

TABLE I
DEHYDROHALOGENATION OF 5-BROMO AND 5,5-DIBROMODIHYDROURACILS

Dihydrouracil	Uracil	Yield	M.P.	Reported M.P.
1-Methyl-5-bromo	1-Methyl	96%	232-233°	232 ⁹⁷
1-Benzyl-5-bromo	1-Benzyl	78%	171-172°	173-174 ⁹⁸
1-Isopropyl-5,5-dibromo	1-Isopropyl-5-bromo	64%	202-204°	—
1-Benzyl-5,5-dibromo	1-Benzyl-5-bromo	78%	203-205°	204 ⁹⁹

Anal. Calcd. for $C_8H_{17}O_2N$: N, 8.80. Found: N, 8.65.

1-Methyldihydrouracil. A solution of 30.0 g. (0.23 mole) of the ethyl ester of *N*-methyl- β -alanine in 30 ml. of water and 23.5 ml. of hydrochloric acid was added dropwise to a cooled solution of 24.3 g. (0.30 mole) of potassium cyanate in 30 ml. of water. This reaction mixture was allowed to stand overnight, the water removed by distillation under vacuum, and the semisolid residue heated at 100-110° (25 mm.) for 1 hr. The solid residue was extracted with boiling absolute alcohol. Upon evaporation of the alcohol a white crystalline solid was obtained. Recrystallization from ethanol yielded 13.0 g. (50%) of 1-methyldihydrouracil, which melted at 173-174°. (Lit. 174-175°).¹²

1-Isopropyldihydrouracil. When 31.8 g. (0.20 mole) of the ethyl ester of *N*-isopropyl- β -alanine was allowed to react with 21.0 g. (0.26 mole) of potassium cyanate and 20.0 ml. of hydrochloric acid according to the procedure described for the preparation of 1-methyldihydrouracil, 20.0 g. (61%) of 1-isopropyldihydrouracil was obtained. The compound after recrystallization from water melted at 140-141°.

Anal. Calcd. for $C_7H_{12}O_2N_2$: N, 17.93. Found: N, 17.68.

1-Benzylidihydrouracil. When 22.0 g. (0.11 mole) of the ethyl ester of *N*-benzyl- β -alanine was allowed to react with 9.7 g. (0.12 mole) potassium cyanate and 10.7 ml. of hydrochloric acid according to the procedure described for the preparation of 1-methyldihydrouracil a water insoluble oil formed. After shaking the mixture overnight, the oil was separated and heated at 110° for 2 hr. Upon cooling the oil solidified and was recrystallized from isopropyl alcohol to yield 15.0 g. (67%) of a white crystalline solid melting at 125-127°.

Anal. Calcd. for $C_{11}H_{12}O_2N_2$: N, 13.72. Found: N, 13.56.

Bromination of 1-substituted dihydrouracils. A well-stirred solution of the 1-substituted dihydrouracil in ten times its weight in acetic acid was heated to boiling. To this boiling solution one or two molecular equivalents of bromine in 3 times its volume of acetic acid was added dropwise. When the bromine color was discharged, most of the acetic acid was removed by distillation, the residue diluted with 20 ml. of water and neutralized with 10% sodium hydroxide solution. A solid precipitated from the neutral solution and was purified by recrystallization.

1-Methyl-5-bromodihydrouracil. When 1-methyldihydrouracil was treated with one molecular equivalent of bromine a 59% yield of 1-methyl-5-bromodihydrouracil was obtained. After recrystallization from ethanol it melted at 132-135°.

Anal. Calcd. for $C_6H_7O_2N_2Br$: N, 13.53; Br, 38.60. Found: N, 13.58; Br, 38.42.

1-Benzyl-5-bromodihydrouracil. 1-Benzylidihydrouracil when treated with one molecular equivalent of bromine gave 1-benzyl-5-bromodihydrouracil in 51% yield. After several recrystallizations from ethanol it melted at 150-152°.

