

*Anal.* Calcd for  $C_{27}H_{37}NO_2$ : C, 79.56; H, 9.15; N, 3.44. Found: C, 79.40; H, 9.12; N, 3.44.

**16 $\beta$ -Anilino-17 $\alpha$  $\beta$ -methyl-D-homoandrost-4-ene-3,17-dione (14).**—A solution of 0.78 g of **12** in 30 ml of toluene and 8 ml of cyclohexanone was treated with 1.0 g of aluminum isopropoxide and stirred and refluxed for 1.5 hr. The cooled solution was diluted with ether, washed several times with potassium sodium tartrate solution, dried, and concentrated under reduced pressure. Trituration of the residual oil with ether afforded, after filtration, 0.23 g (30%) of product,  $\lambda_{\max}$  243  $m\mu$  ( $\epsilon$  28,900). A sample was recrystallized for analysis from methanol-acetone, mp 239–243° dec,  $[\alpha]_D^{25} +42^\circ$ ,  $\lambda_{\max}$  243  $m\mu$  ( $\epsilon$  30,200) and 292  $m\mu$  ( $\epsilon$  1960),  $\lambda_{\max}^{HCl}$  240  $m\mu$  ( $\epsilon$  17,100). The nmr spectrum exhibited two three-proton singlets at 0.87 (18-Me) and 1.17 (19-Me), a three-proton doublet ( $J = 7$  cps) centered at 0.99 (17a-Me), a broad one-proton hump at 3.7–4.2 (16 $\alpha$  proton), a one-proton singlet at 5.80 (4 proton), and a five-proton multiplet at 6.5–7.4 ppm.

*Anal.* Calcd for  $C_{27}H_{35}NO_2$ : C, 79.96; H, 8.70; N, 3.45. Found: C, 80.25; H, 8.58; N, 3.26.

**16 $\beta$ -Dimethylamino-17 $\alpha$  $\beta$ -methyl-D-homoandrost-5-en-3 $\beta$ -ol-17-one (13).**—A solution of 4.24 g of 17 $\alpha$  $\beta$ -dimethylamino-17 $\alpha$  $\beta$ -methyl-D-homoandrost-5-en-3 $\beta$ -ol-17-one (**2c**) in 210 ml of diethylene glycol was treated with 32 ml of dimethylamine and heated in a sealed bomb at 170° for 2 hr. The cooled solution was poured into water, and the precipitate was filtered, washed, and dried. Two recrystallizations from acetonitrile afforded 1.91 g (45%) of **13**, mp 154–156°,  $[\alpha]_D^{25} -94^\circ$  ( $c$  0.5, MeOH),  $\lambda_{\max}$  290  $m\mu$  ( $\epsilon$  36). The nmr spectrum exhibited a three-proton singlet at 0.67 (18-Me), a 1.5 proton singlet at 0.87 and a 4.5 proton singlet at 1.00 (17a-Me doublet and 19-Me singlet overlapping,  $J = 8$  cps), a six-proton singlet at 2.44 (N-Me<sub>2</sub>), a broad two-

proton hump at 2.8–3.8 (3 $\alpha$  and 16 $\alpha$  protons), and a one-proton hump at 5.40 ppm (6 proton).

*Anal.* Calcd for  $C_{23}H_{37}NO_2$ : C, 76.83; H, 10.37; N, 3.90. Found: C, 76.61; H, 10.28; N, 3.95.

The hydrochloride salt, prepared in the usual manner, was recrystallized from isopropyl alcohol-ethyl acetate, mp 282–283° dec (put on the block at 280°),  $[\alpha]_D^{25} -105^\circ$  ( $c$  0.8, MeOH),  $pK'_a$  7.7,  $\lambda_{\max}$  283  $m\mu$  ( $\epsilon$  36).

*Anal.* Calcd for  $C_{23}H_{35}ClNO_2$ : C, 69.76; H, 9.67; Cl, 8.95; N, 3.54. Found: C, 69.50; H, 9.65; Cl, 8.94; N, 3.32.

A solution of 100 mg of **13** in 6 ml of purified dioxane and 6 ml of deuterium oxide was treated with 300 mg of sodium methoxide and heated at 70° under an atmosphere of nitrogen for 16 hr. The solution was concentrated and the steroid was extracted with ether. The ether solution was dried, concentrated to a small volume, and diluted with petroleum ether. The precipitate was collected and dried under reduced pressure, affording 53 mg of 3-O,16 $\alpha$ ,17 $\alpha$  $\beta$ -di-16 $\beta$ -dimethylamino-17 $\alpha$  $\beta$ -methyl-D-homoandrost-3-en-3 $\beta$ -ol-17-one, mp 146–149°. The nmr spectrum exhibited two three-proton singlets at 0.67 (18-Me) and 1.00 (19-Me), a singlet integrating for 2.4 protons at 0.93 (17a-Me), a six-proton singlet at 2.44 (NMe<sub>2</sub>), a broad one-proton hump at 3.2–3.8 (3 $\alpha$ -H), and a one-proton hump at 5.40 ppm (6 proton).

