

Alkylation of *o*- and *p*-Tolunitriles with Halides by Means of Sodium Amide in Liquid Ammonia¹

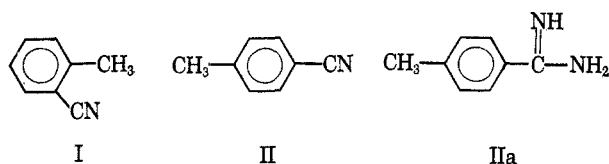
FRED H. RASH,² SANDRA BOATMAN, AND CHARLES R. HAUSER

Department of Chemistry, Duke University, Durham, North Carolina

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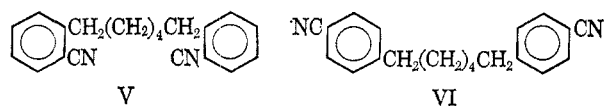
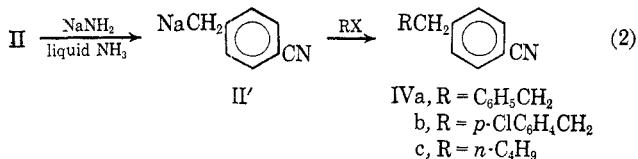
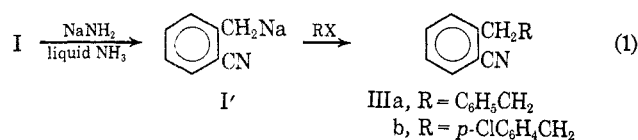
o- and *p*-tolunitriles were converted by sodium amide in liquid ammonia into corresponding carbanions, which were alkylated with certain alkyl, aralkyl, and methylene dihalides to form corresponding alkyl derivatives or bis products in yields of 63–86%. Also, the carbanions were coupled by means of 2,3-dibromo-2,3-dimethylbutane. The benzyl derivative of *o*-tolunitrile was further benzylated to form the dibenzyl derivative, and the benzyl derivative of *p*-tolunitrile was condensed with 1,4-dibromobutane to afford the bis product. The method furnishes a useful route to the synthesis of many new compounds.

o-Tolunitrile (I) and *p*-tolunitrile (II) might conceivably be attacked by an alkali amide at either a methyl hydrogen to form the carbanion or the cyanide group to give the amidine, for example, IIa.



Previously, nitrile I appears to have been converted partly into its carbanion by potassium amide in liquid ammonia since, in the presence of chlorobenzene and excess reagent, phenylation and diphenylation at the methyl group were realized in yields of 32 and 9%, respectively.³ However, nitrile II has been reported to be attacked at its cyanide group by potassium amide in liquid ammonia (sealed tube)⁴ and by sodium amide in refluxing toluene⁵ to form amidine IIa, which was isolated as its potassium salt⁴ and as its carbonate (60% yield),⁵ respectively.

We have now found that nitriles I and II are converted largely into carbanions I' and II', by sodium amide in liquid ammonia, as evidenced by successful alkylations. Thus, carbanion I' was alkylated with benzyl chloride and *p*-chlorobenzyl chloride, and carbanion II' with these halides and *n*-butyl bromide, to give alkyl derivatives IIIa–b and IVa–c, respectively (eq 1 and 2). Similarly, carbanions I' and II' under-

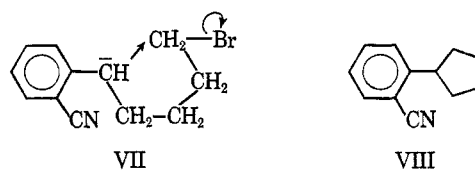


went twofold alkylation with 0.5 molecular equiv of 1,4-dibromobutane to afford the bis products V and VI, respectively. The yields were 63–86% (Table I).

The structures of these alkylation products were supported by analyses and absorption spectra (Tables II and III). The infrared spectra showed absorption peaks for the nitrile group (2257–2203 cm⁻¹, lit.^{6a} 2240–2221 cm⁻¹), and either *ortho* (768–763 cm⁻¹, lit.^{6b} 770–735 cm⁻¹) or *para* (827–815 cm⁻¹, lit.^{6b} 860–800 cm⁻¹) aromatic disubstitution. The nuclear magnetic resonance (nmr) spectra exhibited peaks with area ratios corresponding closely to those calculated for the expected relative numbers of aromatic (δ 6.9–7.7, lit.⁷ δ 6.5–8.0), benzylic (δ 2.5–3.3, lit.⁷ δ 2.2–2.9), and in the case of compounds IVc, V, and VI, aliphatic protons (δ 0.7–1.9, lit.⁷ δ 0.6–1.5).