Anal. Calcd. for $C_{11}H_{11}O_2N_2Br_2$: N, 9.90; Br, 28.22. Found: N, 9.76, Br, 28.36.

1-Isopropyl-5,5-dibromodihydrouracil. 1-Isopropyldihydrouracil when treated with one equivalent of bromine yielded a mixture of brominated compounds which could not be separated. When treated with two molecular equivalents of bromine, a 52% yield of 1-isopropyl-5,5-dibromodihydrouracil

was obtained. After several recrystallizations from ethanol it melted at 129-132°.

Anal. Calcd. for $C_7H_{10}O_2N_2Br_2$: N, 8.92; Br, 50.89. Found: N, 8.88; Br, 50.46.

1-Benzyl-5,5-dibromodihydrouracil. 1-Benzylidihydrouracil when treated with two molecular equivalents of bromine gave 1-benzyl-5,5-dibromouracil in 51% yield. After recrystallization from alcohol it melted at 157-159°.

Anal. Calcd. for $C_{11}H_{10}O_2N_2Br_2$: N, 7.74; Br, 44.14. Found: N, 7.52; Br, 43.79.

Dehydrohalogenation of 5-bromo and 5,5-dibromodihydrouracils. The brominated uracil was added in small portions to ten times its weight of boiling dimethylformamide, and the resulting solution refluxed for one hour. The dimethylformamide was removed by distillation under reduced pressure, and the residue treated with a small quantity of water. The resulting solid was filtered and recrystallized from alcohol (see Table I).

When 4.4 g. (0.014 mole) of 1-isopropyl-5,5-dibromodihydrouracil was dehydrogenated according to the above procedure, 2.3 g. (70%) of 1-isopropyl-5-bromouracil was obtained. It melted at 202-204°.

Anal. Calcd. for $C_7H_9O_2N_2Br$: N, 12.02; Br, 34.28. Found: N, 12.10; Br, 33.99.

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Reduction of Trimethylacetonitrile with Grignard Reagents. II. The Reaction of Trimethylacetonitrile with *t*-Butylmagnesium Chloride at Elevated Temperatures¹

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It has been shown that *t*-butylmagnesium chloride reacts readily with trimethylacetonitrile at high temperature (150°) and pressure to yield the reduction products, trimethylacetaldehyde, 2,2-dimethylpropylidene-2',2'-dimethylpropylamine (I), and higher boiling material of unknown structure. These findings have been interpreted in terms of the six-membered ring transition state mechanism for the "abnormal" Grignard reaction.

In the reaction of Grignard reagents with trimethylacetonitrile it was found² that as the

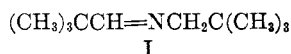
(1) Abstracted from the thesis submitted by Erwin J. Blanz, Jr., to Stanford University in partial fulfillment of the requirements for the M.S. degree, April 1957.

(2) H. S. Mosher and W. T. Mooney, *J. Am. Chem. Soc.*, **73**, 3948 (1951).

(12) G. Hilbert, *J. Am. Chem. Soc.*, **54**, 2076 (1932).

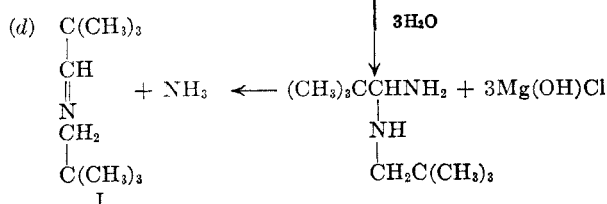
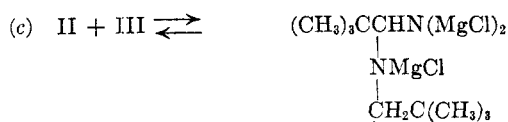
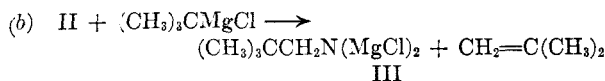
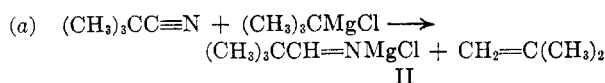
branching on the carbon atom *alpha* to the magnesium increased, the yield of reduction product, trimethylacetaldehyde, increased at the expense of normal addition. This reaction with *t*-butylmagnesium chloride and trimethylacetonitrile was so hindered, however, that under usual conditions (ether solution and room temperature) sixty per cent of the trimethylacetonitrile was recovered unchanged. Since the use of a solvent such as diisobutyl ether introduced certain problems, we decided to study this reaction in a stainless steel rocking autoclave at elevated temperatures.

