 1-Cyclohexyl-2-ethyl-3-methyldiaziridine, a proposed intermediate[18] in the reaction of DENA with cyclohexylmagnesium bromide, was prepared from acetaldehydecyclohexylimine and *N*-chloroethylamine by the method of Schmitz and Schinkowski.[19] When this compound was treated with cyclohexylmagnesium bromide, 1-ethyl-1-(α-cyclohexylethyl)-2-cyclohexylhydrazine (**8**) was not detected by GC. Similarly 1-cyclohexyl-2-methyl-3-ethyldiaziridine[19] did not react with phenylmagnesium bromide under conditions in which Grignard reagents react with nitrosamines.

Reaction path a, which includes the direct formation of a dipolar species, is consistent with our observations using organolithium reagents.[2,3] However, with organomagnesium halides, elimination to give the azomethineimine proceeds readily during the reaction, whereas elimination after the addition of phenyl- or *tert*-butyllithium to the nitroso moiety requires protonation by water or ethanol. This difference apparently diminishes with some primary alkyllithium compounds, as in the reaction of DENA with methyllithium, where elimination during reaction can account for observed products.[20]

Azomethineimines such as **3** can undergo addition with appropriate dipolarphiles to form isolable adducts.[3,14,21-23] Attempts to trap such a species with norbornene[24] during the addition of phenylmagnesium bromide to DMNA were unsuccessful and no observable change in products was detected by NMR. It is interesting to note that the normally intense yellow color that appears during the addition of phenylmagnesium bromide to DMNA was absent when norbornene was present. Optimum yields (75–80%) of the α-C-alkylated trisubstituted hydrazine **7** were obtained after the addition of 2 mol of Grignard reagent (cf. Experimental Section).

Hydrazone Formation. The addition of benzylmagnesium chloride to DMNA gave, after work-up, benzaldehyde dimethylhydrazone in 33–37% yield. Three additional compounds, benzaldehyde 1-methyl-1-(β-phenylethyl)-hydrazone (**5**) and compounds tentatively identified as 1,1-dimethyl-2,2-dibenzylhydrazine and 1-methyl-1-(β-phenylethyl)-2-benzylhydrazine, were detected by gas chromatographic analysis.

The formation of hydrazones appears to be significant in the reaction of primary alkylmagnesium halides with nitrosamines.[5,20] Elimination to form a hydrazone is probably competitive with hydrogen abstraction from an α carbon. Cyclohexylmagnesium bromide, a secondary Grignard reagent, gave only a trace amount of cyclohexanone 1,1-dimethylhydrazone during reaction with DMNA.

Although phenylmagnesium bromide and aliphatic[25] nitrosamines form α-C phenylated products, substantial amounts of *N*-phenylhydrazines without substitution at an α carbon have been found.[5,20] Similarly, we have isolated 1,1-dimethyl-2-phenylhydrazine (20%) from the reaction of phenylmagnesium bromide and DMNA. This may have been formed via reduction of the adduct $Me_2NN(Ph)$-OMgBr by an additional 2 mol of the Grignard reagent.[26]

In addition to products which were discussed above, trace amounts of compounds which incorporated 3 mol of Grignard reagent were detected by mass spectroscopy and NMR.

Experimental Section

Infrared absorption spectra were determined using a Beckman IR5A spectrophotometer and ultraviolet absorption spectra were determined using a Perkin-Elmer 202 ultraviolet–visible spectrophotometer. A Varian A-60 or Jeolco 100 nuclear magnetic resonance spectrometer was used to record the NMR spectra spectra. Mass spectra were obtained on a Hitachi Perkin-Elmer RMU-6D mass spectrometer.

Melting points were determined on a Mel-Temp or Fisher-Johns melting point apparatus. Both melting points and boiling points are uncorrected.

Gas chromatographic analyses were determined on an F & M Model 720 gas chromatograph. The column used was a 2-ft stainless steel column (0.5 in. o.d.) packed with 20% by weight DC-200 on Chromosorb W. The column was conditioned overnight at 220°. Analysis conditions were as follows: the helium flow rate was 60 ml/min and the temperature was programmed at 7.5°/min from 70 to 220° and then maintained isothermally. Microanalysis were performed by Weiler and Strauss, Oxford, England, and Galbraith Laboratories, Knoxville, Tenn.