Previously, nitrile IIIa has been prepared in unstated yields by heating the corresponding acid with lead thiocyanate,⁸ and nitrile IVa by the Sandmeyer reaction on *p*-aminobibenzyl;⁹ the present method appears superior.

It was possible for the intermediate monoalkyl derivatives in the twofold alkylations of carbanions I' and II' with 1,4-dibromobutane to equilibrate with I' or II' to form the carbanion, for example, VII, which might cyclize to give VIII. However, the products isolated were the bis derivatives V and VI, not such a cyclic product as VIII, as evidenced by their nmr spectra, and, especially, by their molecular weights.



Whereas carbanions I' and II' would probably undergo twofold alkylations with 1,3-dihalopropanes and with various higher methylene halides, II' failed to exhibit satisfactorily such alkylations with ethylene and methylene chlorides. The reaction with the ethylene halide appeared to involve β elimination since much of the starting nitrile was recovered. The

(5) A. V. Kirsanov and I. M. Polyakova, *Bull. Soc. Chim. France*, [5] **3**, 1800 (1936).

(6) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958: (a) p 264, (b) pp 75–79.

(7) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959, pp 51–62.

(8) See Table I, footnote a.

(9) See J. v. Braun, *et al.*, Table I, footnote d.

(1) (a) This investigation was supported in part by Public Health Service Research Grant No. CA 04455-07 from the National Cancer Institute. (b) A preliminary report has appeared in a communication: *Chem. Ind.* (London), 1267 (1966); also see W. T. Boyce and R. Levine, *J. Org. Chem.*, **31**, 3807 (1966).

(2) National Science Foundation Predoctoral Fellow, 1962–1965.

(3) P. H. Dirstine and F. W. Bergstrom, *J. Org. Chem.*, **11**, 55 (1946).

(4) E. F. Cornell, *J. Am. Chem. Soc.*, **50**, 3315 (1928).

TABLE I
 ALKYLATIONS OF *o*- AND *p*-TOLUNITRILES

Tolunitrile	Halide	Alkylation time, hr	Product name	Mp or bp (mm) °C	Yield, %
I	C ₆ H ₄ CH ₂ Cl	0.5	<i>o</i> -(β-Phenylethyl)benzotrile (IIIa)	110–114 (0.25) ^a	77 (61) ^b
I	<i>p</i> -ClC ₆ H ₄ CH ₂ Cl	1	<i>o</i> -(<i>p</i> -Chloro-β-phenylethyl)benzotrile (IIIb)	67–68 ^c	64
II	C ₆ H ₄ ClCH ₂ Cl	0.5	<i>p</i> -(β-Phenylethyl)benzotrile (IVa)	147–150 (0.5), ^d 40–42.5	71
II	<i>p</i> -ClC ₆ H ₄ CH ₂ Cl	0.5	<i>p</i> -(<i>p</i> -Chloro-β-phenylethyl)benzotrile (IVb)	111–112 ^e	86 (70) ^b
II	<i>n</i> -C ₄ H ₉ Br	4	<i>p</i> -Pentylbenzotrile (IVc)	94–96 (0.05)	63
I	Br(CH ₂) ₄ Br	1	1,6-Di(<i>o</i> -cyanophenyl)hexane (V)	70.5–72 ^e	67
II	Br(CH ₂) ₄ Br	1	1,6-Di(<i>p</i> -cyanophenyl)hexane (VI)	119–120.5 ^e	63

^a E. Bergmann [*J. Org. Chem.*, **4**, 8 (1939)] reports bp 168° (4 mm). ^b Yields given in parentheses were obtained when only 5 min was allowed for carbanion formation. Usual anion formation times were 15 min for nitrile I and 30 min for nitrile II. ^c A hexane solution of the initial oily product was cooled in Dry Ice, and the resulting precipitate recrystallized from hexane. ^d Reported as an oil [J. v. Braun, H. Deutsch, and O. Koscielski, *Ber.*, **46**, 1511 (1913)]. Some (10%) of the *p*-tolunitrile, bp 83–85° (8.3 mm), was recovered. I. Heilbron ["Dictionary of Organic Compounds," 4th ed., Oxford University Press, New York, N. Y., 1965, p 3078] reports bp 90.5–91° (11 mm). ^e Recrystallized from ethanol.