When the reaction was carried out at 150° for approximately twelve hours with the ratio of *t*-butylmagnesium chloride and trimethylacetonitrile 1.3:1 there was isolated after hydrolysis a 10% yield of trimethylacetaldehyde, a 31% yield of the aldimine 2,2-dimethylpropylidene-2',2'-dimethylpropylamine (I) and a high boiling material of unknown structure; 7% of the unreacted nitrile



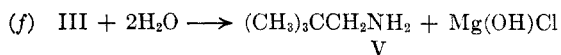
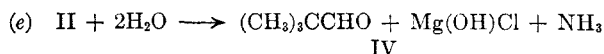
was recovered. No addition product 2,2,4,4-tetramethyl-3-pentanone was isolated. When the ratio of the Grignard reagent to the nitrile was increased to 2.6:1, there was isolated a 17% yield of trimethylacetaldehyde, a 26% yield of the aldimine (I), and material of unknown structure; neither neopentylamine, 2,2,4,4-tetramethyl-3-pentanone, nor unreacted nitrile were isolated.

Although ketimines have been isolated from the reaction of Grignard reagents with nitriles we have found no report of the isolation of an aldimine by this reaction. A possible way of formation of the aldimine is set forth in the following series of equations:



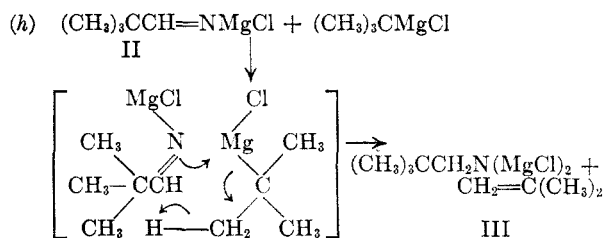
Equations (a) and (b) represent the reduction of the trimethylacetonitrile to the aldimine and amine stage respectively. Equation (c) represents the condensation of the substituted aldimine II and the

substituted amine III. Since aldimines are generally prepared from aldehydes and amines,³ there is a possibility that the aldimine was formed after the hydrolysis of the Grignard reaction. If this is so, the equations for the formation of the aldimine (I) may be represented as follows:



No experimental evidence is available to decide between these two possibilities. The fact that no neopentylamine was found is explained on the reasonable assumption that reactions (e) or (g) are essentially complete as written.

The six-membered ring theory for "abnormal" Grignard reactions⁴ has been used to explain the formation of trimethylacetaldehyde.² This theory also can be readily applied to the formation of neopentylamine derivatives. The following equations represent this postulated mechanism:



Hydrolysis of the magnesium salt III would give neopentylamine or this salt (III) could react further as indicated by Equation (e). Isobutylene was identified by its infrared spectrum as a product of this reaction as required by this mechanism.

The proof of structure of 2,2-dimethylpropylidene-2',2'-dimethylpropylamine (I) has been reviewed in a previous publication.⁵

The high-boiling material from this reaction was shown by gas-partition chromatography on both Carbowax and silicon oil columns to be a complex mixture. In addition it was found that the material was not stable on standing; crystals of trimethylacetamide separated from the high-boiling material after a period of a month. Before the complexity of this material was appreciated the following evidence had been obtained: (a) Hydrolysis of the material gave trimethylacetaldehyde and am-

(3) M. R. Tiollais, *Bull. soc. chim. France*, **14**, 708 (1947).

