amount of *p*-toluenesulfonyl bromide is formed along with a considerable quantity of the insoluble 2:1 salt, bis(*p*-toluenesulfonylhydrazide) hydrobromide. This salt reacts slowly with bromine since, if it is in

$$7\ p\text{-}CH_3C_6H_4SO_2NHNH_2 + 2Br_2 \longrightarrow p\text{-}CH_3C_6H_4SO_2Br + 3(2\ p\text{-}CH_3C_6H_4SO_2N_2H_3\cdot HBr) + N_2$$

contact with a large excess of bromine, the 1:1 salt, *p*-toluenesulfonylhydrazide hydrobromide, forms. When the 2:1 salt is digested in ether partial reversion to the

$$4\ p\text{-}CH_3C_6H_4SO_2N_2H_3 + 2Br_2 \longrightarrow p\text{-}CH_3C_6H_4SO_2Br + 3\ p\text{-}CH_3C_6H_4SO_2N_2H_3\cdot HBr + N_2$$

1:1 salt occurs. The 1:1 salt also has been prepared by bromination in ether.

The identity of the salts follows from the stoichiometry of their formation, analysis for ionizable bromine, bromimetric analysis for the hydrazyl group, and quantitative isolation of the sulfonyl bromide when the salts are brominated in aqueous solution. Hydrazide perbromides, analogous to those isolated by Carpino[9a] when benzoylhydrazide reacted with bromine in nitromethane saturated with hydrogen bromide, were not observed in our experiments.

Our results with bromine in nonaqueous media are in contrast to the experiences of Carpino[9] with hydrazides of carboxylic acids and of Davies, Storrie, and Tucker[10] with nitrobenzenesulfonylhydrazides. They found that chlorination occurred easily and the salts, undoubtedly formed, reacted readily. Thus, *m*- and *p*-nitrobenzenesulfonylhydrazides were converted into the corresponding sulfonyl chlorides in yields of 82 and 88%, respectively, by chlorination at 0° in petroleum ether or chloroform.

It is of considerable interest to note that brominations in water carried out in presence of chloride ions does not lead to serious contamination with sulfonyl chloride as one might expect. Even under conditions believed to be favorable for the formation of sulfonyl chlorides, *i.e.*, adding slowly an aqueous solution of sodium bromide–sodium bromate (mole ratio, 1:2) to a solution of *p*-toluenesulfonylhydrazide in 25% hydrochloric acid saturated with sodium chloride, the sulfonyl halides consisted primarly of the bromide. The mixture of halides (about 95% yield) contained 25.95% bromine and 5.25% chlorine corresponding to 69 and 31 mole % of the respective sulfonyl halides. No attempt was made to ascertain whether chlorine was a consequence of exchange between the sulfonyl bromide and chloride anions or whether the chlorine was incorporated during the transient oxidative phase. The amount of sulfonylhydrazide converted to sulfonyl bromide is essentially the same as that found when sodium bromate is used as the brominative oxidant; the provocative relationship is probably fortuitous. Formation of a sulfonyl chloride is obviated by carrying out the reaction in sulfuric acid solution.

These observations preclude the possibility that cationic species such as $ArSO_2N_2^+$ or $ArSO_2^+$ are important in these brominations. The mechanistic picture, however, is obscure and undoubtedly complex. Higginson[25] has discussed the oxidation of hydrazine and the nature of the intermediates involved.

Chlorination of sulfonylhydrazides has been carried out in nonpolar organic solvents[10]; the reaction with chlorine is rapid in water to give good yields of the sulfonyl chloride. No attempts were made to find conditions suitable for high yields.

The reaction of iodine with sulfonylhydrazide was examined cursorily. In aqueous acidic solution iodine is decolorized slowly at room temperature and rapidly on warming; in acetic acid no perceptible reaction was observed. Others,[8] much earlier, have noted that iodine reacts sluggishly with sulfonylhydrazides to give 1,2-disulfonylhydrazines among other reaction products. Sodium iodide reacts with aromatic sulfonyl halides[26] leading to sodium sulfinate, disulfones, and other products. Thus in presence of iodides or iodine a variety of products containing sulfur in various oxidative states may be produced.

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(25) W. C. E. Higginson, "Recent Aspects of the Inorganic Chemistry of Nitrogen," Spec. Publ. no. 10, The Chemical Society, London, 1957, p. 95.

