Catalytic reduction of XIII *to 2-ethylferrocylacetonitrile.* A solution of 13.2 g. of the nitrile in 50 ml. of methanol containing in suspension 1.3 g. of 10% palladium-on-charcoal was stirred vigorously under hydrogen at atmospheric pressure. In 30 min., 1428 ml. (theo. 1330) of gas had been taken up. The reaction mixture was worked up in the same manner as the other reductions to afford 12.6 g. of a dark oil; λ_{max} 4.4 μ, no absorption at 6.1 μ or 11.1 μ.

Hydrolysis of the saturated nitrile to 1-ethylferrocylacetic acid. A solution of 12.6 g. of the nitrile obtained above and 48 ml. of 50% aqueous potassium hydroxide in 100 ml. of ethanol was brought to reflux. After 30 min. heating no ammonia had been noted. At this point 100 ml. of ethylene glycol was added to the solution and solvent was removed by distillation until the temperature of the distillate reached 100°. The now copious evolution of ammonia had ceased at the end of 2 hr. The hot solution was poured onto 800 ml. of ice water and this solution washed three times with 100 ml. of ether. The alkaline portion was subsequently filtered and acidified with phosphoric acid under a stream of nitrogen. The precipitated solid was collected on a filter, dried, and crystallized from benzene-hexane to afford 9.50 g. (70%) of the acid as stout amber rod-like crystals m.p. 123–125°.

Further crystallization from the same solvent pair gave a sample m.p. 124–125°.

Anal. Calcd. for $C_{14}H_{16}FeO_2$: C, 61.78; H, 6.13; Fe, 20.52. Found: C, 61.91; H, 6.20; Fe, 20.28.

Reaction of the methiodide IX *with sodium hydroxide.* A suspension of 5.0 g. of the quaternary salt[15] in 50 ml. of *N* sodium hydroxide was heated under reflux for 20 hr. At this temperature the salt went into solution. On cooling a crystalline solid came out of solution. This was collected on a filter and washed with ether to yield 3.70 g. (74%) of a material whose infrared spectrum was identical to that of starting material. The aqueous filtrate was extracted with ether and the organic solutions were combined. The residue obtained on removing the ether (0.08 g.) was chromatographed on an alumina column to afford 0.06 g. of a solid m.p. 46–52°, whose infrared spectrum is the same as that of vinylferrocene.

DURHAM, N. C.

(15) C. R. Hauser, J. K. Lindsay, and D. Lednicer, *J. Org. Chem.*, **23**, 358 (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Addition Reactions of the Methiodide of Benzophenonemethylimine and Its 4-Methyl Analog with Nucleophilic Reagents[1]

CHARLES R. HAUSER AND DANIEL LEDNICER

Received August 5, 1958

Benzophenone and 4-methylbenzophenone were condensed with methylamine to form the corresponding methylimines, which were converted to their methiodides. These methiodides were treated with potassium cyanide to give the corresponding α-aminonitriles. The α-aminonitrile from the methiodide of benzophenoneimine was obtained in low yield by the phenylation of the α-aminonitrile prepared from benzaldehyde, dimethylamine, and potassium cyanide. The methiodide of benzophenoneimine also underwent addition reactions with methylmagnesium iodide, potassio phenylacetonitrile, water, and liquid ammonia. The tertiary amine obtained from the methiodide and methylmagnesium iodide was prepared in better yield from the appropriate α-aminonitrile and the same Grignard reagent.

Some time ago, Sommelet[2] reported that the methiodide of benzophenonemethylimine (I) reacts with methylmagnesium iodide to form tertiary amine II, but the experimental details were not given.

$(C_6H_5)_2C{=}\overset{+}{N}(CH_3)_2\ I^-$ (I) $\qquad (C_6H_5)_2C(CH_3)-N(CH_3)_2$ (II)

More recently, the corresponding reaction of the methiodide I with benzylmagnesium chloride was effected in this laboratory[3] as an independent synthesis of tertiary amine III, which had been obtained from a Stevens type of rearrangement.

$(C_6H_5)_2C(CH_2C_6H_5)-N(CH_3)_2$ (III)

(1) Supported by the Office of Ordnance Research, U. S. Army.

