Condensations at the *p*-Methyl Group of N,N-Dimethyl-*p*-toluenesulfonamide by Means of Sodium Amide in Liquid Ammonia[1]

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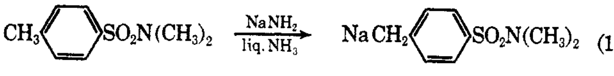
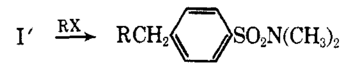
A *p*-methyl hydrogen of N,N-dimethyl-*p*-toluenesulfonamide was ionized by means of sodium amide in liquid ammonia and the resulting carbanion was condensed with electrophilic compounds to form the *p*-methyl derivatives. The carbanion underwent alkylations with benzyl and *p*-chlorobenzyl chlorides, twofold alkylation with 1,4-dibromobutane, coupling with 2,3-dibromo-2,3-dimethylbutane, carbonyl addition reactions with benzophenone and anisaldehyde, and benzoylation with methyl benzoate. The carbonyl addition products were dehydrated. These reactions illustrate a useful method of synthesis of some new types of *para*-substituted N,N-dimethylbenzenesulfonamides.

Since toluene appears to be almost as strong an acid as ammonia,[3] it seemed possible that *p*-toluenesulfonamide I might be sufficiently acidic to be converted by sodium amide in liquid ammonia to carbanion I′, which could be condensed with electrophilic compounds (eq 1). Such condensations to form some new types of *para*-substituted N,N-dimethylbenzenesulfonamides were realized in the present investigation.

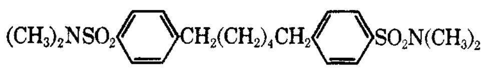

(1)

I I′

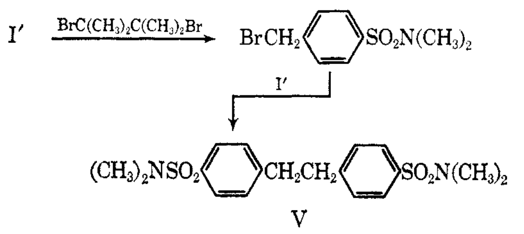
Carbanion I′ underwent alkylations with benzyl and *p*-chlorobenzyl chlorides and twofold alkylation with 1,4-dibromobutane to form II, III, and IV in yields of 72, 44, and 39%, respectively (eq 2). Carbanion I′ was coupled by means of 2,3-dibromo-2,3-dimethylbutane to give bibenzyl disulfonamide V in 47% yield. Presumably part of I′ was converted to an intermediate benzyl-type halide which then alkylated unchanged I′ (Scheme I); the dibromide was converted to 2,3-dimethyl-2-butene.[4] The coupled product V was independently synthesized in 24% yield from bibenzyl through its disulfonyl chloride (Scheme II).


(2)

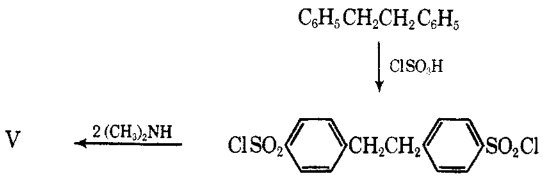
II, $R = CH_2C_6H_5$
III, $R = CH_2C_6H_4Cl\text{-}p$


IV

SCHEME I

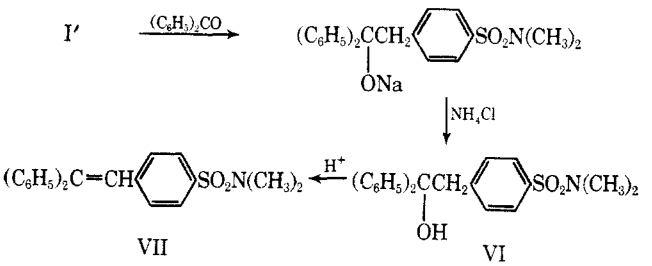


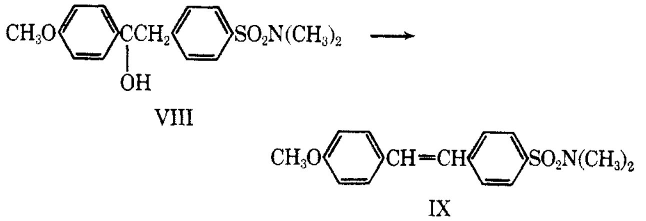
SCHEME II



Carbanion I′ underwent an addition reaction with benzophenone to form carbinol sulfonamide VI in 40% yield; VI was dehydrated by means of a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene to give VII in 84% yield (Scheme III). Similarly, carbanion I′ was condensed with anisaldehyde to form carbinol sulfonamide VIII in 31% yield; VIII was dehydrated to afford IX in 85% yield.