(26)(a) E. Gebauer-Fulnegg, E. Riesz, and S. Ilse, *Monatsh.*, **49**, 41 (1928); (b) E. Gebauer-Fulnegg and F. Riesenfeld, *ibid.*, **47**, 185 (1926).

Oxidation of N,N-Disubstituted Ketohydrazones by Lead Tetraacetate. Carbon–Nitrogen Bond Cleavage[1]

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N,N-Disubstituted ketohydrazones are oxidized with lead tetraacetate to effect carbon–nitrogen cleavage of primary or secondary alkyl groups. A monosubstituted hydrazone intermediate has been demonstrated and an azoacetate and a carbonyl compound are isolated products.

It recently has been shown that azoacetates are produced in good yields when ketohydrazones are added to a solution of lead tetraacetate[3]

$$R_1R_2C{=}N{-}NH{-}R_3 + Pb(OAc)_4 \longrightarrow R_1R_2C(OAc){-}N{=}N{-}R_3 + Pb(OAc)_2 + HOAc$$

It was initially anticipated that N,N-disubstituted ketohydrazones would fail to react with this oxidizing agent.[4] However, benzophenone dimethylhydrazone, benzophenone methylphenylhydrazone, and other simi-

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(1) This research received support by the National Science Foundation, grant G 5789.

(2) From the M.A. thesis of Elisabeth Cerda, Western Michigan University, 1961. Presented in part at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

(3) D. C. Iffland, L. Salisbury, and W. R. Schafer, *J. Am. Chem. Soc.*, **83**, 747 (1961).

(4) Although ketoximes react with lead tetraacetate to yield nitrosoacetates, oxime O-alkyl ethers may be recovered from reaction mixtures containing lead tetraacetate. *Cf.* ref. 3, footnote 9.

lar hydrazones were found to consume lead tetraacetate readily under conditions used in the reactions with monosubstituted hydrazones. Nevertheless, the isolation of reaction products was not achieved until after discovery that a stoichiometry of two to one (lead tetraacetate to hydrazone) was involved in this new reaction. With this modification N,N-disubstituted ketohydrazones also yielded azoacetates (up to 75%) comparable to azoacetates derived from the monosubstituted hydrazones. The reaction was more complex than that obtained with monosubstituted hydrazones and isolation of the azoacetate was occasionally more difficult. Methylene chloride was the solvent of choice for this reaction. Benzene was also used, but because of the lower solubility of the lead tetraacetate, this solvent was somewhat less convenient.

The alkyl group cleaved in this oxidation was converted to the corresponding aldehyde or ketone. Although yields for the low molecular weight carbonyl compounds were not determined, benzaldehyde was produced in at least 62% yield starting from benzophenone benzyl-*t*-butylhydrazone. No cleavage of either *t*-alkyl or aryl groups has been observed. The N,N-disubstituted hydrazones examined in this reaction and a summary of reaction products are listed in Table I.

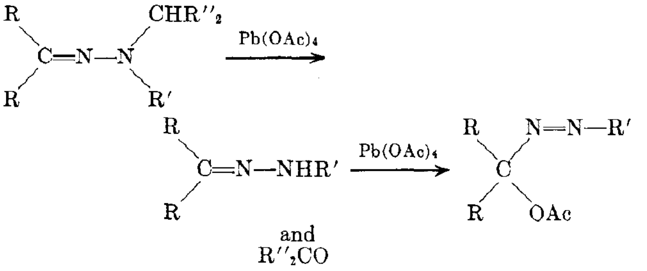
TABLE I

OXIDATION OF N,N-DISUBSTITUTED KETOHYDRAZONES

Hydrazone $R_2C{=}N{-}NR'R''$ R	R′	R″	Azoacetate $R_2C(OAc){-}N{=}N{-}R'$ yield, %	Carbonyl compound (related to R″)	2,4-Dinitrophenylhydrazone, m.p., °C.
C_6H_5-	CH_3-	CH_3-	75	CH_2O	163–164[a]
C_6H_5-	C_6H_5-	CH_3-	56	CH_2O	163–164[a]
C_6H_5-	C_6H_5-	C_2H_5-	50	$CH_3{-}CHO$	154–158[b]
C_6H_5-	C_6H_5-	$(CH_3)_2CH-$	[c]	$CH_3{-}CO{-}CH_3$	123–124[d]
C_6H_5-	$t\text{-}C_4H_9-$	CH_3-	50	[c]	
C_6H_5-	$t\text{-}C_4H_9-$	$C_6H_5{-}CH_2-$	47	$C_6H_5{-}CHO$	233–235[e]
CH_3-	C_6H_5-	CH_3-	[c]	CH_2O	163–164[a]