**Acknowledgment.**—The authors wish to express their appreciation to Mr. C. E. Childs and the staff of our Microanalytical Laboratory, Dr. J. M. Vandenberg and the staff of our Physical Chemistry Laboratory, and Mr. W. M. Pearlman of our High-Pressure Laboratory for their valuable technical assistance.

## Acylated Hydrazine Mustards<sup>1</sup>

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Received August 9, 1966

The synthesis of some new 1-acyl-2,2-dialkylhydrazines (**3a–f**), 1-acyl-2-isopropenylhydrazines (**6a–d**), and 1-acyl-2,2-bis(2-chloroethyl)hydrazines (**8a–c**) is reported. Catalytic reduction of 1-acyl-2,2-bis(2-chloroethyl)hydrazines was found to cause extensive hydrogenolysis of the C–N and C–Cl bonds. Lithium aluminum hydride reduction of acylhydrazones **5b**, **5c**, and **5d** and catalytic reduction of **5a** and **5e** was selective, resulting in 1-acyl-2-alkylhydrazines. However, reduction of  $\alpha$ -haloacylhydrazones **6a** and **6b** was accompanied by considerable hydrogenolysis.

The synthesis and interesting biological activity of bis(2-chloroethyl)hydrazine<sup>2</sup> and a number of its acyl<sup>3</sup> and alkylidene<sup>2c,3a,4</sup> derivatives have recently been reported by other workers. The purpose of the present investigation was to obtain a wider variety of "hydrazine" mustards for screening purposes and to explore new methods of synthesis for these compounds. The syntheses of new acyl derivatives of bis(2-chloroethyl)hydrazine, as well as the synthesis and reduction of acyl derivatives of bis(2-chloroethyl)hydrazines and chlorinated isopropenylhydrazones, were accomplished and are reported herein.

Alkylation of benzoylhydrazine (**1a**)<sup>5</sup> and isonicotinoylhydrazine (**1b**)<sup>6</sup> with alkyl halides has been shown

to give 2,2-dialkylhydrazines (**2a** and **2b**)<sup>5,6</sup> despite earlier reports.<sup>7</sup> A large number of 1-acyl-2,2-dialkylhydrazines have also been prepared in this laboratory,<sup>8</sup> by direct alkylation.

In the present study, the acylhydrazines **1a**, **1c**, **1d**, **1e**, and **1f** were alkylated with 2,3-dichloropropene to give 1-acyl-2,2-dialkenylhydrazines **3a**, **3c**, **3d**, and **3f**, respectively. The nmr spectrum of the product from the reaction of **1a** with 2,3-dichloropropene clearly indicates structure **3a** in having peaks at 3.90 (allylic protons), 5.25 (*trans*-vinyl protons), 5.44 (*cis*-vinyl protons), and complex aromatic absorption above 7.2–8.0 ppm for aromatic and N–H protons. The nmr spectrum of **3d** at first appeared unusual in that splitting

(1) This investigation was supported by Public Health Service Research Grant No. CA-05777 from the National Cancer Institute.

(2) (a) R. Preussman, C. Satzinger, and D. Schmahl, *Angew. Chem.*, **70**, 743 (1958); (b) M. Ishidate, Y. Sakurai, and Y. Kuwanda, *Chem. Pharm. Bull.* (Tokyo), **7**, 391 (1959); (c) W. Schulze and G. Letsch, *J. Prakt. Chem.*, **14**, 11 (1961).

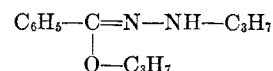
(3) (a) M. Ishidate, Y. Sakurai, and Y. Kuwanda, *Chem. Pharm. Bull.* (Tokyo), **8**, 543 (1960); (b) Y. Sakurai and M. Aoshima, *ibid.*, **10**, 979 (1962); (c) W. Schulze and G. Letsch, *J. Prakt. Chem.*, **16**, 182 (1962).

(4) (a) W. Schulze and G. Letsch, *ibid.*, **17**, 21 (1962); (b) W. Schulze and G. Letsch, *ibid.*, **21**, 272 (1963).

(5) R. L. Hinman and M. C. Flores, *J. Org. Chem.*, **24**, 660 (1959), and references cited therein.

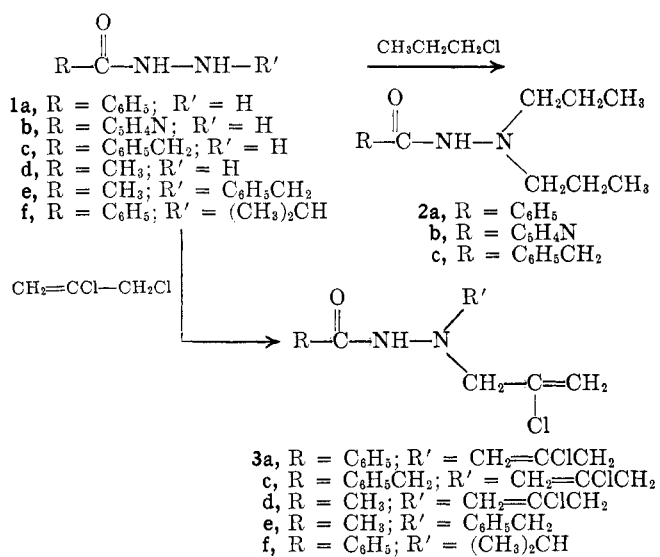
(6) H. Fox, J. T. Gibas, and A. Motchone, *ibid.*, **21**, 349 (1956); H. Fox and J. T. Gibas, *ibid.*, **20**, 60 (1955).