SCHEME III





In the carbonyl additions to form VI and VIII, the reaction mixtures were neutralized inversely after a relatively short time, since certain related processes[5] have been shown to undergo reversion after longer periods. Carbanion I′ was benzoylated with methyl benzoate in the presence of sodium amide to form ketone sulfonamide X in 38% yield (Scheme IV). Such a procedure has been used for certain related Claisen condensations.[6]

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[1] (a) This investigation was supported in part by the National Science Foundation; (b) a preliminary report has appeared in a communication, *Chem. Ind.* (London), 1267 (1966).

[2] Union Carbide Corp. Fellow, 1965–1966.

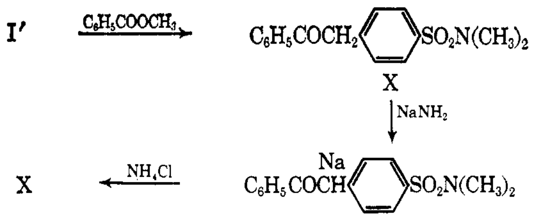
[3] See D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965.

[4] See K. Ziegler and B. Schnell, *Ann.*, **437**, 227 (1924).

[5] See E. M. Kaiser and C. R. Hauser, *Chem. Ind.* (London), 1299 (1965); F. H. Rash, S. Boatman, and C. R. Hauser, *ibid.*, 1267 (1966).

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

SCHEME IV



The benzoylation of sulfonamide I was also effected with methyl benzoate by means of sodium hydride in 1,2-dimethoxyethane (monoglyme), but the yield of X was only 2%.[7] This yield, as well as certain of the other yields reported above, might be improved by further study.

The structures of products II–X were supported by analyses and absorption spectra. Table I summarizes the infrared data. Absorptions appeared for the sulfonamide group at 1337–1314 and 1164–1140 cm^{-1}, for two adjacent aromatic hydrogens (*p*-substitution) near 830 cm^{-1}, and for functional groups introduced through condensation with the electrophilic compounds at 3484–3472 (for hydroxyl), 1245–1235 (for aryl ether), 1294 and 968 (for *trans*-disubstituted ethylene), and 1664 cm^{-1} (for aryl ketone). These values are consistent with the absorptions reported by Bellamy.[8]

TABLE I

SULFONAMIDE INFRARED DATA

Product	Infrared absorption peaks, cm^{-1}
II	2890, 1595, 1337, 1164, 952, 830, 742, 713
III	2865, 1580, 1319, 1148, 954, 833
IV	2882, 1587, 1323, 1149, 952, 832
V	2865, 1580, 1319, 1148, 944, 827
VI	3484, 1587, 1321, 1155, 961, 830, 751, 697
VII	1570, 1318, 1152, 857, 835, 737, 697
VIII	3472, 1597, 1314, 1235, 1147, 958, 830
IX	1590, 1321, 1294, 1245, 1145, 968, 951, 832
X	1664, 1577, 1314, 1140, 952

Table II summarizes the nuclear magnetic resonance (nmr) data for several of the products described above. The spectra of compounds II, III, and V exhibited peaks with integrated area ratios corresponding closely to those calculated. The aromatic multiplets were found at δ 6.9–7.9, the benzylic singlets at 2.9–3.1, and the aminomethyl singlets at 2.7–2.8. The nmr spectrum of compound IV consisted of an aromatic quartet at δ 7.4–7.9, a broad low peak at 1.2–2.0 corresponding to the methylene (nonbenzylic aliphatic) protons, and a singlet at 2.8 with a small shoulder peak at 2.7. If this last singlet is assumed to result from the overlapping of a benzylic triplet with a much larger aminomethyl singlet, the integrated area ratios are consistent with the assigned structure. The spectrum of X was similar to those above, but the benzylic protons are shifted downfield to δ 4.6 by the carbonyl group.