 TABLE II
 ANALYTICAL DATA

Compd	Formula	Calcd, %				Found, %			
		C	H	N	...	C	H	N	...
IIIa	C ₁₅ H ₁₃ N	86.92	6.32	6.75	207.3 ^a	86.91	6.36	6.58	202 ^a
IIIb	C ₁₅ H ₂₁ NCl	74.53	5.00	5.79	14.67 ^b	74.50	5.03	5.66	14.68 ^b
IVa	C ₁₅ H ₁₃ N	86.92	6.32	6.75		86.92	6.31	6.75	
IVb	C ₁₅ H ₁₂ NCl	74.53	5.00	5.79	14.67 ^b	74.45	5.18	5.68	14.66 ^b
IVc	C ₁₂ H ₁₅ N	83.19	8.73	8.08		83.45	8.98	7.86	
V	C ₂₀ H ₂₀ N ₂	83.26	6.99	9.71	288.4 ^a	83.23	7.03	9.66	277 ^a
VI	C ₂₀ H ₂₀ N ₂	83.26	6.99	9.71	288.4 ^a	83.17	7.00	9.67	290 ^a

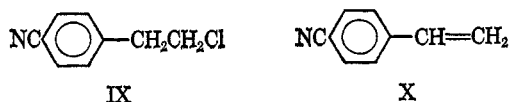
^a Molecular weight. ^b Chlorine (per cent).

 TABLE III
 INFRARED AND NUCLEAR MAGNETIC RESONANCE DATA

Compd	Infrared absorption peaks, cm ⁻¹	Type of protons	Peak type	Chemical shift, ^a δ (ppm)	Integrated area ratio ^b	
					Calcd	Found
IIIa	2217, 1603, 1511, 1456, 764, 700	Aromatic	Multiplet	6.9–7.4	9	9.1
		Benzylic	Multiplet	2.7–3.1	4	3.9
IIIb	2212, 1590, 1475, 815, 768	Aromatic	Multiplet	7.0–7.7	8	7.9
		Benzylic	Multiplet	2.7–3.3	4	4.1
IVa	2257, 1613, 1502, 1458	Aromatic	Multiplet	6.9–7.5	9	9.2
		Benzylic	Singlet	2.9	4	3.8
IVb	2208, 1585, 1471, 826	Aromatic	Multiplet	6.9–7.6	8	8.1
		Benzylic	Singlet	2.9	4	3.9
IVc	2915, 2227, 1618, 1513, 1471, 825	Aromatic	Quartet	7.2–7.6	4	4.0
		Benzylic	Triplet ^b	2.5–2.7	2	2.1
		Aliphatic	Multiplet	0.7–1.8	9	8.9
V	2882, 2203, 1582, 1466, 763	Aromatic	Multiplet	7.1–7.7	8	7.8
		Benzylic	Triplet ^b	2.7–2.9	4	4.1
		Methylenic	Broad singlet	1.2–1.9	8	8.1
VI	2890, 2227, 1610, 1511, 1471, 827	Aromatic	Quartet	7.2–7.6	8	7.9
		Benzylic	Triplet ^b	2.5–2.8	4	4.0
		Methylenic	Broad singlet	1.2–1.9	8	8.1

^a Downfield from tetramethylsilane as internal standard. ^b Coupling constant, ~7 cps.

reaction with the methylene halide might have involved monoalkylation to form IX which underwent β elimination to give the cyanostyrene X, since polymer was produced; X might be expected to undergo polymerization under the conditions employed.



Similar results have recently been obtained with disodio β-diketones, which underwent twofold alkylations with 1,3-dichloropropane and higher methylene halides but reacted with ethylene and methylene halides to

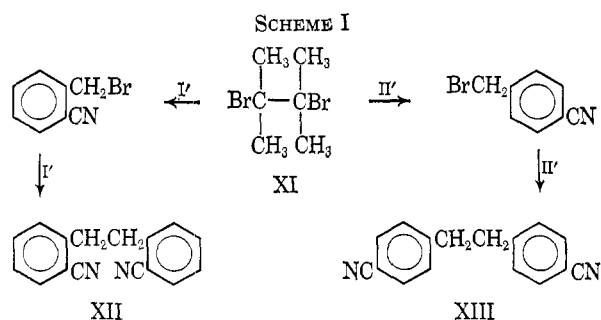
regenerate starting β-diketone and produce polymer, respectively.¹⁰

Also, carbanions I' and II' were coupled with dibromide XI to form XII and XIII in yields of 52 and 55%, respectively; presumably halogenide XI and sodio salts I' and II' underwent halogen-metal interchange to produce 2,3-dimethyl-2-butene¹¹ and *o*- or *p*-cyanobenzyl bromide which alkylated I' or II' (Scheme I).

This method appears equally satisfactory for XII as an earlier one involving Grignard coupling of the

(10) K. G. Hampton, R. J. Light, and C. R. Hauser, *J. Org. Chem.*, **30**, 1414 (1965).

(11) See K. Ziegler and B. Schnell, *Ann.*, **437**, 227 (1924).