(7) D. Liberman, F. Grumbach, and N. Rist [*Compt. Rend.*, **237**, 338 (1953)] and R. Stolle and O. Benrath [*J. Prakt. Chem.*, **70**, 263 (1940)] reported the structure



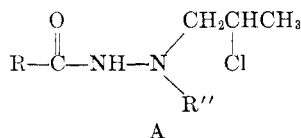
as the product formed by reaction of *n*-propyl chloride and benzoylhydrazine.

(8) Unpublished results of J. McAlvanah and B. Mallinger of this laboratory.



of the acetyl protons was observed. This is similar however, to that observed by Newman and Ungar<sup>9</sup> as well as Baumgarten, *et al.*,<sup>10</sup> in substituted hydrazides.

Reduction of (2-chloroallyl)hydrazides (**3a** and **3c**<sup>11</sup>) was explored as a possible synthetic route to 1-acyl-2-(2-chloropropyl)hydrazines; however, reduction of **3a** and **3c** with rhodium-on-alumina, platinum-on-charcoal or palladium-on-charcoal catalysts gave unpromising results. Reduction of **3c** in ethanol over 5% rhodium on alumina gave a complex mixture of products which was not resolved. Reduction of **3a** or **3c** with platinum or palladium on carbon in neutral or acidic ethanol solution gave hydrochloride salts from which 1-benzoyl-2-*n*-propylhydrazine (**4a**) and 1-phenylacetyl-2-*n*-propylhydrazine (**4c**) were isolated. Structures **4a** and **4c** were proven by comparison with samples prepared by reduction (*vide infra*) of the corresponding hydrazines (**5a** and **5c**). A comparison of the above results with the course of reduction of 1-phenylacetyl-2,2-diallylhydrazine, which was converted largely into di-*n*-propylhydrazine (**2c**) with rhodium on alumina and to **2c** in 78–80% with platinum on charcoal indicated that the chloro group β to the nitrogen of **3a** and **3c** facilitates C–N bond cleavage to a marked extent. The obvious conclusion to be drawn from these results is that C–N bond cleavage proceeds hydrogenolysis of the C–Cl bond or that a 2-chloropropyl hydrazide intermediate, *e.g.*, structure **A**, was suffering hydrogenolysis of a C–N bond. The latter appears unlikely in the light of the reported<sup>4b</sup> reduction of pyruvic acid *N,N*-bis(2-chloroethyl)hydrazone to  $\alpha$ -[*N,N*-bis(2-chloroethylhydrazino)]propionic acid with platinum oxide catalyst and the reported resistance of alkyl chlorides to hydrogenolysis.<sup>11</sup>

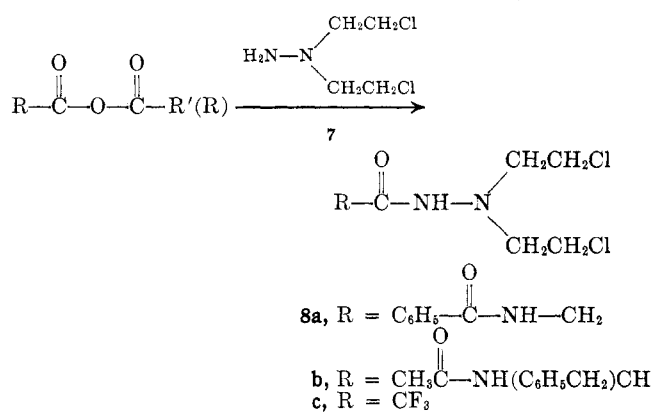
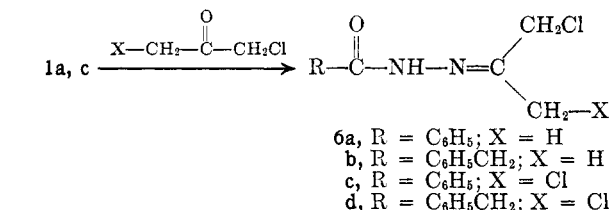
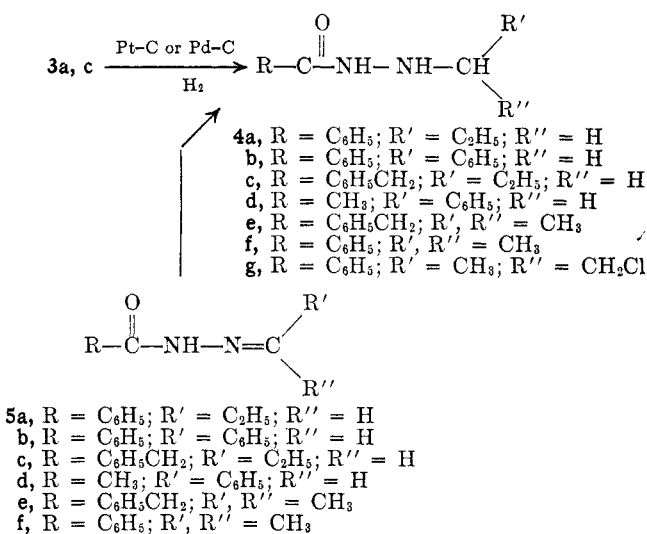