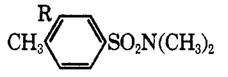
It should be pointed out that the spectral data support the *p*-methyl derivatives represented above, not the possible ring-substituted derivative XI for which resonance form I″ of the carbanion would have been the precursor. Thus both the presence of only one benzylic resonance in the nmr spectrum and the area ratios are consistent with the structures shown above but not with XI. Structure XI should have a more complex spectrum.

TABLE II

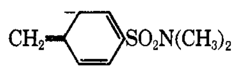
SULFONAMIDE NMR DATA

Compd	Type of protons	Peak type	Chemical shift,[a] δ, ppm	Integrated area ratios Calcd	Integrated area ratios Found
II[b]	Aromatic	Multiplet	7.1–7.8	9	9.1
	Benzylic	Singlet	3.0	4	4.2
	Aminomethyl	Singlet	2.7	6	5.8
III[b]	Aromatic	Multiplet	6.9–7.7	8	8.3
	Benzylic	Singlet	2.9	4	3.8
	Aminomethyl	Singlet	2.7	6	5.9
IV[c]	Aromatic	Quartet	7.4–7.9	8	7.9
	Aminomethyl	Singlet	2.7–2.8	12	16.0
	Benzylic	Masked		4	
	Methylene	Broad low peak	1.2–2.0	8	8.1
V[c]	Aromatic	Quartet	7.4–7.9	8	8.1
	Benzylic	Singlet	3.1	4	4.1
	Aminomethyl	Singlet	2.8	12	11.8
X[c]	Aromatic	Multiplet	7.5–8.2	9	9.1
	Benzylic (ketone)	Singlet	4.6	2	2.0
	Aminomethyl	Singlet	2.8	6	5.9

[a] Downfield from tetramethylsilane as internal standard. [b] Solvent was deuteriochloroform. [c] Solvent was trifluoroacetic acid.

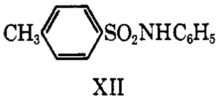


XI

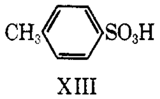


I″

In contrast to sulfonamide I which readily afforded the monocarbanion I′, *p*-toluenesulfonanilide (XII) and *p*-toluenesulfonic acid (XIII) failed to be converted by sodium amide in liquid ammonia to dianions suitable for benzylation at the *p*-methyl position. Thus, treatment of XII with 2 mole equiv of the reagent and of the monosodio salt of XIII with 1 equiv followed by benzyl chloride produced some stilbene (from self-condensation of the halide)[9] and much of the starting XII and XIII was recovered. The purple color associated with the formation of stilbene by sodium amide in liquid ammonia[9] was observed in both cases; XIII was recovered as the S-benzylthiuronium *p*-toluenesulfonate.[10]



XII



XIII

Discussion

The equilibrium of the acid–base reaction of sulfonamide I with sodium amide in liquid ammonia appeared to be far on the side of carbanion I′ (eq 1), since benzylation at the *p*-methyl position was realized in 72% yield (eq 2). Moreover, this alkylation seemed not to be accompanied by self-condensation of the benzyl chloride to form stilbene, which would have been expected had there been appreciable sodium amide present in the equilibrium.[9]

The preferential reaction of sodium amide with the *p*-methyl hydrogen of sulfonamide I rather than with

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[7] Sodium hydride has been more satisfactory than sodium amide for certain other benzoylations; see M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 1007 (1965).

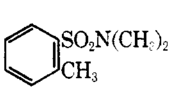
[8] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958.

[9] See C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *J. Am. Chem. Soc.*, **78**, 1653 (1956).

[10] See E. Chambers and G. W. Watt, *J. Org. Chem.*, **6**, 376 (1941).

the sulfonyl group is not especially surprising, since the latter group is known not to be very reactive toward nucleophiles, as illustrated by the difficulty of effecting base-catalyzed hydrolysis of sulfonamides.[11] However, attack of sodium amide at the sulfonyl group of I was possible, as sodium isopentoxide has been reported to cleave I in refluxing isopentyl alcohol to form diisopentyl ether and sodium *p*-toluenesulfonate;[12] presumably the initial reaction involved formation of dimethylamine and isopentyl *p*-toluenesulfonate, with which sodium isopentoxide underwent an SN2 displacement.