[a] Lit.[22] m.p. 166°. [b] Reported value; 168° (stable), 157° (unstable), 148° (mixture) ["Tables for Identification of Organic Compounds," C. D. Hodgman, R. C. Weast, and S. M. Selby, Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p. 68]. Infrared spectrum of this derivative was identical with the spectrum of the derivative prepared from authentic acetaldehyde. [c] Not isolated. [d] Lit.[22] m.p. 126°. [e] Lit.[22] m.p. 237°. This derivative was isolated in 62% yield based on starting benzophenone benzyl-*t*-butylhydrazone.

The course of the reaction has been of considerable interest and speculation. In each oxidation reaction the formation of the monosubstituted hydrazone has been detected. Indeed, when the addition of reagents was reversed and with a ratio of lead tetraacetate to benzophenone methylphenylhydrazone restricted to 0.9–1 mole, benzophenone phenylhydrazone was the principal product along with formaldehyde. This production of hydrazone suggests that it might be an intermediate in the formation of azoacetate according to the following sequence.



Such a reaction with production of lead diacetate and acetic acid in the first step is difficult to comprehend. The possibility that alkylidene diacetate might be a precursor of the carbonyl compound has been considered since methylene diacetate has been shown to be a reaction product in the lead tetraacetate oxidation of methyl acetate.[5] However, when ethylidene diacetate was added to a reaction mixture consisting of benzophenone phenylhydrazone and lead tetraacetate with conditions approximating the reaction at the end of the first step, no acetaldehyde was produced. Nevertheless, the oxidation of benzophenone ethylphenylhydrazone under anhydrous conditions maintained by the addition of acetic anhydride, yielded acetaldehyde as demonstrated by means of g.l.c. Thus, formation of the carbonyl compound by a hydrolytic step was precluded.

The reaction mixtures have been examined for acetic anhydride. Infrared spectra of reaction mixtures failed to show absorption at 1830 and 1130 cm.$^{-1}$ characteristic of the anhydride. Gas–liquid chromatography failed to indicate acetic anhydride, although the anhydride was detectable in the reaction solvent (methylene chloride) at concentration levels below that expected in the reactions.

The oxidative cleavage of the N-alkyl bond appears similar to the manganese dioxide oxidation of dialkyl anilines,[6] and tertiary aliphatic amines[7] described by Henbest for which a free radical mechanism has been suggested.[8] Furthermore, the presence of an enamine in the oxidation of diethylaniline was demonstrated by the development of a blue quinone when the oxidation was conducted in the presence of chloranil.[7] When benzophenone ethylphenylhydrazone containing chloranil was treated with lead tetraacetate in either methylene chloride or benzene solution, colored products attributable to an enamine intermediate failed to develop.

Although the mechanism of this new reaction of disubstituted hydrazones is not clear, it should be pointed out that a similar oxidation may be realized with other oxidizing agents. Treatment of benzophenone methylphenylhydrazone in methylene chloride with benzoyl peroxide slowly produced a mixture from which α-benzoyloxy-α-phenylazodiphenylmethane[3] was isolated in low yield.[9] The same hydrazone reacted with manganese dioxide in chloroform–acetic acid mixture to form a crude product which exhibited all infrared absorption bands of the corresponding azoacetate.

The hydrazines necessary for the preparation of phenylethyl-, phenylisopropyl-, methyl-*t*-butyl-, and benzyl-*t*-butylhydrazones were prepared from appropriate N-nitroso secondary amines. Lithium aluminum

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(5) W. A. Mosher and C. L. Kehr, *J. Am. Chem. Soc.*, **82**, 5342 (1960).

(6) H. B. Henbest and A. Thomas, *J. Chem. Soc.*, 3032 (1957).

(7) D. Buckley, S. Dunstan, and H. B. Henbest, *ibid.*, 4880 (1957).

(8) H. B. Henbest and M. J. W. Stafford, *Chem. Ind.* (London), 1170 (1961).