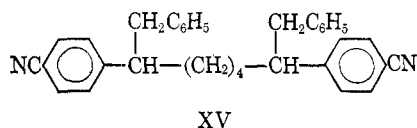
2-cyanobenzyl bromide,¹² and superior for XIII to previous methods involving persulfate oxidation of *p*-tolunitrile¹³ and several-step syntheses from bibenzyl^{14,15} in which the yields were only 6–10% and 20–31%, respectively.

Although carbanions I' and II' were alkylated in good yields when the halide was added to the reaction mixture within 5–30 min, the self-condensation product of nitrile II was apparently produced when the reaction mixture containing carbanion II' in liquid ammonia was allowed to stand for 10 hr.¹⁶ Moreover, when the liquid ammonia of the reaction mixture containing carbanion II' was replaced by tetrahydrofuran within a few minutes and the resulting suspension was refluxed, there was obtained the amidine IIa, which was isolated as its hydrochloride salt and picrate. This result is similar to that reported previously with sodium amide in refluxing toluene.⁵

Next, the benzyl derivative IIIa, which was obtained by benzylation of carbanion I' (see eq 1), was further alkylated by treatment with sodium amide in liquid ammonia followed by benzyl chloride to form the dibenzyl derivative XIV in 44% yield (eq 3). Structure XIV was supported by analysis and absorption spectra.



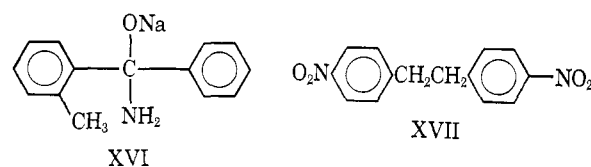
Similarly, the monobenzyl derivative IVa (see eq 2) was treated with sodium amide in liquid ammonia followed by 1,4-dibromobutane to form the bis product XV in 20% yield, which is probably not the maximum obtainable. Structure XV, which appeared to consist of a mixture of diastereoisomers (see melting points), was supported by analysis, absorption spectra, and molecular weight.



In these further alkylations, the time allowed for conversion into carbanions appeared to be critical, since certain attempted alkylations of IVa and IVb after 30 min, rather than after 15 min, failed to afford isolable products.

- (12) R. C. Fuson, *J. Am. Chem. Soc.*, **48**, 830 (1926).
 (13) (a) P. Kattwinkel and R. Wolfenstein, *Ber.*, **34**, 2423 (1901); (b) P. Kattwinkel and R. Wolfenstein, *ibid.*, **37**, 3221 (1904).
 (14) J. N. Ashley, H. J. Barber, A. J. Ewins, G. Newberry, and A. D. H. Self, *J. Chem. Soc.*, 103 (1942).
 (15) G. J. Sloan and W. R. Vaughan, *J. Org. Chem.*, **22**, 750 (1957).
 (16) This reaction is being further investigated.

It should be mentioned that, in contrast to *o*- and *p*-tolunitriles, *m*-tolunitrile, *o*-tolylphenyl ketone, and *p*-nitrotoluene failed to afford an isolable amount of the corresponding benzyl derivative on treatment with 1 molecular equiv of sodium amide in liquid ammonia, followed by 1 equiv of benzyl chloride. The *m*-tolunitrile afforded unidentified material. The ketone appeared to undergo an addition reaction with the alkali amide to form XVI, since stilbene was not produced and the ketone and benzyl chloride were largely recovered; stilbene would probably have been produced through self-condensation of the benzyl chloride had the alkali amide been present when this halide was added.¹⁷ The nitrotoluene apparently was converted through its carbanion into a radical, since dimer XVII was obtained in 34% yield; this dimer has been prepared from *p*-nitrotoluene by other bases in liquid ammonia¹⁸ and, especially, by passing air through a methanolic hydroxide solution of this nitro compound.¹⁹



Incidentally, *o*-nitrotoluene couples similarly to the *para* isomer¹⁸ and several substituted *o*-nitrotoluenes undergo ethoxide-catalyzed condensation with ethyl oxalate²⁰ but neither isomer appears to have been alkylated successfully.

Similarly, *o*-toluamide and *p*-toluic acid failed to undergo benzylation on treatment with 2 molecular equiv of sodium amide in liquid ammonia followed by 1 equiv of benzyl chloride, and the starting amide and acid were largely recovered. The purple color associated with the formation of stilbene was observed,¹⁷ and some of this hydrocarbon was isolated.

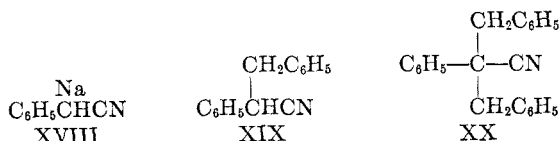
Discussion

These results show that, although the amidine and the self-condensation product may be produced under certain conditions, *o*- and *p*-tolunitriles are converted initially by sodium amide in liquid ammonia into their carbanions, which can be alkylated in good yields. Also, further alkylations may be realized in fair to good yields.