The present method of condensation at the *p*-methyl group of sulfonamide I by means of sodium amide in liquid ammonia could probably be extended, not only to other electrophilic compounds, but also to the isomeric sulfonamides XIV and XV and perhaps to sulfonamide XVI; I and XIV may be regarded as vinylogs of XVI.



XIV

$C_6H_5CH_2SO_2N(CH_3)_2$

XV

$CH_3SO_2N(CH_3)_2$

XVI

Previously, sulfonamides XV and XVI have been alkylated with certain halides by means of sodium amide in toluene[13] and sulfonamide XVI has been condensed with some carbonyl compounds by means of *n*-butyllithium in tetrahydrofuran.[14]

Experimental Section[15]

Conversion of N,N-Dimethyl-*p*-toluenesulfonamide (I) to Carbanion I′.—To a stirred suspension of 0.055 mole of sodium amide, prepared from 0.055 g-atom of sodium in 500 ml of commercial, anhydrous liquid ammonia,[6] was added 9.97 g (0.05 mole) of solid N,N-dimethyl-*p*-toluenesulfonamide (I) through Gooch tubing; the solid was rinsed in with about 50 ml of anhydrous ether. The color of this sulfonamide carbanion solution varied from red to olive, apparently depending on the amount of iron catalyst used to form the sodium amide. Conversion to the anion was assumed to be complete after the mixture had been stirred for 30 min. The resulting solution, which was assumed to contain 0.05 mole of carbanion I′, was then treated with an electrophilic compound as described below.

Alkylations of Carbanion I′. A. With Benzyl Chloride to Form II.—To a stirred solution of carbanion I′ (0.05 mole) was added 6.33 g (0.05 mole) of benzyl chloride in about 50 ml of anhydrous ether. The color of the carbanion was discharged and a precipitate formed. After 1.5 hr, 5 g of ammonium chloride was added and the liquid ammonia was evaporated (steam bath). The residue was stirred with ether and water. The undissolved solid was removed by filtration and the two layers of the filtrate were separated. The ethereal layer was combined with an ethereal extract and two methylene chloride extracts of the aqueous layer. The organic solution was dried over anhydrous magnesium sulfate and the solvents were removed. The residual solid and filtered solid (see above) were combined and recrystallized from ethanol to give 10.40 g (72%) of N,N-dimethyl-*p*-(β-phenylethyl)benzenesulfonamide (II), mp 137–141° and 140–142° after further recrystallization.

Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.40; H, 6.62; N, 4.84; S, 11.08. Found: C, 66.21; H, 6.84; N, 4.87; S, 10.85.

B. With *p*-Chlorobenzyl Chloride to Form III.—This reaction was carried out as described above for benzyl chloride to give, after recrystallization from ethanol, 10.24 g of product, mp 103–118°. Two recrystallizations from cyclohexane–ethanol afforded 7.12 g (44%) of N,N-dimethyl-*p*-(*p*-chloro-β-phenylethyl)benzene sulfonamide (III), mp 118–121° and 119–121.5° after further recrystallization.

Anal. Calcd for $C_{16}H_{18}NO_2SCl$: C, 59.34; H, 5.60; N, 4.33; S, 9.90; Cl, 10.95. Found: C, 59.15; H, 5.61; N, 4.48; S, 9.53; Cl, 10.98.

Twofold Alkylation of Carbanion I′ with 1,4-Dibromobutane to Form IV.—To a stirred solution of 0.05 mole of carbanion I′ was added 5.4 g (0.025 mole) of 1,4-dibromobutane in about 50 ml of anhydrous ether. The color of the reaction mixture was discharged and a precipitate formed. After 1 hr, 3 g of ammonium chloride was added and the liquid ammonia evaporated. The residue was stirred with water and methylene chloride and the layers were separated. The organic layer was evaporated to give a pale tan solid which was recrystallized from acetonitrile to give 5.11 g of crystals, mp 171–179°. Another recrystallization afforded 4.40 g (39%) of white 1,6-bis(N,N-dimethyl-*p*-sulfamylphenyl)hexane (IV), mp 179–182° and 181.5–183.5° after further recrystallization.