Materials. The Grignard reagents[27] were standardized according to the method of Gilman.[28] The nitrosmines,[3] benzaldehyde

N,N-dimethylhydrazone,[29] 2-phenylpyrrolidine,[30] and 1-cyclohexyl-2-methyl-3-ethyldiaziridine[19] were prepared by previously described methods or purchased.

Reaction of Nitrosamines with Grignard Reagents. The reaction between DENA and cyclohexylmagnesium bromide is representative and will be described in detail. The product hydrazines were usually converted to the hydrochloride salt, which gave well-defined solids which were readily recrystallized.

1-Ethyl-1-(α-cyclohexylethyl)-2-cyclohexylhydrazine (8). A solution of DENA (8.16 g, 80 mmol) in 500 ml of anhydrous ether was cooled to 0° under an argon atmosphere. Cyclohexylmagnesium bromide (165 ml of a 1.95 *M* solution) was added slowly with stirring. The reaction mixture was stirred for 2 hr and then quenched with water. The ether layer was separated, dried, and evaporated in vacuo. The yellow liquid was distilled and the fraction boiling at 106–110° (0.25 mm) was collected (9.4 g, 47%). Redistillation at 0.35 mm gave pure **8**: bp 122–124°; ir (neat) 3.10 (w), 6.9 (s), 7.3 (s), 11.25 (m), 11.82 (m), and 13.5 μ (m); NMR (100 MMz, CCl_4) δ 0.79 (d), 0.94 (t), 1.16 (br m), 1.64 (br m) (27 H), 1.96 (s, 1 H), and 2.1–2.7 (m, 4 H); mass spectrum (70 eV) *m/e* 252 (M^+, 10%), 169 (100%). The hydrochloride salt was recrystallized from 1-propanol: mp 159–160°; ir (Nujol) 3.74 (m), 6.30 (m), 7.25 (m), and 13.05 μ (w). Anal. Calcd for $C_{16}H_{33}N_2Cl$: C, 66.52; H, 11.51; N, 9.70. Found: C, 66.61; H, 11.37; N, 9.63.

1-Methyl-1-(cyclohexylmethyl)-2-cyclohexylhydrazine (7). A. Preparation. The reaction between DMNA (3.85 g, 52 mmol) and cyclohexylmagnesium bromide (208 mmol) gave **7** as a pale yellow oil. The product was distilled and the fraction which boiled at 113–115° (1.8 mm) was collected (5.7 g, 48%): ir (neat) 3.10 (w), 6.92 (s), 9.07 (m), 11.45 (m), and 12.7–13.1 μ (m); NMR (CCl_4) δ 0.8–2.2 (m, 24 H), 2.25 (s, 3 H), and 2.4–2.8 (br m, 1 H); mass spectrum (70 eV) *m/e* 224 (M^+, 18%), 141 (100%). The hydrochloride salt was recrystallized from ethyl acetate and sublimed (140°, 0.3 mm): mp 199–201°; ir (Nujol) 6.30 (m), 6.65 (m), 6.86 (s), 7.26 (s), and 12.13 μ (m). Anal. Calcd for $C_{14}H_{29}N_2Cl$: C, 64.46; H, 11.21; N, 10.74. Found: C, 64.57; H, 11.42; N, 10.61.

B. Stoichiometric Determination. DMNA (1.45 g, 19.6 mmol) and biphenyl (1.54 g, 10 mmol) were dissolved in 250 ml of anhydrous ether in a stirred flask fitted with a rubber septum and a 50-ml burette which contained 40 ml of cyclohexylmagnesium bromide (1.96 mequiv/ml). The system was maintained under an argon atmosphere and kept at 2–5° throughout the reaction.

The Grignard reagent was added slowly, and at each 5-ml interval an aliquot of approximately 1 ml was removed from the reaction mixture by syringe. The sample was quenched and 10–15 μl of the ether layer was analyzed by GC by comparing the ratio of dimethylnitrosamine and 1-methyl-1-(methylcyclohexyl)-2-cyclohexylhydrazine to the biphenyl standard. A ratio of 2:1 (cyclohexylmagnesium bromide:DMNA) was found to give the highest yield of **7** (75–80%).