These successful alkylations illustrate a useful route to the synthesis of many new products. This method of introducing an alkyl or related group at the methyl substituent of the readily available *o*- or *p*-tolunitrile appears more convenient than that of introducing the cyanide group through the appropriate aromatic amine (Sandmeyer), acid (lead thiocyanate fusion), amide (dehydration), or aldoxime (dehydration); such methods have been employed for preparations of IIIa, IVa, XII, and XIII (see above).

- (17) See C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *J. Am. Chem. Soc.*, **78**, 1653 (1956).
 (18) F. W. Bergstrom, I. M. Granara, and V. Erickson, *J. Org. Chem.*, **7**, 98 (1942).
 (19) H. O. House, *Org. Syn.*, **34**, 35 (1954).
 (20) H. R. Snyder and F. J. Pilgrim, *J. Am. Chem. Soc.*, **70**, 3787 (1948), and references therein.

Finally, the present alkylations are of interest in connection with previous alkylations of phenylacetonitrile and acetonitrile, to which *o*- and *p*-tolunitriles are related as isomers and vinyls, respectively. Whereas the monoalkylations of carbanions I' and II' were readily effected without appreciable dialkylation, those of the carbanions of phenylacetonitrile and acetonitrile have generally been accompanied by considerable dialkylation²¹ (and some trialkylation in case of acetonitriles²²) under similar conditions even though only molecular equivalents of the reactants were employed. For example, treatment of sodiophenylacetonitrile (XVIII) with 1 molecular equiv of benzyl chloride has afforded about equal amounts of the monobenzyl derivative XIX, the dibenzyl derivative XX, and regenerated phenylacetonitrile.²¹



The lack of appreciable dialkylation in the monoalkylation of carbanions I' and II' is presumably due to insufficient equilibration of the monoalkyl derivative with I' or II' and/or to a lower nucleophilicity of the carbanion of the monoalkyl derivative. Apparently, the acidity of the benzylic hydrogen of the benzyl derivative IIIa is somewhat less than that of the methyl hydrogen of *o*-tolunitrile since the further benzylation of the monobenzyl derivative was realized in much lower yield. Although the acidity of the monobenzyl derivative of phenylacetonitrile (XIX) is probably also less than that of phenylacetonitrile, the conversion of XIX to its carbanion by sodium amide is still essentially complete, since further alkylation may be achieved in high yield.²³

Experimental Section²⁴

Alkylations of *o*- and *p*-Tolunitriles.—To a stirred suspension of 0.11 mole of sodium amide, prepared from 0.11 g-atom of sodium in 600 ml of commercial, anhydrous liquid ammonia,²⁵ was added 11.72 g (0.1 mole) of *o*- or *p*-tolunitrile in 50 ml of anhydrous ether. The resulting grape-red solution of sodio-*o*-tolunitrile was stirred for 15 min, and the red-orange solution of sodio-*p*-tolunitrile for 30 min; then 0.1 mole of alkyl or aralkyl halide or 0.05 mole of 1,4-dibromobutane in 100 ml of anhydrous ether was added. After 30–60 min, the liquid ammonia was evaporated (steam bath) and the residue was stirred with ether and water. The two layers were separated. The ethereal layer, with which was combined two ethereal extracts of the aqueous layer, was dried over anhydrous magnesium sulfate, and the solvent was removed. The residue was distilled or recrystallized from an appropriate solvent. In certain cases some of the original nitrile was recovered. The results are summarized in Tables I–III.

(21) C. R. Hauser and W. R. Brasen, *J. Am. Chem. Soc.*, **78**, 494 (1956).

(22) F. W. Bergstrom and R. Agostinho, *ibid.*, **67**, 2152 (1945).

(23) W. G. Kenyon, E. M. Kaiser, and C. R. Hauser, *J. Org. Chem.*, **30**, 4135 (1965).

(24) Melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes and are uncorrected. Analyses are by Janssen Pharmaceutica, Beerse, Belgium, and Triangle Chemical Laboratories, Inc., Chapel Hill, N. C. Nmr spectra were obtained with 10–20% solutions in deuteriochloroform (unless otherwise noted) with tetramethylsilane as internal standard using a Varian A-60 spectrometer. Infrared spectra were determined with a Perkin-Elmer Infracord with potassium bromide pellets of solids and with neat samples of liquids on sodium chloride plates.

(25) See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 122 (1954).