(2) M. Sommelet, *Compt. rend.*, **183**, 302 (1926).

(3) C. R. Hauser, R. M. Manyk, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **20**, 1119 (1955).

In the present investigation a further study along these lines was carried out. The methiodide I was prepared as indicated in Equation 1.[3]

$$(C_6H_5)_2C{=}O \xrightarrow[180°]{CH_3NH_2} (C_6H_5)_2C{=}NCH_3 \xrightarrow{CH_3I} I \quad (1)$$

The yield of the intermediate benzophenonemethylimine was 89%, which is somewhat higher than that (49%) reported previously.[3] The methiodide of this imine was obtained as an ether-insoluble, crystalline solid.

Similarly 4-methylbenzophenone was condensed in 68% yield with methylamine to give the corresponding imine IV, which was methylated to form the methiodide V.

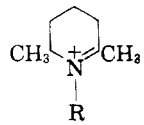
p-$CH_3C_6H_4C(C_6H_5){=}NCH_3$ (IV) $\qquad p$-$CH_3C_6H_4C(C_6H_5){=}\overset{+}{N}(CH_3)_2\ I$ (V)

The methiodides I and V are ternary iminium salts whose cationic fragment may be represented by resonance forms such as Ia and Ib.

$$(C_6H_5)_2C{=}\overset{+}{N}(CH_3)_2 \longleftrightarrow (C_6H_5)_2\overset{+}{C}{-}N(CH_3)_2$$
Ia Ib

Since the cannonical form representing the carbonium ion Ib should make a significant contribution to the structure of the cation,[4] this ion might be expected to be especially reactive toward nucleophilic reagents. This expectation was borne out by the present results.

It should be mentioned that Leonard and coworkers[5] have recently shown in an excellent series of papers that such an alicyclic ternary ion as VI, which was prepared by oxidative dehydrogenation

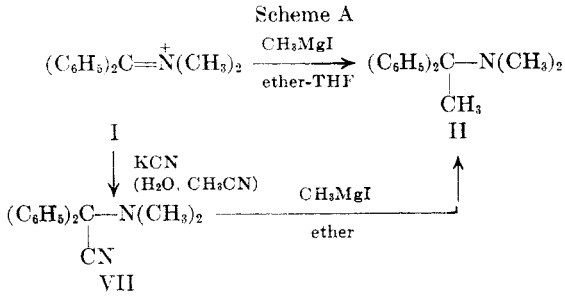


VI

of the corresponding substituted piperidine, likewise reacts readily with nucleophilic reagents including methylmagnesium iodide and potassium cyanide.

The cation Ia–b readily underwent addition reactions with methylmagneisum iodide in ether-tetrahydrofuran and with potassium cyanide in aqueous acetonitrile to form tertiary amine II and the α-aminonitrile VII in yields of 75% and 99% respectively (Scheme A).

Scheme A



The tetrahydrofuran was employed in the reaction with the Grignard reagent in order to facilitate solution of the ternary salt I. Actually the tertiary amine II was obtained in better over-all yield (95%) by first preparing the α-aminonitrile VII and then treating it with the same Grignard reagent in ether alone (see Scheme A). The latter step was realized in 96% yield. Both of these Grignard reactions were accompanied by transient purple colors.

The substitution type of reaction observed with the diphenylaminonitrile VII and the Grignard reagent (see Scheme A) is known[6] to be characteristic generally of such a monoarylaminonitrile as VIII, which is readily prepared from benzaldehyde, dimethylamine, and potassium cyanide (Equation 2).

$$C_6H_5CHO \xrightarrow[KCN]{(CH_3)_2NH} C_6H_5CH(CN){-}N(CH_3)_2 \qquad (2)$$
VIII

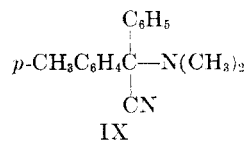
Incidentally, the corresponding direct preparation of the diphenylaminonitrile VII from benzophenone and these reagents appears not to have been realized.