(9) M. S. Newman and I. Ungar, *J. Org. Chem.*, **27**, 1238 (1962).

(10) H. E. Baumgarten, P. L. Creger, and R. L. Zey, *J. Am. Chem. Soc.* **82**, 3979 (1960).

(11) The hydrogenolysis of allylic and vinyl halides has recently been investigated by G. E. Ham and W. P. Coker [*J. Org. Chem.*, **29**, 194 (1954)] and E. J. McMullen, H. R. Henze, and R. W. Wyatt [*J. Am. Chem. Soc.*, **76**, 5636 (1954)].

1-Acyl-2-(chloroisopropyl)hydrazines are potentially available *via* the selective reduction of hydrazones (*e.g.*, **6a**) prepared from 1-chloro-2-propanone and acylhydrazines. Reduction of hydrazone **6b** in glacial acetic acid over a platinum-on-charcoal catalyst gave after absorption of 1 mole of hydrogen unreacted hydrazone **6b** and two other components, the component having the lower *R<sub>f</sub>* value on tlc plates had the same *R<sub>f</sub>* value as 1-phenylacetyl-2-isopropylhydrazine (**4e**). The mixture was not characterized further. Reduction of **6a** or **6b** in absolute ethanol over platinum-on-charcoal catalyst was accompanied by extensive hydrogenolysis of the C–Cl bond, indicated by the absorption of 1.8 molar equiv of hydrogen. The reac-



tion mixture was concentrated and the residue was partitioned between ethyl ether and water. The ether layer contained 1-benzoyl-2-(2-chloroisopropyl)hydrazine (**4g**), the purification of which was difficult, because of contamination with **4f**. The compound **4f** was isolated from the aqueous extract.

The reduction of hydrazones **5b**, **5c**, and **5d** with 2 molar equiv of lithium aluminum hydride was selective, reducing the C=N bond and giving good yields of the 1-acyl-2-monoalkylhydrazines **4b**, **4c**, and **4d**,

respectively. Reduction of chlorinated hydrazone **6b** under these conditions gave oily products which were not resolved.

The compounds, 1-(*N*-benzoylglycyl)-2,2-bis(2-chloroethyl)hydrazine (**8a**) and 1-(*N*-acetyl-*dl*-phenylalanyl)-2,2-bis(2-chloroethyl)hydrazine (**8b**), were prepared by the mixed anhydride synthesis using 1,1-bis(2-chloroethyl)hydrazine (**7**). The 1-trifluoroacetyl-2,2-bis(2-chloroethyl)hydrazine (**8c**) was prepared from trifluoroacetic anhydride and **7** in ethyl ether.

### Experimental Section<sup>12</sup>

**1-Phenylacetyl-2,2-bis(2-chloroallyl)hydrazine (3c).**—Phenylacetylhydrazide (25.25 g) in 35 ml of sodium ethoxide solution (prepared from 1.61 g of sodium metal in 50 ml absolute ethanol) was treated with 2,3-dichloropropene (8.6 g) and the mixture was heated at reflux for 2 hr. After cooling, the mixture was filtered and the filtrate was concentrated *in vacuo* to an oil which crystallized in ethyl ether-petroleum ether (bp 30–60°) as brown needles (9.07 g), melting at 63–68°. Several recrystallizations from aqueous ethanol (Nuchar) gave thick colorless needles of **3c**: mp 71–72.5°;  $\lambda_{\max}$  3.08, 3.23, 5.97, 6.12  $\mu$ .

*Anal.* Calcd for  $C_{14}H_{16}Cl_2N_2O$ : C, 56.20; H, 5.39; N, 9.37. Found: C, 56.54; H, 5.64; N, 9.36.

**1-Benzoyl-2,2-bis(2-chloroallyl)hydrazine (3a).**—Compound **3a** was prepared by the above method from 2.72 g of **1a** and 4.50 g of 2,3-dichloropropene in 86.7% yield, mp 70–72°. An analytical sample was prepared from benzene-petroleum ether solvent as colorless needles: mp 72–73.5°;  $\lambda_{\max}$  2.99, 3.21, 6.04, 10.88  $\mu$ .