Anal. Calcd for $C_{22}H_{32}N_2O_4S_2$: C, 58.38; H, 7.13; N, 6.19; S, 14.17; mol wt, 452.6. Found: C, 58.18; H, 6.97; N, 6.35; S, 14.36; mol wt, 450.6.

Coupling of Carbanion I′ to Form V.—To a stirred solution of carbanion I′ (0.05 mole) was added, during 20 min, 6.1 g (0.025 mole) of 2,3-dibromo-2,3-dimethylbutane[16] in about 45 ml of anhydrous ether. After 2 hr, the reaction mixture was treated with 5 g of ammonium chloride and worked up as described above for the twofold alkylation to afford 4.60 g (47%) of pale tan 1,2-bis(N,N-dimethyl-*p*-sulfamylphenyl)ethane (V), mp 208–214° and 216–218° (sintered at 213°) after further recrystallization.

Anal. Calcd for $C_{18}H_{24}N_2O_4S_2$: C, 54.52; H, 6.10; N, 7.07; S, 16.17. Found: C, 54.44; H, 6.09; N, 7.15; S, 16.04.

Independent synthesis of V was effected by treating 5 g (0.0275 mole) of bibenzyl (which had been melted and then cooled until solid) with 18 ml (0.275 mole or 31.9 g) of chlorosulfonic acid.[17] When the initial reaction had subsided, the mixture was heated on the steam bath for about 45 min. The dark oil was cooled and added dropwise to a stirred mixture of ice and water. The resulting suspension was neutralized with sodium bicarbonate and stirred with methylene chloride. The undissolved solid was collected and heated for 30 min on the steam bath with 100 ml of 25% aqueous dimethylamine. The resulting mixture was cooled and filtered. The solid was recrystallized from acetonitrile to afford 2.58 g (24%) of disulfonamide V, mp 215–217.5° (sintered at 213°). A mixture melting point with a sample of compound V prepared from carbanion I′ was undepressed. The infrared spectra of the two samples were superimposable. Evaporation of the methylene chloride layer of the filtrate (see above) and treatment of the residue with aqueous dimethylamine afforded no more of V.

Carbonyl Additions of Carbanion I′. A. With Benzophenone to Form VI.—To a stirred solution of carbanion I′ (0.05 mole) was added, during 1 min, 9.11 g (0.05 mole) of benzophenone in about 50 ml of anhydrous ether. After 1 min more, the reaction mixture (light brown) was neutralized inversely by pouring it into a solution of 5 g (excess) of ammonium chloride in about 200 ml of liquid ammonia. The ammonia was evaporated and the residue was stirred with ether and water. The precipitate was collected by filtration[18] and recrystallized from acetonitrile to afford 6.78 g of N,N-dimethyl-*p*-(2,2-diphenyl-2-hydroxyethyl)benzenesulfonamide (VI), mp 214–217°. A second crop (0.93 g) melted at 213–217° after two recrystallizations from acetonitrile; the total yield was 40%. An analytical sample melted at 216.5–218°.

Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.26; H, 6.08; N, 3.67; S, 8.40. Found: C, 69.26; H, 6.12; N, 3.69; S, 8.12.

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[11] See R. S. Schreiber and R. L. Shriner, *J. Am. Chem. Soc.*, **56**, 114 (1934); M. Pezold, R. S. Schreiber, and R. L. Shriner, *ibid.*, **56**, 696 (1934).

[12] D. Klamann, *Angew. Chem.*, **67**, 719 (1955); D. Klamann and H. Bertsch, *Ber.*, **91**, 212 (1958).

[13] O. Eisleb, *Ber.*, **B74**, 1433 (1941); O. Eisleb, German Patent 735,866 (1943); *Chem. Abstr.*, **38**, 4101 (1944).

[14] E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965).