In connection with the present work, the monophenylaminonitrile VIII was phenylated with bromobenzene by means of two molecular equivalents of potassium amide in liquid ammonia to form the diphenylaminonitrile VII in 25% yield (Equation 3).[7]

$$C_6H_5CH(CN){-}N(CH_3)_2 \xrightarrow[2.\ C_6H_5Br,\ KNH_2]{1.\ KNH_2\ (Liq.\ NH_3)} VII \qquad (3)$$
(VIII)

The procedure employed in this reaction was similar to that used by Leake and Levine[8] for the phenylation of certain carbanions, in which benzyne was considered to be an intermediate.

The preparation of the diphenylamnionitrile VII illustrated in Scheme A appears to be general. Thus the cation of the methiodide V similarly underwent the addition reaction with potassium cyanide to form the diarylaminonitrile IX in 93% yield.



An attempt to resolve this asymmetric aminonitrile by means of D - 10 - camphorsulfonic acid was unsuccessful because of the ease with which this nitrile undergoes hydrolysis. Thus with one-half an equivalent of the acid, 4-methylbenzophenone was obtained from IX along with optically inactive recovered starting material. Similarly, treatment of the aminonitrile with ethanolic picric acid led to the isolation of the picrate of dimethylamine rather than that of IX.

The cation of the methiodide I underwent ready reaction with the carbanion of phenylacetonitrile in tetrahydrofuran. The product of this reaction, which was obtained in good yield, is formulated as the β-aminonitrile X (Equation 4).

(4) Since the methiodide I has salt-like properties, the possible addition of the iodide anion to the cation to form an ether-soluble halide appears not to occur appreciably.

(5) See N. J. Leonard and F. Hanck, Jr., *J. Am. Chem. Soc.*, **79**, 5279 (1957).

(6) L. H. Goodson and H. Christopher, *J. Am. Chem. Soc.*, **72**, 358 (1950).

(7) The alkylation of the monophenylaminonitrile VIII with benzyl chloride has been accomplished by means of an equivalent of potassium amide in liquid ammonia to give a 90% yield of the benzylation product, which underwent dehydrocyanation on further treatment with the alkali amide or even on distillation to form the corresponding enamine; unpublished result of G. T. Ledford and C. R. Hauser.

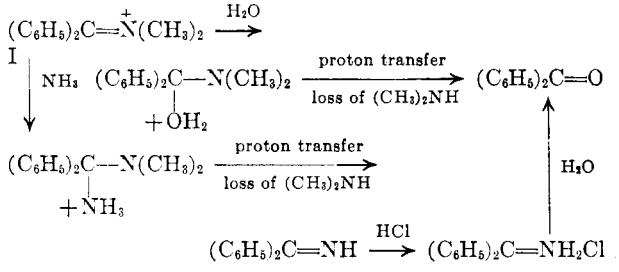
(8) W. W. Leake and R. Levine, abstracts of the ACS meeting, New York, September 1957, p. 37.

$$C_6H_5CH_2CN \xrightarrow[\text{liq. } NH_3]{KNH_2} \underset{K}{C_6H_5\overset{-}{C}HCN} \xrightarrow[THF]{I} \underset{X}{C_6H_5\overset{(C_6H_5)_2C-N(CH_3)_2}{\overset{|}{C}}HCN} \quad (4)$$

Unsuccessful attempts were made to effect the elimination of dimethylamine from X to form the corresponding acrylonitrile.

Finally the cation of the methiodide I reacted quite readily with water at room temperature and with liquid ammonia at −33° to form benzophenone and benzophenoneimine respectively. Presumably the water and ammonia functioned as nucleophilic reagents in these reactions to form intermediate addition complexes which then eliminated dimethylamine or the dimethylammonium ion to give the products isolated (Scheme B).

Scheme B



EXPERIMENTAL[9]

Conversion of the ketones to the imines. A stream of methylamine was passed through a melt of the appropriate ketone maintained at 180–185°. At the end of about 10 hr., the evolution of water had ceased. The oily product was allowed to cool and dissolved in ether. This solution was then quickly extracted with ice cold 2*N* hydrochloric acid. Each portion of the extract was immediately made alkaline with 40% sodium hydroxide. The resulting oil was extracted with ether, dried, and the solvent removed *in vacuo*. The pure imine was obtained by distillation at reduced pressure.