(4) Whitmore and George, "The Common Basis of the Reaction of Grignard Reagents with Carbonyl Compounds; Addition, Reduction, Enolization and Condensation." Paper presented at the 102nd Meeting of the American Chemical Society, September 9, 1941. For further details see the Ph.D. thesis of R. S. George, The Pennsylvania State College, July 1943; available from University Microfilms, Ann Arbor, Mich.

(5) H. S. Mosher and E. J. Blanz, Jr., *J. Org. Chem.*, **22**, 445 (1957).

monium chloride; (b) hydrogenation of this material gave dieneopentylamine; (c) the infrared spectrum of the material showed a very narrow, pronounced absorption at 6.01μ characteristic of the C=N group and a wider, less pronounced absorption at 3.00μ indicating the presence of NH.

EXPERIMENTAL^{6,7}

t-Butylmagnesium chloride and trimethylacetonitrile. To a titrated ether solution of 0.172 mole of *t*-butylmagnesium chloride in a stainless steel autoclave was added 11.6 g. (0.135 mole) of trimethylacetonitrile (b.p. $104\text{--}105^\circ$). The autoclave was quickly sealed under a blanket of nitrogen and heated for 12 hr. at 150° . After the autoclave was cooled, the contents were hydrolyzed in an aqueous solution of ammonium chloride at 0° , and the ether layer and ether extracts of the aqueous layer were dried over anhydrous sodium sulfate. The ether was removed by fractionation through a sixteen-plate column and the residue was fractionated further from a column of small holdup to give the following cuts: 1-3 ether; cuts 4-5, b.p. $68\text{--}71^\circ$, n_D^{21} 1.3803-1.3829, 1.10 g., impure trimethylacetaldehyde; cut 6, b.p. $71\text{--}92^\circ$, n_D^{21} 1.3900, 0.45 g.; cuts 7-8, b.p. $92\text{--}118^\circ$, n_D^{21} 1.3860-1.3898, 0.81 g., impure trimethylacetonitrile and hexamethylethane; cut 9, b.p. $118\text{--}141^\circ$, n_D^{21} 1.4029, 0.36 g.; cuts 10-15, b.p. $141\text{--}145^\circ$, n_D^{21} 1.4080-1.4099, 3.42 g., 2,2-dimethylpropylidene-2',2'-dimethylpropylamine; cuts 16-19, b.p. $110\text{--}115^\circ$ (15 mm.), n_D^{21} 1.4334-1.4376, 3.58 g., high boiling mixture of unknown structure; residue 0.59 g. The material from cuts 4-5 gave a 2,4-dinitrophenylhydrazone, m.p. $205\text{--}206^\circ$; melting point when mixed with an authentic sample of 2,4-dinitrophenylhydrazone of trimethylacetaldehyde. $206\text{--}207^\circ$.

Cuts 10-15 were further purified by means of gas-liquid partition chromatography. The infrared spectrum of the aldimine (I) was identical to the aldimine prepared from trimethylacetaldehyde and neopentylamine.⁵ Infrared spectrum included bands at $3.40(s)$, $3.56(s)$, $5.98(s)$, $6.77(s)$, $6.95(m)$, $7.18(m)$, $7.33(s)$, $8.00(w)$, $8.26(m)$, $9.38(m)$, $9.89(w)$, $10.52(w)$, $11.13(m)$, and $13.42(w) \mu$.

Infrared analysis of the gas collected when the autoclave was vented showed that it consisted of a mixture of isobutylene and ether.

A second experiment in which 2.6 molar equivalents of Grignard reagent were used was carried out as indicated above starting with 10 g. (0.120 mole) of trimethylacetonitrile and 0.316 mole of *t*-butylmagnesium chloride. After fractionation there was obtained trimethylacetaldehyde 1.72 g. (17%), 2,2-dimethylpropylidene-2',2'-dimethylpropylamine 2.39 g. (26%) and 4.42 g. b.p. $86\text{--}90^\circ$ (9 mm.) of the high-boiling material of unknown structure.