1-Methyl-1-neopentyl-2-*tert*-butylhydrazine (6). The reaction between DMNA (2.5 g, 34 mmol) and *tert*-butylmagnesium bromide (130 mmol) gave **6** as a pale yellow oil. Distillation of 0.8 mm gave a fraction (2.9 g, 50%), bp 25–28°, which was redistilled: bp 30–32° (1.6 mm); ir (neat) 3.03 (w), 6.73 (s), 7.20 (m), 7.35 (s), and 11.46 μ (s); NMR (CCl_4) δ 0.95 (s, 9 H), 1.08 (s, 9 H) 1.90 (br s, 1 H), and 2.49 (s, 5 H); mass spectrum (70 eV) *m/e* 172 (M^+, 46%), 59 (100%). Anal. Calcd for $C_{10}H_{24}N_2$: C, 69.70; H, 14.04; N, 16.26. Found: C, 69.48; H, 13.88; N, 16.56.

***N*-Cyclohexylamino-2-cyclohexylpiperidine (9).** This compound was obtained from PipNA (3.42 g, 33 mmol) and cyclohexylmagnesium bromide (132 mmol): bp 124–127° (0.3 mm) (4.5 g, 52%); ir (neat) 3.1 (w), 6.89 (s), 7.27 (m), 8.98 (m), 11.25 (m), 11.55 (m), and 13.24 μ (m); NMR (CCl_4) δ 0.9–2.2 (br m) and 2.2–3.0 (br m) (31 H) and 3.4 (br m, 1 H); mass spectrum (70 eV) *m/e* 264 (M^+, 8%), 99 (100%). The hydrochloride salt was recrystallized from ethyl acetate–methanol: mp 216–217.5°; ir (Nujol) 3.12 (m), 6.41 (w), 6.88 (s), 7.24 (m), 11.42 (m), and 12.15 μ (m). Anal. Calcd for $C_{17}H_{32}N_2Cl$: C, 67.86; H, 11.05; N, 9.31. Found: C, 67.87; H, 10.89; N, 9.38.

***N*-Anilino-2-phenylpyrrolidine (10).** This compound was obtained from PyrNA (12.0 g, 120 mmol) and phenylmagnesium bromide (324 mmol), bp 129–132° (0.60 mm) (12 g, 51%). The viscous oil solidified and was recrystallized from heptane: mp 67–68°; ir (Nujol) 3.1 (w), 6.24 (s), 6.68 (s), 7.95 (m), 11.31 (m), 13.2–13.4 (s), 14.25 (s), and 14.45 μ (s); NMR (100 MHz, CCl_4) δ 1.88 (m) and 2.3 (m) (5 H), 3.6 (t overlapping m, 2 H), 3.84 (br s, 1 H), and 6.4–7.4 (m, 10 H); mass spectrum (70 eV) *m/e* 238 (M^+, 79%), 77 (100%). Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76. Found: C, 80.48; H, 7.67; N, 11.85.

Reaction of DMNA with Phenylmagnesium Bromide. DMNA (5.85 g, 79 mmol) and phenylmagnesium bromide (32 mmol) were reacted as described above. After quenching with water and drying over anhydrous potassium carbonate, the ether solution was cooled in a Dry Ice–acetone bath. Hydrogen chloride was passed into the solution until precipitation was complete. The ether was decanted and the oil was washed with ether and then an additional 100 ml of ether was added. A concentrated solution of sodium hydroxide was added dropwise to the stirred mixture cooled in ice until the water layer was strongly basic. The ether layer was separated, dried, and evaporated, and the residue was distilled. The fractions boiling at 71° (2.7 mm) and 149–151° (3.0 mm) were collected.

The higher boiling fraction was redistilled to give 1-methyl-1-benzyl-2-phenylhydrazine (**4**, 5.0 g, 30%): bp 135–136° (1.7 mm); ir (neat) 3.07 (w), 6.24 (s), 6.69 (s), 6.98 (m), 11.4 (m), 13.4 (s), and 14.45 μ (s); NMR (CCl_4) δ 2.20 (s, 3 H), 3.55 (s, 2 H), 4.10 (s, 1 H), and 6.5–7.3 (m, 10 H); mass spectrum (70 eV) *m/e* 212 (M^+, 52%), 121 (100%).