Benzophenone (66.5 g. ,0.36 mole), when subjected to this treatment afforded 55.3 g. (82%) of the imine as a colorless oil, b.p. 126–128° at 2.5 mm.; lit. 93° at 0.4 mm.

In the same way, 50.0 g. (0.25 mole) of 4-methylbenzophenone afforded 38.8 g. (68%) of IV as a clear oil, b.p. 140–142° at 2.4 mm. A small amount (5.1 g., 10%) of starting material was recovered from the neutral portion. A sample was redistilled to afford the analytical sample, b.p. 138–140° at 2.4 mm.

Anal. Calcd. for $C_{15}H_{15}N$: C, 86.08; H, 7.22; N, 6.69. Found C, 86.31; H, 7.36; N, 6.70.

Preparation of the ternary iminium salts. (*a*) *From benzophenone imine.* The liquid imine (62.7 g., 0.32 mole) was mixed with 30 ml. (0.48 mole) of methyl iodide. Within about 1 hr. the solution had set to a hard cake. After standing overnight, the yellowish solid was pulverized and washed well with ether to give 103 g. of I. The solid on heating slowly decomposes without showing a reproducible melting or decomposition point.

(*b*) *From 4-methylbenzophenone imine (IV).* Methyl iodide (21 ml., 0.34 mole) was added to 38.0 g. of the imine IV. Heat was evolved as an extremely viscous sirup V formed. Various attempts at crystallizing this taffy-like sirup were unsuccessful. This product was used without further purification.

(9) All melting points are uncorrected. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

α-Dimethylaminodiphenylacetonitrile VII. (*a*) *From the ternary salt.* A solution of 9.75 g. (0.29 mole) of the ternary salt from benzophenone (I) in 50 ml. of acetonitrile was added to a well stirred solution of 10 g. of potassium cyanide in 200 ml. of water. A solid came out almost immediately. After a total contact time of 30 min. the solid was removed by filtration and dried to yield 6.71 g. (99%) of the aminonitrile VII, m.p. 98–99.5°. The mixed melting point of this with a sample prepared by the direct phenylation was 98–99°.

(*b*) *By direct phenylation.* A solution of 48.0 g. (0.30 mole) of the aminonitrile of benzaldehyde in 50 ml. of ether was added to 0.3 mole of potassium amide (from 11.7 g. of the metal) in 300 ml. of liquid ammonia. To the resulting dark green solution there was added 47.1 g. (0.30 mole) of bromo benzene in 50 ml. of ether. Over the period of 25 min. another equivalent of potassium amide in 300 ml. of liquid ammonia was added to the reaction mixture by means of an inverse addition flask. The brown mixture was then stirred for an additional 5 min. and the base destroyed with 18 *g.* of ammonium chloride. The mixture was then taken to dryness on the steam bath. The grayish residue was washed with ether and these extracts separated from the inorganic salts by filtration. The solvent was removed from the ethereal solution to leave a dark oil. On standing the product separated from this oil as large cubic crystals. One crystallization from hexane afforded 18.2 g. (25%) of the aminonitrile VII, m.p. 99–100°.

A sample of this was recrystallized again from the same solvent to afford the analytical sample, m.p. 99–100°.

Anal. Calcd. for $C_{16}N_{16}N_2$: C, 81.32; H, 6.83; N, 11.86. Found: C, 81.50; H, 7.06; N, 11.88.

Formation of tertiary amine II. (*a*) *From the ternary salt.* Methylmagnesium iodide was prepared from 7.8 g. (0.055 mole) of methyl iodide and 1.34 g. of magnesium in 50 ml. of ether. To this solution there was then added 80 ml. of tetrahydrofuran. The solid salt I (8.3 g.)was added to this from a flask by means of Gooch tubing. A grape juice colored suspension developed immediately. Within 10 min. the intense coloration faded to light yellow. At the end of 2 hr. water was added and the ethereal layer separated. The aqueous portion was again extracted with ether. The combined organic solutions were then washed with 3 portions of 60 ml. of 3*N* hydrochloric acid. The oil which came out on making the washes alkaline was taken up in ether and dried. The solvent was then removed to leave behind 4.85 g. (85%) of the tertiary amine m.p. 27–30°. This solid was recrystallized twice from low boiling petroleum ether (cooling in Dry Ice–acetone) to afford 4.29 g. (75%) of crystalline solid, m.p. 40–41°.