(9) The infrared spectrum of the reaction mixture derived from benzophenone phenylhydrazone and benzoyl peroxide also indicated the presence of the azobenzoate. Isolation and characterization of the azobenzoate formed in this reaction has been accomplished also by Professor J. T. Edwards, McGill University. Private communication.

hydride reductions of N-nitrosoethylaniline and N-nitrosoisopropylaniline were accomplished following the procedure of Hanna and Schueler.[10] Attempted reductions of N-nitrosomethyl-*t*-butylamine of N-nitrosobenzyl-*t*-butylamine with lithium aluminum hydride either without catalyst or with aluminum chloride or bismuth chloride catalysts,[11] or sodium with ethanol and low pressure hydrogenation over platinum catalyst, all failed to produce isolable amounts of dialkylhydrazine. Extensive recovery of the nitroso compound was possible in each instance.

An acidic reduction medium was initially avoided in anticipation of extensive alkene formation by acid-catalyzed elimination on the *t*-alkylhydrazine product.[12] Nevertheless, powdered zinc in acetic acid produced a 24% yield of methyl-*t*-butylhydrazine and a 67% yield of benzyl-*t*-butylhydrazine.

Experimental[13]

Preparation and Properties of N,N-Disubstituted Hydrazones.—Acetone methylphenylhydrazone, benzophenone methylphenylhydrazone, benzophenone diphenylhydrazone, and benzophenone dimethylhydrazone were prepared by reaction of the commercially available ketones and disubstituted hydrazines in the usual manner.[14] Benzophenone dimethylhydrazone, not previously reported, distilled at 146–148° (1 mm.); $n^{28}\text{D}$ 1.6048; $\lambda_{\max}$ 241 (4.13), 320 mμ (log ϵ 3.60).

Anal. Calcd. for $C_{15}H_{16}N_2$: N, 12.51. Found: N, 12.47.

N-Nitrosoethylaniline[15] was reduced with lithium aluminum hydride[10] to form ethylphenylhydrazine, b.p. 95–100° (6 mm.), which was treated with benzophenone in absolute alcohol to provide the hydrazone, m.p. 72–73° (from 95% ethanol).

Anal. Calcd. for $C_{21}H_{20}N_2$: N, 9.33. Found: N, 9.27.

Isopropylaniline was prepared in 35% yield by platinum-catalyzed hydrogenation of a mixture of nitrobenzene and acetone in acetic acid according to Emerson and Uranek.[16] Reaction of the amine with nitrous acid[15] gave N-nitrosoisopropylaniline in 83% yield; b.p. 114° (5 mm.), $n^{27}\text{D}$ 1.5253.

Anal. Calcd. for $C_9H_{12}ON_2$: N, 17.06. Found: N, 16.98.

With lithium aluminum hydride the nitrosocompound was converted to isopropylphenylhydrazine in 62% yield[17]; b.p. 112–116° (10 mm.); $n^{25}\text{D}$ 1.5474.

Anal. Calcd. for $C_9H_{14}N_2$: N, 18.65. Found: N, 18.84.

Adapting the procedure for preparing benzophenone hydrazones from diphenyldichloromethane,[18] isopropylphenylhydrazine, and diphenyldichloromethane gave the crude hydrazone (78% yield) which, as indicated by the infrared spectrum, contained benzophenone. The hydrazone was purified by conversion to the perchlorate salt in acetic anhydride.[18] After being washed with anhydrous ether, the salt (m.p. 149–150°) was treated with 5% potassium hydroxide solution and the hydrazone was collected in ether. The ether solution was dried over anhydrous potassium carbonate and evaporated under vacuum to leave a residue which solidified. Recrystallization from aqueous methanol gave pure benzophenone isopropylphenylhydrazone, m.p. 78–79°.

Anal. Calcd. for $C_{22}H_{22}N_2$: N, 8.91. Found: N, 8.79.