The hydrochloride salt was recrystallized from ethanol: mp 177.5–180.5°; ir (Nujol) 3.15 (m), 6.24 (m), 12.9 (m), 13.33 (m), and 14.43 μ (s). Anal. Calcd for $C_{14}H_{17}N_2Cl$: C, 67.60; H, 6.89; N, 11.26; Cl, 14.25. Found: C, 67.71; H, 6.82; N, 11.23; Cl, 14.34.

The lower boiling fraction (2.0 g, 19%) was identified as 1,1-dimethyl-2-phenylhydrazine: ir (neat) 3.08 (m), 6.24 (s), 13.30, and 14.45 μ (s); NMR (CCl_4) δ 2.34 (s, 6 H), 4.0 (br s, 1 H), and 6.7–7.3 (m, 5 H).

Benzaldehyde *N,N*-Dimethylhydrazone. Benzaldehyde *N,N*-dimethylhydrazone was produced in 33–37% yield (GC) from the reaction between DMNA and a fourfold excess of benzylmagnesium chloride. It was identical with a known sample.[29] Three additional products with longer retention times were detected by GC. These compounds were separated from benzaldehyde *N,N*-dimethylhydrazone by distillation. The fraction boiling at 130–133° (0.2 mm), which contained the three additional compounds, was chromatographed on silica gel (100–200 mesh) using the following solvent sequence: hexane, CCl_4, benzene, and $CHCl_3$.

Benzaldehyde 1-Methyl-1-(β-phenylethyl)hydrazone (5). The least polar of the three products was present in the chloroform fraction (vide supra) and solidified after evaporation of solvent, mp 43–44°. Recrystallization from water–1-propanol and sublimation (55°, 0.55 mm) gave **5** as a white solid: mp 45–45.5°; ir (neat) 6.27 (m), 6.41 (m), 9.55 (m), 13.30 (s), and 14.40 μ (s); NMR (100 MHz, CCl_4) δ 2.78 (s) overlapping 2.81 (t) (5 H), 3.42 (m, 2 H), and 7.0–7.5 (m, 11 H); mass spectrum (70 eV) *m/e* 238 (M^+, 87%), 147 (100%). Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.75. Found: C, 80.32; H, 7.69; N, 11.88.

1-Cyclohexyl-2-ethyl-3-methyldiaziridine. According to the method of Schmitz and Schinkowski[19] for the synthesis of diaziridines, a solution of acetaldehydecyclohexylimine[31] (15 g, 0.12 mol) and cyclohexylamine (10 g, 0.12 mol) in 100 ml of ether was cooled in an ice bath with stirring. *N*-Chloroethylamine[19] (0.12 mol) in 130 ml of ether was added and the reaction mixture was stirred overnight at room temperature. The precipitate of cyclohexylamine hydrochloride was filtered with suction and the solution was concentrated and filtered until no precipitate formed. The solution was extracted with aqueous saturated sodium bicarbonate, dried, and concentrated to an oil. Fractional distillation gave unreacted imine and amine at 30–40° (10 mm). The pressure was then reduced to 0.3 mm and the fraction boiling at 75–78° was collected. Further purification via the hexacyanoferrate salt[16b] and GC gave 1-cyclohexyl-2-ethyl-3-methyldiaziridine as a colorless oil: ir (neat) 6.90 (m), 7.12 (m), 9.09 (m), 11.19 (m), and 12.91 μ (w); NMR (neat) δ 0.9–2.1 (m), 1.30 (d), and 2.1–2.7 (m); mass spectrum (70 eV) *m/e* 168 (M^+, 11%), 71 (100%). Anal. Calcd for $C_{10}H_{20}N_2$: C, 71.37; H, 11.98; N, 16.64. Found: C, 70.95, 71.01; H, 11.67, 11.80; N, 16.15, 16.32.

Addition of Cyclohexylmagnesium Bromide to 1-Cyclohexyl-2-ethyl-3-methyldiaziridine. A solution containing 50 ml of ether and 200 mg (1.2 mmol) of 1-cyclohexyl-2-ethyl-3-methyldiaziridine was cooled to 0° under a nitrogen atmosphere. Cyclohexylmagnesium bromide (6.0 mmol) in 15 ml of ether was added dropwise to this solution. After 15 min the solution was quenched with water, and the ether layer was separated, dried, and evaporated in vacuo. Gas chromatographic analysis of the liquid residue showed only starting material and no 1-ethyl-1-(α-cyclohexylethyl)-2-cyclohexylhydrazine when compared to a standard sample.

