TABLE I

CHARACTERIZATION OF $CH_3CN(CH_3)_2 \cdot HX$

X	Mode of formation	Calcd Equiv wt	Calcd X, %	Found Equiv wt	Found X, %	Mp,[a] °C	Lit. Mp, °C	Lit. Ref
Cl	Gas phase	123.5	28.7	123.6	28.8	120–121	121–122	*b*
Cl	Ether			124	28.8	120–121		
Br	Gas phase	168	47.6	169	47.6	169–170	167–168	*b*
Br	Ether			168	47.6	167–168[c]		
Br[d]	Gas phase	196	...	187	...	120–124	120–124	*e*
I	Gas phase	215	59.1	216	59.0	140–143 dec	140–143 dec	*b*
I[f]	Gas phase	233	54.5	230	54.8	64–68		

[a] Sealed tube unless otherwise indicated. [b] Reference 5. [c] Unsealed tube. [d] Reaction with diethylamine to give $CH_3CON(C_2H_5)_2 \cdot HBr$. [e] E. H. White, *J. Amer. Chem. Soc.*, **77**, 6215 (1955). [f] Monohydrate.

methylacetamide and hydrogen chloride, reaction-vessel walls became coated with small droplets which rapidly crystallized. Since it seemed reasonable that the liquid might have been the desired amide and the observed crystallization might have been due to increasing contamination with dimethylammonium chloride, vacuum distillation of the amide from the sides of the flask was attempted. Instead, sublimation occurred with separation of two crystalline phases: a colorless residue identified as dimethylammonium chloride, and a similar, but acidic, sublimate which proved to be the hydrochloride of N,N-dimethylacetamide. Yields of the adduct vary with reaction conditions but can approach quantitative amounts.

The adduct was also prepared by reaction of dimethylamine with acetyl chloride in ether at 0°. Filtration of the colorless precipitate and sublimation yielded 70% of the adduct. Infrared spectra of the adducts prepared by the two methods are identical and consistent with the reported[5] spectrum of $CH_3CON(CH_3)_2 \cdot HCl$.

Sensitivity of the reaction to amine stoichiometry may account for earlier doubts concerning the utility of this approach to preparation of the adducts.[9] Successful preparations require not only use of 1 equiv or less of the amine, but also a mode of mixing which precludes a local excess of amine. Thus in gas-phase reactions the amine must be diluted with helium and added to the acyl halide. In solution reactions the amine must be added slowly to a well stirred acyl halide solution. In general, the adduct must be formed in the presence of a local excess of acetyl halide. On formation, the adduct presumably separates from the reaction medium, effectively preventing its reaction with local excesses of free amine as suggested by Cook.[9]

Experimental Section

Gas-Phase Preparation of N,N-Dimethylacetamide Hydrochloride.—Adducts were prepared in a glass reactor consisting of two bulbs, individually connected to an existing vacuum system and connected to each other by a stopcock. In a typical preparation acetyl chloride (20 cm pressure, 0.011 mol) and dimethylamine (0.011 mol) were transferred, respectively, through the vacuum system into thoroughly dried bulbs. The flask containing amine was charged with dry helium to a total pressure of 40 cm and the connecting stopcock was opened rapidly to permit reaction. The rapid flow of the dimethylamine–helium mixture into the acetyl chloride provided a crude means of mixing the two reactants.

The reactor pressure began dropping immediately and reached 15.3 cm (equivalent to 73% completion) 30 sec after the stopcock had been opened. Concurrent with the pressure drop, a white solid began forming on the walls of the flask containing the acetyl chloride. In other experiments this condensed phase appeared originally as a colorless liquid which rapidly solidified. When the reactor pressure had dropped to 10 cm, the calculated limit for the reaction, dry helium was added to a pressure of 76 cm. The flask containing most of the solid product was removed quickly and fitted with a cold-finger condenser. Vacuum sublimation of the solids at 40° yielded an acidic, colorless, crystalline sublimate.