[15] Melting points were taken on a Thomas–Hoover melting point apparatus in open capillary tubes and are uncorrected. Analyses were by Janssen Pharmaceutica, Beerse, Belgium, and Triangle Chemical Laboratories, Inc., Chapel Hill, N. C. Nmr spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as internal standard and deuteriochloroform or trifluoroacetic acid as solvent. Infrared spectra were determined with a Perkin-Elmer Model 137 Infracord with potassium bromide pellets of the compounds.

[16] See A. V. Grosse and V. N. Ipatieff, *J. Org. Chem.*, **8**, 438 (1943).

[17] This procedure is adapted from that in L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, pp 152–153.

[18] Evaporation of the ether layer of the filtrate and of ethereal extracts of the aqueous layer left a brown oil, which was not investigated.

Dehydration was effected by refluxing 3 g of the benzophenone adduct VI with 0.2 g of *p*-toluenesulfonic acid in 200 ml of dry benzene for 12 hr. The benzene solution was cooled, washed twice with aqueous sodium bicarbonate and twice with water, and dried over anhydrous magnesium sulfate. The solvent was removed. The residue was recrystallized from ethanol–acetonitrile to afford 2.10 g of N,N-dimethyl-*p*-(2,2-diphenylvinyl)-benzenesulfonamide (VII), mp 166–167.5°. A second crop (0.30 g) melted at 164–167.5°; the total yield was 84%. After four recrystallizations from acetonitrile, a sample melted at 166–168°.

Anal. Calcd for $C_{22}H_{21}NO_2S$: C, 72.70; H, 5.82; N, 3.85; S, 8.82. Found: C, 72.56; H, 5.83; N, 3.85; S, 8.77.

B. With Anisaldehyde to Form VIII.—This reaction was carried out essentially as described above for benzophenone. After 1.5 min, the clear dark gray reaction mixture was inversely neutralized. The ammonia was evaporated; then water and ether were added. Undissolved solid was collected by filtration and recrystallized from ethanol to give 4.74 g of white crystals, mp 141–145°. Evaporation of the ether layer of the filtrate and of ethereal extracts of the aqueous layer gave, on cooling, some solid, which was collected and recrystallized from ethanol to give 0.66 g of crystals, mp 139–148°. The two crops were combined and recrystallized from ethanol to afford 5.14 g (31%) of N,N-dimethyl-*p*-(2-hydroxy-2-*p*-methoxyphenylethyl)benzenesulfonamide (VIII), mp 143–148° and 147.5–150° after further recrystallization.

Anal. Calcd for $C_{17}H_{21}NO_4S$: C, 60.87; H, 6.31; N, 4.18; S, 9.56. Found: C, 60.73; H, 6.08; N, 3.90; S, 9.89.

Dehydration of 2 g of VIII was effected as described above for that of adduct VI to give 1.61 g (85%) of N,N-dimethyl-4′-methoxy-*trans*-4-stilbenesulfonamide (IX), mp 213.5–215.5°.

Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41; S, 10.10. Found: C, 64.29; H, 6.00; N, 4.46; S, 9.95.

Benzoylation of Sulfonamide I with Methyl Benzoate to Form X. A. By Sodium Amide.—To a stirred suspension of 0.105 mole (2.1 mole equiv) of sodium amide in 500 ml of liquid ammonia was added 9.97 g (0.05 mole) of N,N-dimethyl-*p*-toluenesulfonamide; the solid was rinsed in with a little ether. The resulting dark red mixture was stirred 30 min. Then 13.61 g (0.1 mole or 2 equiv) of methyl benzoate in ether was added. The color became pale green and a precipitate appeared. After 2 hr, 8 g of ammonium chloride was added, the ammonia evaporated, and the residue stirred with ether and water. Insoluble solid was collected by filtration. Ether extraction of the filtrate gave only an oil which did not crystallize. The filtered solid was recrystallized from acetonitrile to afford 5.79 g (38%) of N,N-dimethyl-*p*-phenacylbenzenesulfonamide (X), mp 191–195° and 192.5–195° after further recrystallization.

Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; N, 4.62; S, 10.57. Found: C, 63.11; H, 5.61; N, 4.80; S, 10.50.