Catalytic hydrogenation of N-methylene-*t*-butylamine[19] in 1-butanol provided methyl-*t*-butylamine. The amine was converted to N-nitrosomethyl-*t*-butylamine as described by Heath and Mattocks[20]; b.p. 63–64° (7 mm.); $n^{25}\text{D}$ 1.4462; $\lambda_{\max}$ 230 (3.95); 348 mμ (log ϵ 1.82) [lit.[20] b.p. 66° (5 mm.)]. The amine (0.125 mole) in acetic acid (2.0 moles) solution was treated with powdered zinc (0.5 g.-atom). The zinc was added in portions during 1 hr. to maintain the temperature at 40°. After standing 5 hr. at room temperature, the mixture was added to 500 ml. of 50% aqueous sodium hydroxide solution. An oil was collected with pentane and dried over solid sodium hydroxide. After the solvent was removed, the oil was distilled to yield 3.4 g. (26%) of methyl-*t*-butylhydrazine; b.p. 116–118°; $n^{25}\text{D}$ 1.4252.

Anal. Calcd. for $C_5H_{14}N_2$: N, 27.52. Found: N, 27.47.

Benzophenone methyl-*t*-butylhydrazone was prepared from the hydrazine and diphenyldichloromethane and converted to the perchlorate salt by the procedure indicated before,[18] m.p. (perchlorate salt) 148–149°.

Anal. Calcd. for $C_{19}H_{22}N_2 \cdot HClO_4$: N, 7.64. Found: N, 7.78.

Benzophenone benzyl-*t*-butylhydrazone[21] was prepared analogous to the benzophenone methyl-*t*-butylhydrazone. From benzaldehyde and *t*-butylamine, N-benzylidene-*t*-butylamine was obtained in 92% yield; b.p. 101–102 (15 mm.); $n^{25}\text{D}$ 1.5184.

Anal. Calcd. for $C_{11}H_{15}N$: N, 8.69. Found: N, 8.70.

Low pressure hydrogenation over platinum gave benzyl-*t*-butylamine (86%); b.p. 91–93° (9 mm.); $n^{25}\text{D}$ 1.4975.

Anal. Calcd. for $C_{11}H_{17}N$: N, 8.58. Found: N, 8.53.

Conversion to the N-nitrosobenzyl-*t*-butylamine was completed in 80% yield; b.p. 141° (5 mm.); m.p. 42°; $\lambda_{\max}$ 236 (2.80); 360 mμ (log ϵ 0.92).

Anal. Calcd. for $C_{11}H_{16}ON_2$: N, 14.57. Found: N, 14.39.

Reduction with zinc and acetic acid led to the isolation (67%) of benzyl-*t*-butylhydrazine; b.p. 102–103° (5 mm.); $n^{25}\text{D}$ 1.5084.

Anal. Calcd. for $C_{11}H_{18}N_2$: N, 15.72. Found: N, 15.54.

With diphenyldichloromethane the hydrazone was formed in 50% yield; m p. 89–91°.

Anal. Calcd. for $C_{24}H_{26}N_2$: N, 8.18. Found: N, 7.99.

Reaction of Benzophenone N-Methyl-N-phenylhydrazone with Lead Tetraacetate.—The following procedure is typical for the reaction of lead tetraacetate with the hydrazones indicated in Table I.

A. Normal Addition.—A solution of 4.29 g. (0.015 mole) of benzophenone N-methyl-N-phenylhydrazone in 50 ml. of methylene chloride was added dropwise to a stirred solution of 16.83 g. (0.038 mole) of lead tetraacetate dissolved in methylene chloride. The reaction was somewhat exothermic, and the temperature of the reaction mixture was maintained between 0 and 5° by immersing the reaction flask in an ice–water bath. After a few milliliters of the hydrazone solution had been added, turbidity and a yellow color developed. Toward the end of the addition a gummy, orange-colored substance formed, which changed on further stirring to a flaky white precipitate of lead diacetate. The reaction mixture was stirred at room temperature for an additional 20–30 min. before 250 ml. of water was added. The methylene chloride layer was separated, washed successively with water and saturated sodium bicarbonate solution, and then dried over anhydrous sodium sulfate. The solvent was vacuum evaporated, leaving a yellow-brown oil. A seed crystal of α-acetoxy-α-phenylazodiphenylmethane induced crystallization. Recrystallization from petroleum ether (b.p. 60–110°) gave 2.74 g. (56%) of bright yellow crystals, m.p. 97–100°, identical with authentic α-acetoxy-α-phenylazodiphenylmethane.[3]

The presence of formaldehyde in the water layer as one of the reaction products was confirmed by Tollens test and formation of the 2,4-dinitrophenylhydrazone, m.p. 163–164° (lit.[22] m.p. 166°).