Preparations of other adducts were similar except that lower pressures were used occasionally. Variations of molar ratios of the reactants markedly decreased the yields of adducts, particularly when excess amine was used. Because several adducts proved extremely hygroscopic, all handling of sublimed products was carried out in an atmosphere of dry nitrogen. The monohydrate of the HI· adduct was prepared by allowing the newly formed adduct to stand overnight in the presence of 2 cm of water vapor. Results are summarized in Table I.

No adducts were obtained from gas-phase reactions of acetyl cyanide and either dimethylamine or diethylamine, nor from oxalyl chloride and dimethylamine (which produces N,N,N′,N′-tetramethyloxamide).

Preparations in Ether.—The HCl and HBr adducts were prepared in *ca.* 70 and 50% yields, respectively, by slow addition of an ethereal solution of the amine to a similar solution of the acetyl halide. The reaction mixture, protected by a drying tube, was stirred continuously and cooled in an ice–water bath during addition. Filtration, removal of ether under reduced pressure, and repeated sublimation of all solids gave material described in Table I. The hydrogen iodide adduct could not be prepared in good yield by a similar procedure.

Registry No.—N,N-Dimethylacetamide hydrochloride, 920-54-7; N,N-dimethylacetamide hydrobromide, 920-53-6; N,N-dimethylacetamide hydriodide, 920-55-8.

The Sulfonation of Negatively Substituted *t*-Butylbenzene Derivatives

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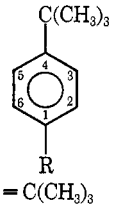
The possibility of ring sulfonation *ortho* to a *t*-butyl group is of special interest because of the high steric requirements of both moieties. 2,6-Di-*t*-butylpyridine is the only compound known to react in this manner.[1,2]

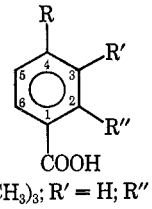
(1) N. Muller and W. J. Wallace, *J. Org. Chem.*, **24**, 1151 (1959).

(2) Dr. H. Cerfontain has suggested (privately) that the explanation may lie in ring deformation.

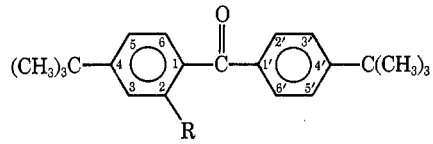
Although 1,4-di-*t*-butylbenzene (Ia) was at first thought to undergo *ortho* sulfonation, later work showed that the only product is 4-*t*-butylbenzenesulfonic acid (Ib), which is obtained with various reaction conditions and reagents.[3,4] Since no other attempts to obtain *o*-*t*-butylbenzenesulfonic acid derivatives have been reported, the present study was undertaken to explore the possibility of their preparation by direct sulfonation. Substrates with negative substituents (nitro, carbonyl, sulfonyl) *para* to the *t*-butyl group were selected (compounds Ic–h, IIIa), since such groups desirably inhibit the otherwise facile removal of the *t*-butyl moiety by protodealkylation. In addition, the directive influence of both substituents would favor entry of the sulfonic groups in the desired position *ortho* to the *t*-butyl group. Although identifiable reaction products were obtained from four substrates, in no case was sulfonation *ortho* to the *t*-butyl group observed. Compounds Ic and IIIa underwent sulfonation *ortho* to the carbonyl group, even though it is electronegative and ordinarily considered to be *meta* directing. This was shown unequivocally in the case of IIa by independent synthesis *via* 6-*t*-butylsaccharin, as well as by comparison of its nmr and ir spectra with those of the isopropyl



Ia, R = $C(CH_3)_3$
b, R = SO_3H
c, R = COOH
d, R = SO_2CH_3
e, R = $SO_2C_6H_4C(CH_3)_3$
f, R = NO_2
g, R = $C(OH)(CF_3)_2$
h, R = $C(F)(CF_3)_2$



IIa, R = $C(CH_3)_3$; R′ = H; R″ = SO_3Na
b, R = $CH(CH_3)_2$; R′ = SO_3Na; R″ = H



IIIa, R = H
b, R = SO_3Na

analog IIb which was found in past work[5] to sulfonate normally *meta* to the carboxyl group. Spectral data likewise showed that IIIa underwent sulfonation *ortho* to the carbonyl group.