*Anal.* Calcd for  $C_{13}H_{14}Cl_2N_2O$ : C, 54.74; H, 4.95; Cl, 24.87; N, 9.83. Found: C, 54.87; H, 5.11; Cl, 24.85; N, 9.87.

**1-Acetyl-2,2-bis(2-chloroallyl)hydrazine (3d).**—The **3d** was prepared by the above method from **1d** and 2,3-dichloropropene in 56.6% yield, mp 60–63°. An analytical sample was prepared by recrystallization from ethyl ether-petroleum ether as colorless needles: mp 60–63°;  $\lambda_{\max}$  3.15, 3.21, 5.97, 6.11, 11.11  $\mu$ .

*Anal.* Calcd for  $C_8H_{12}Cl_2N_2O$ : C, 43.06; H, 5.42; Cl, 31.79; N, 12.56. Found: C, 43.17; H, 5.53; Cl, 31.78; N, 12.48.

**1-Acetyl-2-(2-chloroallyl)-2-benzylhydrazine (3e).**—Compound **3e** was prepared by the above method from **1e** and 2,3-dichloropropene in 58% yield, mp 67–72°. An analytical sample was prepared by recrystallization from benzene-petroleum ether as colorless needles: mp 73.5–75.5°;  $\lambda_{\max}$  3.10, 3.20, 6.12, 10.96  $\mu$ .

*Anal.* Calcd for  $C_{12}H_{16}ClN_2O$ : C, 60.37; H, 6.33; N, 11.73. Found: C, 60.23; H, 6.35; N, 11.57.

**1-Benzoyl-2-(2-chloroallyl)-2-isopropylhydrazine (3f).**—Compound **3f** was prepared by the above method from **1f** and 2,3-dichloropropene in 78% yield, mp 132–137°. A sample for analysis was obtained from chloroform-petroleum ether as colorless needles: mp 136–138°;  $\lambda_{\max}$  2.99, 3.22, 6.03, 10.87  $\mu$ .

*Anal.* Calcd for  $C_{13}H_{17}ClN_2O$ : C, 61.77; H, 6.78; N, 11.08. Found: C, 61.69; H, 6.08; N, 10.98.

**1-Phenylacetyl-2,2-di-*n*-propylhydrazine (2c).**—Using the above method, *n*-propyl chloride and **1c** gave compound **2c** in 79% yield, mp 64–78°. A pure sample of **2c** was prepared for analysis by recrystallization from benzene-petroleum ether as colorless needles: mp 76–78°;  $\lambda_{\max}$  3.10, 3.22, 6.02  $\mu$ .

*Anal.* Calcd for  $C_{14}H_{22}N_2O$ : C, 71.73; H, 9.48; N, 11.96. Found: C, 72.05; H, 9.10; N, 11.86.

**Hydrogenation of 3c. Method A.**—Compound **3c** (0.90 g) was dissolved in 25 ml of absolute ethanol which contained 50 mg of 5% rhodium-on-alumina catalyst. The mixture was stirred under hydrogen until absorption ceased. An additional 50 mg of catalyst was then added and stirring under hydrogen was continued until absorption again ceased. The catalyst was filtered and the filtrate was concentrated to a semisolid mass, mixed with sodium bicarbonate solution, and extracted with ethyl ether. The dried ether extract was concentrated to an oil

(0.74 g) which solidified on standing. A tlc plate of this material indicated that five or more components were present.

**Method B.**—Compound **3c** (0.60 g) in 20 ml of absolute ethanol containing hydrogen chloride (3 ml of 5 *N* hydrogen chloride in isopropyl alcohol) and 100 mg of 5% platinum-on-charcoal catalyst was stirred under hydrogen. The mixture absorbed 4.7 molar equiv of hydrogen. After separation of the catalyst by filtration, the reaction mixture was concentrated *in vacuo* to a slurry which was shaken with sodium bicarbonate solution and ethyl ether. The dried ether extracts were concentrated to an oil which crystallized from ethyl ether-petroleum ether. This substance (mp 93–96°) was identical<sup>13</sup> with a sample of **4c** prepared by reduction of hydrazone **5c**.

**Method C.**—Two grams of **3c** was hydrogenated over 5% palladium on charcoal (200 mg) in the same manner as method B. The oily product gave 0.75 g of colorless needles, mp 93–96° from benzene-petroleum ether, which was identical<sup>13</sup> with a sample of **4c** prepared from **5c**.

**1-Phenylacetyl-2-propylidenehydrazine (5c).**—Compound **5c** was prepared in good yield from phenylacetylhydrazide (**1c**) and propionaldehyde in ethanol, mp 119–121°.<sup>14</sup>

**Hydrogenation of 5c.**—One gram of **5c** was hydrogenated in ethanol over 50 mg of 5% palladium-on-charcoal catalyst. Several recrystallizations of the residue after evaporation of the filtrate gave colorless needles of **4c**, mp 94–95°.<sup>14</sup>

*Anal.* Calcd for  $C_{11}H_{16}N_2O$ : C, 68.71; H, 8.39; N, 14.57. Found: C, 68.88; H, 6.67; N, 14.74.