B. By Sodium Hydride.—To a stirred slurry of 15 g (0.4 mole) of sodium hydride reagent[19] in 100 ml of refluxing 1,2-dimethoxyethane (monoglyme), under dry nitrogen, was added a mixture of 19.93 g (0.1 mole) of N,N-dimethyl-*p*-toluenesulfonamide (I) and 13.61 g (0.1 mole) of methyl benzoate in 100 ml of monoglyme. After 6 hr, most of the solvent was removed under reduced pressure and the residue worked up to give 0.70 g (2.3%) of X, melting point and mixture melting point with a sample prepared by the sodium amide method, 192.5–196°. The infrared spectra of the two samples were identical. Most (65%) of the starting sulfonamide I was recovered. Some (6%) benzoic acid was isolated.

Registry No.—I′, 13952-53-9; II, 10517-63-2; III, 13952-54-0; IV, 13952-55-1; V, 13952-56-2; VI, 13952-57-3; VII, 13952-58-4; VIII, 13952-59-5; IX, 13952-60-8; X, 13952-61-9; N,N-dimethyl-*p*-toluenesulfonamide, 599-69-9; sodium amide, 12125-45-0; ammonia, 7664-41-7.

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[19] Obtained from Metal Hydrides, Inc., as an approximately 60% dispersion of sodium hydride in mineral oil.

Formation and Reactions of Trisodio-N-acetylsalicylamide[1]

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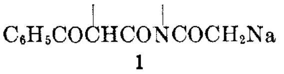
N-Acetylsalicylamide was converted, by means of sodium amide in liquid ammonia, into trisodio salt **3′**. This salt underwent alkylation with certain primary halides, carbonyl addition with various aromatic ketones and aldehydes, and aroylation with methyl benzoate exclusively at its terminal carbanion site. These reactions furnish a convenient new synthetic route to several known compounds as well as a method for the preparation of a number of new compounds.

Recently, several types of active hydrogen compounds have been converted into synthetically useful 1,3,5-trialkali salts by means of 3 molecular equiv of alkali amide in liquid ammonia.[2] For example, N-acetyl-α-benzoylacetamide was converted into trisodio salt **1** which underwent a carbonyl addition reaction with benzophenone to afford carbinol **2**.[2c]



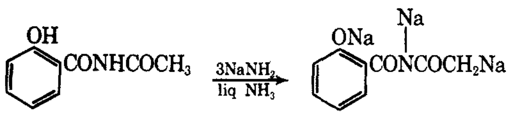
$$C_6H_5CO\overset{Na}{\overset{|}{C}}HCO\overset{Na}{\overset{|}{N}}COCH_2Na$$

1

$$C_6H_5COCH_2CONHCOCH_2\overset{OH}{\overset{|}{C}}(C_6H_5)_2$$

2

In view of the structural similarity between N-acetyl-α-benzoylacetamide and N-acetylsalicylamide (**3**), where the phenolic OH may be regarded as a completely enolized carbonyl group, it seemed possible that **3** might likewise undergo threefold metalation to form the reactive trialkali salt **3′** (eq 1). This has been



3 **3′** (1)

verified in the present study, as evidenced by condensations at the original terminal methyl position with electrophilic compounds.

Trisodio salt **3′** underwent alkylations with the appropriate halides to afford alkyl derivatives **4a–e** in yields of 31–74% (eq 2).[3] The results of these alkylations are summarized in Table I.

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[1] (a) Acknowledgment is made to the donors of the Petroleum Research Fund administered by the American Chemical Society and to the Committee on Grants-in-Aid of Research of the Society of The Sigma Xi for partial support of this work; (b) abstracted from the Ph.D. dissertation of C.-L. Mao, Virginia Polytechic Institute, 1967.

[2] (a) K. G. Hampton, T. M. Harris, C. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 4263 (1965); (b) J. F. Wolfe, C. L. Mao, D. R. Bryant, and C. R. Hauser, *ibid.*, **31**, 3725 (1966); (c) J. F. Wolfe and C. L. Mao, *ibid.*, **32**, 1977 (1967).

[3] Addition of benzyl chloride was not accompanied by stilbene formation which would have been expected if essentially all of the sodium amide had not been consumed in the threefold ionization of **3**. See S. Boatman, T. M. Harris, and C. R. Hauser, *ibid.*, **30**, 3593 (1965).