Similarly, 0.1 mole of sodio-*p*-tolunitrile in liquid ammonia was treated with 0.05 mole of ethylene or methylene chloride and the reaction mixture was worked up after 1 hr to give recovered *p*-tolunitrile, bp 84–86° (8.5 mm), mp 27–29°, lit.²⁶ bp 90.5–91° (11 mm), mp 29°, in yields of 58 and 50%, respectively. Also, the experiment with ethylene chloride afforded some (<1 g) of pot residue, and that with methylene chloride produced some very insoluble powder, presumably polymer.

Coupling of I with Dibromide XI to Form XII.—To a solution of 0.1 mole of *o*-tolunitrile carbanion (10-min anion formation) was added 12.2 g (0.05 mole) of 2,3-dibromo-2,3-dimethylbutane²⁷ in 150 ml of anhydrous ether. During a 10-min addition of the dibromide, the grape-red color became almost black and a precipitate formed. After 1.5 hr, the reaction mixture was treated with 7 g of ammonium chloride and the ammonia was evaporated. Ether and water were added. Ether and methylene chloride extracts gave a black solid. Recrystallization from ethanol afforded 6.08 g (52%) of *o,o'*-dicyanobenzyl (XII) as tan crystals, mp 133–139°. A further recrystallization from ethanol and one from benzene afforded pale tan crystals of XII, mp 138.5–141.5°, lit.¹² mp 139°. The nmr spectrum showed a multiplet at δ 7.2–7.7 (aromatic) and a singlet at 3.2 (benzylic) with an area ratio of 8.1:3.9 (based on 12 expected protons); the calculated area ratio is 8:4. The infrared spectrum showed peaks at 2212 cm^{-1} (nitrile), lit.^{6a} 2240–2221 and 768 cm^{-1} (*ortho* substitution), lit.^{6b} 770–735 cm^{-1} .

Coupling of II with Dibromide XI to Form XIII.—To a solution of 0.1 mole of *p*-tolunitrile carbanion (10-min anion formation) was added, during 5 min, 12.2 g (0.05 mole) of 2,3-dibromo-2,3-dimethylbutane in 100 ml of ether to form a brown mixture. After 2 hr, the reaction mixture was worked up as described above for XII to give a tan powder, which was removed by filtration. This powder was treated with two portions of hot benzene to give, on cooling, 3.29 g of *p,p'*-dicyanobenzyl (XIII) as pale yellow crystals, mp 195–202°. Two methylene chloride extracts of aqueous layer were combined with original organic layer, and the solvents were removed. The crude product was dissolved in boiling benzene, some tarry material was removed by filtration, and the solution was cooled to give 3.09 g of XIII, mp 195–202°. Total yield of XIII was 55%. Recrystallization from acetonitrile afforded very pale tan crystals, mp 200–202.5°, lit.^{13a} mp 198°, lit.¹⁵ mp 196–200°. The nmr spectrum (deuteriochloroform-trifluoroacetic acid) showed essentially a quartet (with some fine splitting) at δ 7.7–7.7 (aromatic) and a singlet at 3.1 (benzylic) with an area ratio of 8.3:3.7; the expected ratio is 8:4. The infrared spectrum showed peaks at 2179 cm^{-1} (C≡N), lit.^{6a} 2240–2221 and 831 cm^{-1} (*para* substitution), lit.^{6b} 860–800 cm^{-1} .

Anal. Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$: mol wt, 232.3. Found: mol wt, 200.1.

Further Benzylation of IIIa to Form XIV.—To a suspension of 0.039 mole of sodium amide in 500 ml of liquid ammonia was added 7.33 g (0.035 mole) of *o*-(β -phenylethyl)benzonitrile (IIIa) in 50 ml of ether to form a deep purple solution. After 15 min, 4.47 g (0.035 mole) of benzyl chloride in 50 ml of ether was added in portions. The purple color was changed to olive green. After 1 hr, the reaction mixture was treated with 3 g of ammonium chloride and the ammonia was evaporated. The residue was stirred with ether and water. On evaporation, the ether layer gave a slushy, yellow solid which was recrystallized twice from cyclohexane to afford 4.59 g (44%) of 1,3-diphenyl-2-(*o*-cyanophenyl)propane (XIV) as pale tan crystals, mp 107–111°. An analytical sample melted at 109–112°. The nmr spectrum showed a multiplet at δ 6.8–7.4 (aromatic protons), a multiplet at 3.4–4.0 (methynyl proton), and a doublet (coupling constant, \sim 7 cps) at 2.9–3.1 (benzylic protons) with area ratios of 14.3:1.0:3.7. The calculated area ratios are 14:1:4. The infrared spectrum showed peaks at 2203 cm^{-1} (CN), lit.^{6a} 2240–2221 cm^{-1} ; 768 cm^{-1} (*ortho* substitution), lit.^{6b} 770–735 cm^{-1} ; 743 and 694 cm^{-1} (monosubstituted phenyl), lit.^{6b} 760–740 and 710–690 cm^{-1} .

Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{N}$: C, 88.85; H, 6.44; N, 4.71. Found: C, 88.46; H, 6.37; N, 4.58.

Further Alkylation of IVa with 1,4-Dibromobutane to Form XV.—To a suspension of 0.043 mole of sodium amide in 400 ml

(26) See I. Hellbron, Table I, footnote *d*.

(27) This compound was prepared by bromination of 2,3-dimethylbutane, essentially as described by A. V. Grosse and V. N. Ipatieff, *J. Org. Chem.*, **8**, 438 (1943).

of liquid ammonia was added 8.15 g (0.039 mole) of *p*-(β -phenylethyl)benzotrile (IVa) in a little ether to give a bright red solution. After 15 min, 4.22 g (0.020 moles) of 1,4-dibromobutane in ether was added portionwise. About one-fourth of the dihalide solution was required to change the color to orange-brown. After 1 hr, the reaction mixture was worked up to give a mixture of a solid and an oil. The solid was removed by filtration to give 1.46 g of 1,8-diphenyl-2,7-di(*p*-cyanophenyl)octane (XV), mp 121.5–127.5°. After two recrystallizations from ethanol the white solid melted at 135–137.5°. The remaining oil was distilled up to 150° (0.07 mm) to remove starting nitrile IVa. Pot residue was recrystallized from ethanol (Norit), extracted into hot hexane, then recrystallized from acetic acid to give 0.33 g of white solid, mp 112–127°. Recrystallization from ethanol raised the melting point to 120–128°. The total crude yield was 20%. The very wide melting ranges are possibly indicative of a mixture of diastereomers. The nmr spectrum of compound XV exhibited peaks at δ 6.8–7.5 (multiplet, aromatic), at 2.8 (singlet, benzylic), and at 0.8–1.8 (multiplet, methylenic) with area ratios 17.3:5.8:8.9. The calculated area ratios are 18:6:8. Infrared absorption peaks were found at 2194 cm^{-1} (CN), lit.^{6a} 2240–2221 cm^{-1} ; 818 cm^{-1} (*para*

substitution), lit.^{6b} 860–800 cm^{-1} ; 750 and 699 cm^{-1} (mono-substituted phenyl), lit.^{6b} 760–740 and 710–690 cm^{-1} .

Anal. Calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2$: C, 87.14; H, 6.88; N, 5.96; mol wt, 468.6. Found: C, 86.70; H, 6.91; N, 6.02; mol wt, 449.

Conversion of *p*-Tolunitrile into Amidine IIa.—To a suspension of 0.11 mole of sodium amide in 300 ml of liquid ammonia was added 11.72 g (0.1 mole) of *p*-tolunitrile in anhydrous tetrahydrofuran (THF). The liquid ammonia was replaced by THF and the resulting mixture was refluxed for 5–10 min. After cooling (ice bath), 11 g (*ca* 0.1 mole) of 12 *M* hydrochloric acid was added, and the mixture was filtered. The filtrate was acidified with about 15 g of 12 *M* hydrochloric acid to precipitate 6.94 g (41%) of crude *p*-toluamidine hydrochloride, which was reprecipitated twice from methanol with dry ether, mp 213.5–215.5°, lit.^{28,29} mp 213° and 215–216°. The amidine hydrochloride was also converted into the picrate, mp 225–228°, lit.³ mp 219°.

(28) G. Glock, *Ber.*, **21**, 2650 (1888).

(29) P. E. Fanta and E. A. Hedman, *J. Am. Chem. Soc.*, **78**, 1434 (1956).

The Proton Magnetic Resonance Spectra of α -Chloroacetamidinium Chlorides and Their Corresponding Thiolsulfates (Bunte Salts)¹

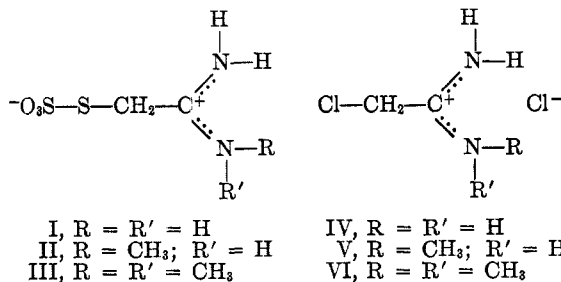
LUDWIG BAUER, CHARLES L. BELL, KAREN ROVER SANDBERG,² AND A. P. PARULKAR

Department of Chemistry, College of Pharmacy, University of Illinois, Chicago, Illinois 60680