Hydrogenation of the high-boiling material. The material from cuts 16-19, 548 mg., methanol, 15 ml., and Raney nickel catalyst, approximately 150 mg., were stirred under one atmosphere of hydrogen in a microhydrogenation apparatus for 34 hr. A total uptake of 100.9 ml. of hydrogen at 18° was recorded. This corresponds to an equivalent weight of 128 ± 5 . The basic product from this reduction was separated by extraction with acid and was regenerated with base. The phenylthiourethane melted at $138\text{--}140^\circ$; melting point when mixed with a known sample of the phenylthiourethane of dieneopentylamine,⁵ $138\text{--}140^\circ$.

Hydrolysis of the high-boiling material. To 20 ml. of 6*N* hydrochloric acid was added 500 mg. of high boiling material. The reaction mixture was heated for 30 min. at 100°

(6) All melting points and boiling points are uncorrected; microanalysis was done by Microchemical Specialties Company, Berkeley, Calif.

(7) Infrared spectra were taken with a Perkin-Elmer Model 21 Recording Infrared Spectrophotometer.

because the material appeared to be quite unreactive in the acid solution. The ether extract gave a 2,4-dinitrophenylhydrazone, m.p. $205\text{--}206^\circ$; melting point when mixed with an authentic sample of the 2,4-dinitrophenylhydrazone of trimethylacetaldehyde, $205\text{--}206^\circ$. Ammonium chloride was isolated from the aqueous acid layer by evaporation. After standing one month white crystals had separated in the vial containing the high boiling material. These crystals were separated, washed with petroleum ether and sublimed; m.p. $153.5\text{--}154.5^\circ$; melting point when mixed with an authentic sample of trimethylacetamide $154\text{--}155^\circ$.

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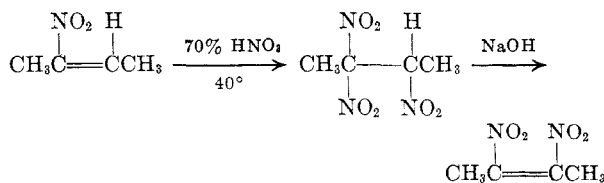
Nitration of Nitroolefins with Nitric Acid

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The addition of dinitrogen tetroxide to simple olefins has been studied extensively by Levy and Scaife¹ who isolated and characterized three types of reaction products—dinitroalkanes, nitroalcohols, and nitroalkylnitrates. This reaction has also been applied to nitroolefins. The addition of dinitrogen tetroxide to 2-nitro-2-butene and 2,3-dinitro-2-butene has given 2,2,3-trinitrobutane² and 2,2,3,3-tetranitrobutane,³ respectively. The nitration of olefins with nitric acid has been studied by various workers,⁴ but to our knowledge the reaction of nitroolefins and nitric acid has not been reported.

We have studied the reaction of 2-nitro-1-propene, 2-nitro-1-butene, and 2-nitro-2-butene with 70% nitric acid under various conditions. Mixtures were obtained from these reactions and only in the case of 2-nitro-2-butene, where a solid product was obtained, was it possible to purify and identify the major product. When the nitric acid was warmed to 40° and 2-nitro-2-butene was added dropwise at this temperature, there was isolated a 25.3% yield of a white solid, m.p. $46\text{--}48^\circ$. The analysis of this product corresponded to an empirical formula of $C_4H_7N_3O_6$, a trinitrobutane. The structure of the trinitrobutane was established as 2,2,3-trinitrobutane by degradation with base to the known 2,3-dinitro-2-butene:



(1) N. Levy and C. W. Scaife, *J. Chem. Soc.*, 1093, 1096, 1100 (1946).

(2) OSRD Rept. 2016, Nov. 15, 1943.

(3) C. E. Gabriel, D. E. Bisgrove, and L. B. Clapp, *J. Am. Chem. Soc.*, **77**, 1293 (1955).

(4) H. Wieland and E. Sakellarios, *Ber.*, **53**, 201 (1920); A. D. Petrov and M. A. Bulygina, *Doklady Akad. Nauk, S.S.S.R.*, **77**, 1031 (1951).