The analytical sample, m.p. 40–41°, was obtained by one further crystallization in the same manner.

Anal. Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22 Found: C, 85.11; H, 8.39; N, 6.30.

The picrate was formed in the usual manner from 0.25 g. of the amine and 5 ml. of saturated ethanolic picric acid and recrystallized from ethanol to a constant m.p. of 154–155°.

Anal. Calcd. for $C_{22}H_{22}N_4O_7$: 58.14; H, 4.88; N, 12.33. Found; C, 58.09; H, 5.24; N, 12.18.

(b) *From the aminonitrile.* A solution of 6.71 g. (0.029 mole) of the aminonitrile of benzophenone (VII) in 100 ml. of ether was added to 0.62 mole of methylmagnesium iodide in 100 ml. of ether. The addition was accompanied by gentle refluxing and the formation of a transient purple coloration. After 2 hr. stirring, 50 ml. of water was added to the colorless reaction mixture. The ethereal layer was separated, washed with water, and then extracted with two 90-ml. portions of dilute hydrochloric acid. The extract was then made strongly alkaline and the resulting oil taken into ether. Drying of the ethereal solution followed by evaporation of the solvent afforded the tertiary amine as an oil which on scratching yielded 6.12 g. (96%) of colorless crystals, m.p. 40–41°. The mixed melting point of this product with that obtained above was 40–41°.

Aminonitrile of 4-methylbenzophenone IX. A solution of the iminium salt V (prepared from 38.0 g. of the corresponding imine) in 180 ml. of acetonitrile was added to a stirred solution of 33.0 g. of potassium cyanide in 300 ml. of water. An oil almost immediately separated from the solution. At the end of 30 min. the oil was taken up in ether and the extract washed with water. The residue obtained when the solvent was removed from the dried extract was distilled at 2.0 mm. to afford 38.6 g. (91% based on imine) of the extremely viscous colorless product, b.p. 158–160°.

A sample was redistilled at the same pressure, b.p. 157–159°. All attempts to crystallize this very pure sample failed.

Anal. Calcd. for $C_{17}H_{16}N_2$: C, 81.56; H, 7.25; N, 11.19. Found: C, 81.31; H, 7.41; N, 10.94.

Reaction of the aminonitrile IX *with acids. (a) d-10-Camphorsulfonic acid.* A solution of 20.0 g. (0.08 mole) of the aminonitrile and 8.5 g. (0.037 mole) of the acid in 30 ml. of ethanol was warmed at reflux for 1 hr. The hot solution was then poured into water and the resulting oil taken into ether. The ethereal solution was washed with water, dried by percolation through sodium sulfate, and evaporated *in vacuo*. The residual oil was fractionally distilled at 2.2 mm. to afford 5.78 g. of 4-methylbenzophenone b.p. 147–150°, 5.06 g. of a middle cut b.p. 150–155°, and 5.03 g. of recovered starting material. The first cut was recrystallized first from ethanol and then from low boiling (30–60°) petroleum ether to afford the ketone of m.p. 54–55°, mixed melting point with an authentic smple, 54–55°.

The infrared spectrum of the high boiling sample was superimposable on one of the starting aminonitrile.

(b) Picric acid. A small sample of the aminonitrile was dissolved in a saturated ethanolic solution of picric acid. In 2 hr. large crystals slowly formed. The melting point of this picrate (158-160°) was not depressed on admixture with authentic sample of the picrate of dimethylamine.