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The nmr parameters of the α -chloroacetamidinium chlorides, $\text{ClCH}_2\text{C}(=\text{NH}_2^+)\text{NRR}'\text{Cl}^-$ ($\text{R} = \text{R}' = \text{H}$; $\text{R} = \text{H}$; $\text{R}' = \text{CH}_3$; and $\text{R} = \text{R}' = \text{CH}_3$), and the corresponding Bunte salts, $^-\text{O}_3\text{S}_2\text{CH}_2\text{C}(=\text{NH}_2^+)\text{NRR}'$, are recorded and the chemical shifts and coupling constants are interpreted in terms of the functional groups present in these molecules. Hindered rotation about the CN bond in these amidinium ions was observed in all these salts and the coalescence temperatures of the NH and NCH_3 protons were determined in a number of solvents. The collapse of these signals is discussed in terms of proton exchange and barriers to rotation. Long-range coupling of the NCH_3 to the methylene group in the N,N-dimethylacetamidinium salts was used to assign the NCH_3 group *cis* and *trans* to the CH_2 group.

This study was initiated at the time when a number of α -chloroamidinium chlorides and α -amidinium thiolsulfates (Bunte salts) were synthesized,³ and it became evident from their nuclear magnetic resonance (nmr) spectra that there existed hindered rotation in the amidinium moiety of these salts. At that time, the then unknown α -amidinium Bunte salts were presented as zwitterions (I), this assignment being



supported by their infrared spectra.⁴ It was hoped that the nmr spectra would support the zwitterionic struc-

ture of these Bunte salts and in general reveal some additional information about hindered rotation in the amidinium cation. Toward this end the nmr spectra of the simplest unsubstituted monomethyl and N,N-dimethylacetamidinium Bunte salts (I–III) were examined in detail in a number of different solvents and at various temperatures and their chemical shifts and coupling constants are compiled in Table I. The nmr spectra of the corresponding α -chloroamidinium chlorides, IV to VI, served as model compounds since their structure was well established and their nmr data are recorded in Table I also.

Although hindered rotation about a CN bond has not been observed in amidines,⁵ this phenomenon is evident in amides, their salts and complexes,^{5–7} thio-

Can. J. Chem., **37**, 1260 (1959); R. Mecke and W. Kutzelnigg, *Spectrochim. Acta*, **16**, 1216 (1960); P. Bassignana, C. Cogrossi, G. Polla, and S. Franco, *Ann. Chim.*, (Rome), **1212** (1963)]. In addition, I showed two strong bands near 1030 and 1220 cm^{-1} attributable to the thiolsulfate anion from a study of the spectra of sodium and potassium S-alkylthiolsulfates [A. Simon and D. Kunath, *Chem. Ber.*, **94**, 1980 (1961)] and in a number of S-(β -aminoethyl)thiolsulfuric acids [T. P. Johnston and A. Gallagher, *J. Org. Chem.*, **27**, 2452 (1962)].

(5) R. C. Neuman, Jr., and L. B. Young, *J. Phys. Chem.*, **69**, 2570 (1965).

(6) For some recent leading references, see (a) T. H. Sidall, III, and W. E. Stewart, *Chem. Commun.*, 612 (1966); (b) A. J. Carty, *Can. J. Chem.*, **44**, 1881 (1966); (c) E. S. Gore, D. J. Blears, and S. S. Danyluk, *ibid.*, **43**, 2135 (1965); (d) S. J. Kuhn and J. S. McIntyre, *ibid.*, **43**, 375 (1965); (e) R. M. Moriarty, *J. Org. Chem.*, **28**, 1296 (1963); (f) L. A. LaPlanche and M. T. Rogers, *J. Am. Chem. Soc.*, **85**, 3728 (1963); (g) R. J. Gillespie and T. Birchall, *Can. J. Chem.*, **41**, 148 (1963).

(7) (a) R. C. Neuman, Jr., and L. B. Young, *J. Phys. Chem.*, **69**, 1777 (1965); (b) W. Walter, G. Maerten, and H. Rose, *Ann.*, **691**, 25 (1966).

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(2) Taken in part from the M.S. thesis of K. R. Sandberg, University of Illinois at the Medical Center, Chicago, Ill., June, 1964.

(3) (a) L. Bauer and T. L. Welsh, *J. Org. Chem.*, **27**, 4382 (1962); (b) L. Bauer and K. R. Sandberg, *J. Med. Chem.*, **7**, 766 (1964).

(4) The infrared spectra (Nujol) of all α -amidinium thiolsulfates (I) exhibited a characteristic strong band around 1700 cm^{-1} which has been assigned to the $>\text{C}=\text{N}^+<$ stretching mode [see J. C. Grivas and A. Taurins,