Examination of the ultraviolet spectrum of the crude reaction mixture after removal of the methylene chloride confirmed the presence of benzophenone phenylhydrazone. A maximum characteristic of benzophenone phenylhydrazone was observed at 340 mμ where the absorption of the azoacetate is insignificant. A benzene solution of the crude reaction mixture obtained, starting from benzophenone ethylphenylhydrazone, was purified by

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(10) C. Hanna and F. W. Schueler, *J. Am. Chem. Soc.*, **74**, 3693 (1952).

(11) G. A. Olah, *ibid.*, **81**, 3165 (1959).

(12) P. A. S. Smith, J. M. Clegg, and J. Lakritz, *J. Org. Chem.*, **23**, 1595 (1958).

(13) Microanalyses were by Galbraith Laboratories, Knoxville, Tenn. All ultraviolet spectra were determined using a Beckman DU spectrophotometer. Solvent was 95% ethanol in every instance. Infrared spectra were obtained with Perkin-Elmer Model 21 spectrophotometer.

(14) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 131.

(15) W. W. Hartman and L. J. Roll, "Organic Syntheses," Coll. Vol. II, A. H. Blatt (Ed.), John Wiley and Sons, Inc., New York, N. Y., 1946, p. 460.

(16) W. S. Emerson and C. A. Uranek, *J. Am. Chem. Soc.*, **63**, 750 (1941).

(17) Attempts to reduce this nitroso compound using zinc and acetic acid lead to a 63% conversion to isopropylaniline. Also, we have noted methylaniline to be a significant by-product in the reduction of N-nitrosomethylaniline by the method of Hartman and Roll (ref. 15, p. 418).

(18) W. Theilacker and O. R. Leichtle, *Ann.*, **572**, 121 (1951).

(19) M. D. Hurwitz, U. S. Patent 2,582,128 (1952).

(20) D. F. Heath and A. R. Mattocks, *J. Chem. Soc.*, 4226 (1961).

(21) We are indebted to Mr. Thomas Davies for assistance in completing the preparation of this compound and its reaction with lead tetraacetate.

(22) Ref. 14, pp. 111, 283.

chromatography on a 1 × 24 cm. neutral alumina (Fisher Scientific Co. no. A540) column and provided a 22% yield (based on the starting hydrazone) of benzophenone phenylhydrazone, m.p. 134–137° (lit.[22] m.p. 137°).

B. Reverse Addition, Approximate 1:1 Ratio of Reactants.—A solution of 8.39 g. (0.018 mole) of lead tetraacetate in 60 ml. of methylene chloride was added to a cooled, stirred solution of 5.72 g. (0.02 mole) of benzophenone N-methyl-N-phenylhydrazone[23] in 50 ml. of methylene chloride over a period of 1.5 hr. keeping the temperature between 0 and 5°. Turbidity developed almost immediately, followed by the formation of a white precipitate. The reaction mixture was stirred at room temperature for 1 hr. The solvent and all volatile products were then evaporated under reduced pressure and condensed in a trap cooled by a Dry Ice–trichloroethylene mixture. The condensate gave a positive Tollens test. Extraction with water and treatment of the extract with 2,4-dinitrophenylhydrazine reagent[22] gave formaldehyde 2,4-dinitrophenylhydrazone, m.p. 163–164°.

The residue left after removal of the volatile material was washed with benzene to separate the organic fraction from the lead diacetate. In order to remove acetic acid, the benzene solution was chromatographed on a 1 × 24 cm. neutral alumina (Fisher Scientific Co. no. A540) column and developed with benzene. The yellow eluate was collected and concentrated by vacuum evaporation. The residue weighed 5.90 g. and crystallized on standing. The ultraviolet spectrum of this material showed absorption maxima at 240, 300, and 340 mμ, characteristic of benzophenone phenylhydrazone. This residue was washed with three 15-ml. portions of cold pentane to leave 3.25 g. (71%, based on lead tetraacetate) of benzophenone phenylhydrazone, m.p. 132–135° (lit.[24] m.p. 137°).

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[23] This procedure was not extended to other hydrazones.

[24] Reference 14, p. 318.