**Hydrogenation of 3a.**—One gram of **3a** and 100 mg of 5% palladium-on-charcoal catalyst in 25 ml of absolute ethanol were stirred under hydrogen until absorption ceased (4 molar equiv). After work-up as described in method C above, the crude, concentrated ether extract was diluted with petroleum ether. The pale yellow needles which formed (mp 64–70°, 0.45 g) gave only one prominent spot on tlc plates. Purification of this product by tlc and sublimation gave 1-benzoyl-2-*n*-propylhydrazine (**4a**): mp 67–70°;  $\lambda_{\max}$  3.09, 6.13  $\mu$ .

*Anal.* Calcd for  $C_{10}H_{14}N_2O$ : C, 67.40; H, 7.92; N, 15.71. Found: C, 67.25; H, 7.77; N, 16.11.

A sample of **4a** prepared by reduction of 1-benzoyl-2-propylidenehydrazine (**5a**) proved to be identical<sup>13</sup> with the reduction product of **3a**.

The reduction of **3a** was repeated but after removal of the catalyst by filtration, the filtrate was concentrated to an oil which crystallized from ethanol-ethyl ether to give 0.38 g, mp 145–151°. This hydrochloride salt of **4a** (immediate heavy precipitate with alcoholic silver nitrate) ( $\lambda_{\max}$  3.11, 3.90, 4.10, 4.35  $\mu$ ) was not purified further.

**1-Benzoyl-2-propylidenehydrazine (5a).**—Compound **5a** was prepared in good yield from **1a** and propionaldehyde, mp 117–120°.<sup>15</sup>

**Hydrogenation of 5a.**—One gram of **5a** was hydrogenated over 50 mg of 5% platinum-on-charcoal catalyst. The residue after filtering the catalyst and concentration of the filtrate melted at 49–60°. Recrystallization from benzene-petroleum ether gave colorless needles melting at 64–69° identical<sup>13</sup> with **4a** from the reduction of **3a**.

**Reduction of 1-Phenylacetyl-2,2-diallylhydrazine.<sup>16</sup> Method A.**—The title compound (0.92 g) was stirred in 25 ml of ethanol over 55 mg of 5% rhodium-on-alumina catalyst under hydrogen until 2 molar equiv of hydrogen was absorbed. After separation of the catalyst, the filtrate was concentrated *in vacuo* to 0.86 g of yellow residue, mp 65–74°. Absorption on alumina (Fisher, 80–200 mesh) and elution with benzene gave 0.77 g of **2c**, mp 74–77°.<sup>13</sup> Fractions eluted with benzene-ethyl ether contained two components having  $R_f$  (tlc plates, 9:1 ethyl ether-petroleum ether) values identical with those of **2c** and **4c**.

**Method B.**—The title compound (0.92 g) was hydrogenated over 50 mg of platinum on charcoal as in the previous experiment. The mixture absorbed 2.25 molar equiv of hydrogen. The crude product (0.86 g, mp 45–53°) was estimated to contain 70–80%

(12) Melting points were observed on a Fisher-Johns block with a calibrated thermometer. Infrared spectra were obtained on a Perkin-Elmer Infracord as Nujol mulls. Plates for thin layer chromatography (tlc) were prepared from silica gel G and the spots were visualized with iodine vapor. All hydrogenations were at atmospheric pressure. Microanalyses were by Dr. A. Bernhardt, Mülheim (Ruhr), Germany. Organic solutions were dried over anhydrous sodium sulfate. The nmr spectra were determined on a Varian A-60 in  $CDCl_3$  with tetramethylsilane as an internal standard.

(13) Established by mixture melting point determination, infrared spectral comparison, and comparison of  $R_f$  values on tlc plates.

(14) H. Takamatsu, S. Umemoto, S. Kano, and K. Tatsumi [Japanese Patent 3676 (1954)] report mp 119–121° for **5c**, 94–95° for **4c**, and 84–85° for **4e**.

(15) T. Curtius and G. Struve [*J. Pract. Chem.*, **60**, 295 (1894)] report mp 117–120°.

(16) Mp 65–67°. *Anal.* Calcd for  $C_{14}H_{18}N_2O$ : C, 73.01; H, 7.88; N, 12.16. Found: C, 73.20; H, 7.80; N, 11.89. Cf. footnote 8.

2c and 20–30% 4c by comparison on tlc plates with standard mixtures of 2c and 4c.

**1-Phenylacetyl-2-(1-chloroisopropenyl)hydrazine (6b).**—A solution of 1.5 g of 1c in 15 ml of ethanol was mixed with 1-chloro-2-propanone (0.93 g) under nitrogen. Crystallization began after 1 hr and was completed by chilling. After collection by filtration, the colorless plates (2.1 g, mp 110–112° dec) were recrystallized from benzene–petroleum ether: mp 113–116° dec;  $\lambda_{\max}$  3.11, 3.21, 5.96, 6.14  $\mu$ .