Addition of Phenylmagnesium Bromide to Cyclohexyl-2-methyl-3-ethyldiaziridine. A solution of 1.89 g (11.25 mmol) of 1-cyclohexyl-2-methyl-3-ethyldiaziridine in 75 ml of anhydrous

ether was cooled to 0–5° under a nitrogen atmosphere. To this solution was added 45 mmol of phenylmagnesium bromide in 50 ml of ether with stirring. After 1 hr the solution was quenched with water. The ether layer was separated and dried over anhydrous potassium carbonate and then evaporated in vacuo. The liquid residue was identical with starting material.

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Registry No.—**4,** 54193-54-3; **4** HCl, 54193-55-4; **5,** 54193-56-5; **6,** 54193-57-6; **7,** 54193-58-7; **7** HCl, 54193-59-8; **8,** 54193-60-1; **8** HCl, 54193-61-2; **9,** 54193-62-3; **9** HCl, 54193-63-4; **10,** 54193-64-5; DMNA, 62-75-9; DENA, 55-18-5; PipNA, 100-75-4; PyrNA, 930-55-2; PhBr, 108-86-1; $PhCH_2Cl$, 100-44-7; *t*-BuBr, 507-19-7; $C_6H_{11}Br$, 108-85-0; 1-cyclohexyl-2-ethyl-3-methyldiaziridine, 54193-65-6; acetaldehydecyclohexylimine, 1193-93-7; cyclohexylamine, 108-91-8; *N*-chloroethylamine, 24948-82-1.

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Reductive Cyclization of Aminobenzoic Acids

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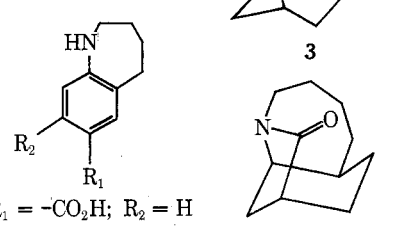
Hydrogenation of 3- and 4-aminobenzoic acids over a ruthenium catalyst at 150° under 1600 psig of hydrogen gave fair yields of the bicyclic lactams **8** and **6,** respectively. Cyclization also occurs on hydrogenation of 3-methyl-4-aminobenzoic acid, but on hydrogenation of the 3,4-diaminobenzoic acid one of the amine groups is lost. The 4-amine is lost twice as readily as is the 3-amine. With the 3-hydroxy-4-aminobenzoic acid complete hydrogenolysis of the amine group occurs.

It was previously found that on hydrogenation of the carboxybenzazepines **1**[1] and **2**[2] good yields were obtained of the cyclic lactams **3** and **4,** respectively. Since this reaction was of general synthetic interest, the hydrogenation of other aminobenzoic acids was also run to determine whether the simpler bicyclic lactams would be formed.



1, $R_1 = -CO_2H$; $R_2 = H$
2, $R_1 = H$; $R_2 = -CO_2H$

3

4

Hydrogenation of 4-aminobenzoic acid (**5**) occurred readily in methanol over a ruthenium on charcoal catalyst at 160° and 1600 psig to give a 40–50% yield of isoquinuclidone (**6**). 3-Aminobenzoic acid (**7**), on hydrogenation under these same conditions, afforded a 35–45% yield of the bicyclo[3.2.1]lactam, **8,** along with a small amount of another material.

The mass spectrum of **6** was analogous to that of 2-piperidone[3] with fragmentation occurring by the successive loss of the two C_2H_4 bridges giving a base peak at mass 69 ($M - C_4H_8$) and a strong peak at mass 97 ($M - C_2H_4$). Fragmentation of **8** followed the pattern observed in the mass spectrum of ε-caprolactam[4] with a base peak at mass 83 ($M - C_2H_4N$) and no other large peaks present. The minor component obtained on hydrogenation of **7** had a mass spectrum which was unlike that of **8** but similar to that of *N*-methylcaprolactam,[4] a base peak at mass 97 ($M - C_2H_4N$) and strong peaks at mass 110 ($M - CH_3N$) and 96 ($M - C_2H_5N$). On this basis, this material was tentatively identified as the *N*-methyllactam, **9.**

Hydrogenation of 3-methyl-4-aminobenzoic acid (**10**) gave four compounds in 8.5, 5, 65, and 10% yields, respectively, as determined by gas chromatographic analysis