Reduction of Ketones with Triisobutylaluminum. The Stereochemistry of Reduction of 3,3,5-Trimethylcyclohexanone

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The reduction of 3,3,5-trimethylcyclohexanone (dihydroisophorone) with triisobutylaluminum yields *trans*-3,3,5-trimethylcyclohexanol as the predominant epimer in an initially kinetically controlled process. The initial reduction step is followed, in the presence of excess ketone, by epimerization to the more stable *cis*-3,3,5-trimethylcyclohexanol (equatorial epimer). When cyclohexanone is added to the reduction mixture the 3,3,5-trimethylcyclohexanol (aluminum salt) is oxidized back to dihydroisophorone. The mechanism and stoichiometry of the reduction is discussed in relation to the above observations.

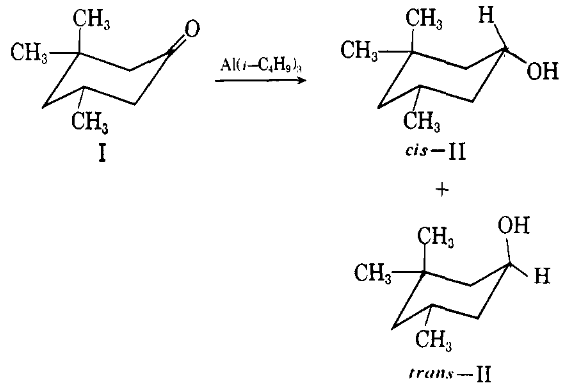
The reactivity and scope of reductions of organic compounds with aluminum alkyls[1] and dialkylaluminum hydrides[1,2] is reminiscent of reductions with lithium aluminum hydride. There are, however, several interesting aspects of the reduction of ketones with triisobutylaluminum in particular. Although this reagent is highly reactive toward the carbonyl group, there exists no aluminum–hydrogen bond analogous to that present in lithium aluminum hydride. Furthermore, in the reduction of ketones with triisobutylaluminum (and also with diisobutylaluminum hydride), only one of the possible three reducing equivalents is utilized[1] (equation 1). After the reaction of equimolar amounts of the reagent with ketone, the product, presumably diisobutylaluminum alkoxide, can apparently no longer function as a reducing agent.

$$R_2C{=}O + Al(i\text{-}C_4H_9)_3 \longrightarrow R_2CHO\text{-}Al(i\text{-}C_4H_9)_2 + (CH_3)_2C{=}CH_2 \quad (1)$$

This report describes the results of experiments which were carried out to elucidate the stereospecificity of reduction of ketones with triisobutylaluminum. The system chosen for initial study was 3,3,5-trimethylcyclohexanone (dihydroisophorone) (I), the reduction of which may lead to two epimeric alcohols, *cis*-3,3,5-trimethylcyclohexanol (*cis*-II) and *trans*-3,3,5-trimethylcyclohexanol (*trans*-II), the equatorial and axial epimers, respectively (Chart I).

CHART I

Reduction of dihydroisophorone to epimeric alcohols



The reduction of I with triisobutylaluminum in benzene at 42° was found to be highly stereospecific. However, either *cis*-II or *trans*-II could be formed as the predominant product depending on the reaction conditions. When a solution of I in benzene was added to triisobutylaluminum and an aliquot was removed while the aluminum alkyl was in excess, the product was found to consist of 96% *trans*-II and 4% *cis*-II by gas chromatographic analysis, with no detectable amount of ketone. If, on the other hand, excess ketone was present, the composition of the reaction mixture changed from predominant *trans*-II to exclusively *cis*-II.

Eliel and Rerick had previously shown that the reduction of 4-*t*-butylcyclohexanone with a reagent consisting of ethereal aluminum chloride–lithium aluminum hydride in the ratio of 3:1, or preferably 4:1, led to equilibration of the *cis* and *trans* aluminum alcoholates in the presence of excess ketone.[3] The equilibrium lay overwhelmingly in favor of the *trans* (equatorial) iso-

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[1] (a) K. Ziegler, British Patent 803,178 (1958); (b) K. Ziegler, "Organometallic Chemistry," H. Zeiss, Ed. Reinhold Publishing Corp., New York, N. Y., 1960, pp. 236–238; (c) K. Ziegler, K. Schneider, and J. Schneider, *Ann.*, **623**, 9 (1959).

[2] A. E. G. Miller, J. W. Biss, and L. H. Schwartzman, *J. Org. Chem.*, **24**, 627 (1959).

[3] (a) E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960); (b) E. L. Eliel, *Record Chem. Prog.*, **22**, 129 (1961).