*Anal.* Calcd for  $C_{11}H_{13}ClN_2O$ : C, 58.80; H, 5.83; Cl, 15.78, N, 12.47. Found: C, 59.04; H, 5.66; Cl, 15.66; N, 12.39.

**1-Phenylacetyl-2-(1,3-dichloroisopropenyl)hydrazine (6d).**—The preceding experiment was repeated employing 1.5 g of 1c and 1.27 g of 1,3-dichloro-2-propanone. Compound 6d (78%) was collected as glistening plates, mp 130–133° dec. An analytical sample was prepared from benzene–petroleum ether: mp 130–133° dec;  $\lambda_{\max}$  3.11, 3.19, 5.94, 6.22  $\mu$ .

*Anal.* Calcd for  $C_{11}H_{12}Cl_2N_2O$ : C, 50.98; H, 4.67; N, 10.81. Found: C, 51.26; H, 4.81; N, 10.67.

**1-Benzoyl-2-(1-chloroisopropylidene)hydrazine (6a).**—Compound 6a was prepared by the method used for preparation of 6b. From benzhydrazide and 2.0 g of 1-chloro-2-propanone was obtained an 82% yield of 6a, mp 120–122° dec. Recrystallization of 6a from chloroform–petroleum ether gave colorless plates, mp 120.5–123° dec.

*Anal.* Calcd for  $C_{10}H_{11}ClN_2O$ : C, 57.01; H, 5.26; Cl, 16.33, N, 13.29. Found: C, 56.91; H, 5.18; Cl, 17.00; N, 13.17.

**1-Benzoyl-2-(1,3-dichloroisopropylidene)hydrazine (5c).**—Compound 5c was prepared in 95% yield from 2.72 g of 1a and 1,3-dichloro-2-propanone by the above method, mp 133–136° dec. An analytical sample of 5c was prepared by recrystallization from benzene–petroleum ether, mp 136–138°.

*Anal.* Calcd for  $C_{10}H_{10}Cl_2N_2O$ : C, 49.00; H, 4.11; Cl, 28.93; N, 11.43. Found: C, 49.17; H, 4.23; Cl, 28.75; N, 11.36.

**Hydrogenation of 6b. Method A.**—One gram of 6b and 50 mg of 5% platinum on charcoal in 20 ml of glacial acetic acid was stirred under hydrogen until 1.1 molar equiv of hydrogen was absorbed. After filtering, acetic acid was removed *in vacuo* leaving an oil which was extracted with sodium bicarbonate and ethyl ether. The dried ether extract was concentrated to 0.87 g of a colorless oil which slowly solidified, mp 42–56°. This solid contained compounds having the same  $R_f$  values on tlc plates as 6b and 4e and a third unidentified compound. Crystallization from ethyl ether gave 0.30 g of colorless plates, mp 105–112° which did not depress the melting point of 6b.

**1-Phenylacetyl-2-isopropylidenehydrazine (5e).**—Three grams of 1c refluxed in 20 ml of acetone for 1 hr gave after concentration 3.8 g of colorless needles, mp 108–110°.

*Anal.* Calcd for  $C_{11}H_{14}N_2O$ : C, 69.45; H, 7.42. Found: C, 69.41; H, 7.55.

**Reduction of 5e.**—One gram of 5e was reduced in the same manner as 5c. Two recrystallizations of the product from benzene–petroleum ether gave an analytical sample of 4e, mp 84–85°. <sup>14</sup>

*Anal.* Calcd for  $C_{11}H_{16}N_2O$ : C, 68.71; H, 8.39. Found: C 68.70; H, 8.42.

**Reduction of 1-Benzoyl-2-(1-chloroisopropylidene)hydrazine (6a).**—When 1 g of 6a and 100 mg of 5% platinum-on-charcoal catalyst in 30 ml of absolute ethanol was stirred under hydrogen, absorption ceased at 1.8 molar equiv of hydrogen. After filtering and washing the catalyst, the ethanol solution was concentrated *in vacuo* to a white solid (0.96 g) which was diluted with water and benzene. The dried benzene extract was concentrated to 0.36 g of white solid, mp 95–100°. A tlc plate showed two prominent spots, the larger having the higher  $R_f$  value, and the smaller having the same  $R_f$  value as 4g. Five recrystallizations from ethyl ether–petroleum ether gave colorless needles, mp 103.5–105°, assumed to be 1-benzoyl-2-(1-chloroisopropyl)hydrazine (4g):  $\lambda_{\max}$  3.02, 6.09  $\mu$ .

*Anal.* Calcd for  $C_{10}H_{13}ClN_2O$ : C, 56.47; H, 6.16; Cl, 16.67; N, 13.17. Found: C, 56.41; H, 6.66; Cl, 14.92; N, 14.92.

The aqueous extract was made basic to litmus with 1 *N* sodium hydroxide and extracted with ethyl ether. The dried ether extract was concentrated to give 0.32 g of colorless needles, mp 103–109°. A thin layer chromatograph indicated the substance consisted largely of 4f. Three recrystallizations from benzene–petroleum ether gave colorless needles of 4f, <sup>13</sup> mp 110–113°.