Reaction of the ternary salt of benzophenone I *with potassio phenylacetonitrile.* A solution of 0.05 mole of potassium amide was prepared from 1.95 g. of the metal in 200 ml. of liquid ammonia. To this there was then added a solution of 5.85 g. (0.05 mole) of phenylacetonitrile in 50 ml. of tetrahydrofuran. An additional 150 ml. of tetrahydrofuran was then added to the green solution and the ammonia allowed to evaporate by bringing the solution to the reflux temperature of tetrahydrofuran. The tetrahydrofuran was allowed to distill over until free of the odor of ammonia. The salt (17.6 g. 0.05 mole) was then added from a flask through a piece of Gooch tubing. A transitory lavender color accompanied the exothermic reaction. At the end of an additional 1 hr. stirring, the solid was removed by filtration and washed with ether. The volume of the filtrate was reduced to about 50 ml. *in vacuo*, and this solution treated with ether. This solution was washed once with water and then extracted with concentrated hydrochloric acid. The acid solution was then made strongly alkaline with potassium hydroxide pellets, and the resulting solid collected by filtration. The crude product (13.5 g.) was recrystallized from hexane to afford 10.6 g. (62%) of colorless crystals of X, m.p. 132–140°. Since this product apparently decomposes on simply heating in ethanol, no picrate was prepared. When a sample was treated with an excess of methyl iodide in acetonitrile for 24 hr. the only isolable product was recovered starting material (53%).

A sample of the β-aminonitrile was recrystallized from cyclohexane to a constant m.p. of 142–144°.

Anal. Calcd. for $C_{23}H_{22}N_2$: C, 84,62; H, 6.79; N, 8.58. Found: C, 84.74, H, 6.75; N, 8.47

Reaction of the ternary salt I *with water.* One gram of the salt prepared from benzophenone was added to a small amount of water covered by ether. Within 20 min. the solid was completely in solution. The ethereal layer was separated, washed with water, and taken to dryness. Upon scratching, the residue afforded 0.45 g. (87%) of benzophenone, m.p. 45–46.5°; mixed melting point with authentic sample, 45–46°.

Reaction of the ternary salt I *with ammonia.* Two grams of the solid was added to 50 ml. of liquid ammonia in a potassium hydroxide drying tube protected flask. A white solid formed which slowly went into solution. The oil which remained when the ammonia had evaporated was washed with ether. The residue from the ether extracts (λ, 2.9μ, 3.0μ and 6.0μ) formed crystals from 10 ml. of dilute hydrochloric acid. Enough water (20 ml.) was added to produce a solution. On further standing, 0.92 g. (89%) of benzophenone, m.p. 45–46°, was deposited from the solution.

DURHAM, N. C.

[CONTRIBUTION FROM THE NATIONAL RESEARCH COUNCIL OF CANADA, PRAIRIE REGIONAL LABORATORY]

Hydrogenolysis of Carbohydrates. VI. Cyclic Ketals and Related Compounds

P. A. J. GORIN

Received August 4, 1958

Some alkylidene-sugar derivatives have been hydrogenolyzed using copper chromite catalyst in dioxane. Carbon-oxygen bonds in the 1,3-dioxolane rings of carbons-5 and -6 of 1,2-5,6-di-*O*-isopropylidene- and 1,2-5,6-di-*O*-cyclohexylidene-D-glucofuranoses being cleaved. *O*-Isopropylidene groups attached to the reducing center of a sugar molecule, however, do not hydrogenolyze to *O*-isopropyl derivatives in a similar manner. The 1,3-dioxolane ring of 1,6-anhydro-D-glucopyranose is split, reductive fission of the carbon-2 hydroxyl group also taking place. The inversion of configuration of hydroxyl groups under hydrogenolysis conditions is considered.

In the course of investigating possible applications of hydrogenolysis reactions to carbohydrate synthesis, various types of sugar derivatives are being investigated as substrates.[1] In a previous publication, 1,2-*O*-isopropylidene-D-glucofuranose was hydrogenated at 180° in dioxane using Adkin's copper chromite catalyst.[2] The main products were 1,2-*O*-isopropylidene-L-idofuranose and a crystalline 3,4-dideoxy-hexitol. In the present paper, the reactions of 1,2,5,6-di-*O*-isopropylidene- and 1,2-5,6-di-*O*-cyclohexylidene-D-glucofuranoses, 1,6-anhydro-D-

(1) Presented at the 134th meeting of the American Chemical Society, Chicago, September 1958; issued as N.R.C. No. 5013.

(2) P. A. J. Gorin and A. S. Perlin, *Can. J. Chem.*, **36**, 661 (1958).