**1-Benzoyl-2-isopropylhydrazine (4f).**—Compound 4f, mp 115–117°, was prepared from 5f by the method of Manjakunnel: <sup>17</sup>  $\lambda_{\max}$  3.06, 6.09  $\mu$ .

**Reduction<sup>17</sup> of 5c with Lithium Aluminum Hydride.**—To a stirred solution of 1.90 g of 5c in 25 ml of dry THF was added dropwise a solution of lithium aluminum hydride in 7.5 ml of THF containing 2.3 molar equiv of hydride. After stirring at room temperature for 45 min the mixture was treated with 30% aqueous potassium tartrate, then filtered with suction. Combined filtrate and washings were concentrated until crystals formed, then the solution was diluted with petroleum ether to give a 79% yield of 4c, mp 90–94°, identical<sup>13</sup> with a sample of 4c prepared by catalytic reduction of 5c.

**Reduction<sup>17</sup> of 5b with Lithium Aluminum Hydride.**—The preceding experiment was repeated using 2.24 g of 5b. The product, 1-benzoyl-2-benzylhydrazine (4b), was obtained in 81% yield, mp 114–116°. <sup>18</sup>

**Reduction<sup>17</sup> of 5d with Lithium Aluminum Hydride.**—The reduction of 1.62 g of 5d was carried out by the above method. 1-Acetyl-2-benzylhydrazine<sup>17</sup> was obtained in 71% yield, mp 69–81°. Recrystallization from benzene–petroleum ether raised the melting point to 78–80.5°.

**1,1-Bis(2-chloroethyl)hydrazine Hydrochloride (7·HCl).**—This compound was prepared by the method of Schulze and Letsch. <sup>26</sup>

**1-(N-Benzoylglycyl)-2,2-bis(2-chloroethyl)hydrazine (8a).**—A solution of 1.08 g of ethyl chloroformate in dry THF was added at –10° with stirring to a solution of 1.8 g of hippuric acid and triethylamine in THF. After 15 min an ethereal solution of 7 (prepared by neutralization of 7 hydrochloride with cold 1 *N* sodium hydroxide) was added at –10°. After stirring for 2 hr at room temperature, the solution was concentrated to an oil and diluted with water and ethyl ether. The dried ether extract was concentrated to an oil which gave a white powder from ethyl ether, mp 129–132°. An analytical sample of 8a was prepared from ethanol–ethyl ether: mp 133.5–134.5°,  $\lambda_{\max}$  2.99, 3.10, 3.26, 5.97, 6.11  $\mu$ .

*Anal.* Calcd for  $C_{13}H_{17}Cl_2N_3O_2$ : C, 49.07; H, 5.39; Cl, 22.29; N, 13.20. Found: C, 49.24; H, 5.37; Cl, 22.28; N, 13.18.

**1-(N-Acetyl-DL-phenylalanyl)-2,2-bis(2-chloroethyl)hydrazine (8b).**—Four grams of N-acetyl-DL-phenylalanine was treated with 2.1 g of ethyl chloroformate and 7 by the method of the preceding experiment. Recrystallization of the product (3.1 g, mp 137–144°) from THF gave a white powder: mp 155–157° dec;  $\lambda_{\max}$  2.99, 3.10, 5.98, 6.08  $\mu$ .

*Anal.* Calcd for  $C_{15}H_{21}Cl_2N_3O_2$ : C, 52.02; H, 6.11; Cl, 20.48; N, 12.13. Found: C, 52.20; H, 6.23; Cl, 20.45; N, 12.06.

**1-Trifluoroacetyl-2,2-bis(2-chloroethyl)hydrazine (8c).**—Trifluoroacetic anhydride (1.6 g) in 5 ml of ethyl ether was added dropwise to a stirred ether solution of 7, prepared by neutralizing 1.0 g of 7 hydrochloride. After 3 hr, sodium bicarbonate solution was added to the reaction. The solution was extracted with ether and the combined ether extracts were dried and concentrated to a white solid, 1.03 g, mp 75–78°. Three recrystallizations of the crude solid from ethyl ether–petroleum ether gave flat, colorless needles: mp 78–79°;  $\lambda_{\max}$  3.08, 3.22, 5.79, 8.55 (broad)  $\mu$ .

*Anal.* Calcd for  $C_8H_9Cl_2F_3N_2O$ : C, 28.47; H, 3.59; Cl, 28.06; N, 11.07. Found: C, 28.25; H, 3.57; Cl, 28.03; N, 10.97.

(17) C. M. Manjakunnel [Ph.D. Thesis, Duquesne University, 1962] showed that the lithium aluminum hydride reduction of acylalkylidenehydrazines furnish acylalkylhydrazines in good yield.

(18) J. S. Aggarwal, N. L. Darborni, and J. N. Ray [J. Chem. Soc., 1945 (1929)] reported mp 114–115°.