This observation is not without precedent, since the formation of at least minor amounts of *ortho*-substituted sulfonic acids has been observed in several instances, including those of benzoic,[6] 3-toluic,[7] and 3,5-dimethylbenzoic acids.[8] *ortho* sulfonation has also been noted with benzophenone,[9] acetophenone,[10] and 3-methylbenzaldehyde.[11] Cerfontain has suggested in explanation that the sulfur trioxide complex with the carbonyl group could easily rearrange, *via* a five-membered cyclic transition state, to the corresponding σ complex for *ortho* substitution.[12]

The two sulfones Id and Ie underwent protodesulfonylation to 4-*t*-butylbenzenesulfonic acid (Ib) or its chloride. The only known precedent for this type of cleavage is the behavior of diphenyl sulfone upon treatment with concentrated sulfuric acid at 230°[13] (eq 1). The presence of the *para* *t*-butyl group ap-

$$C_6H_5SO_2C_6H_5 + H_2SO_4 \longrightarrow 2C_6H_5SO_2OH \qquad (1)$$

parently greatly facilitates desulfonylation, since this occurred in our case at *ca.* 120°. In contrast with carbonyl compounds, there is no precedent for sulfonation *ortho* to a sulfone or sulfonic acid group.

No definite products could be isolated in repeated attempts to sulfonate compounds If–h. Sulfonation of these compounds would involve reaction *ortho* to a *t*-butyl, nitro, or highly fluorinated isopropyl group. There is only one questionable reported instance of sulfonation *ortho* to a nitro group,[14] and reaction *ortho* to the fluorinated groups in Ig and Ih would not be expected, since they are highly electronegative and, as shown by a recent report,[15] have unusually large steric requirements.

Experimental Section[16]

4-*t*-Butylnitrobenzene (If) was prepared by a published procedure.[17]

4,4′-Di-*t*-butylbenzophenone (IIIa).—A published procedure[18] was modified as follows. Carbon tetrachloride (46 g, 0.3 mol) and 13 g of anhydrous aluminum chloride were mixed and cooled to 5° with magnetic stirring. *t*-Butylbenzene (18 g, 0.14 mol) was added all at once. After *ca.* 10 min, hydrogen chloride gas was evolved and the mixture turned red and became too thick to stir. After the mixture had been kneaded for 5 min with a heavy stirring rod, it was hydrolyzed to the yellow ketone by boiling with water; it solidified upon cooling to room temperature. The yield was quantitative (20 g). The analytical sample was recrystallized from 1-butanol: mp 132–134° (lit. mp 133–134°,[18] 135–135°[19]); nmr (C_3D_6O) δ 1.37 [s, 18, $(CH_3)_3C$)], 7.60 (d, J = 9.0 Hz, 4, H-3, -5, -3′, -5′), and 7.70 (d, 4, J = 9.0 Hz, H-2, -6, -2′, -6′).

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(16) Melting points were taken in capillary tubes on a Mel-Temp apparatus and are uncorrected. The proton nmr spectra were obtained on a Varian Associates Model A-60 spectrometer with tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal reference. Infrared spectra were taken on a Perkin-Elmer Model 521 spectrophotometer.
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4-*t*-Butylphenyl Methyl Sulfone (Id).—4-*t*-Butylphenyl methyl sulfide was prepared by a published procedure[20] from purchased 4-*t*-butylbenzenethiol. To a solution of 18 g (0.1 mol) of the sulfide in 50 ml of acetic acid was added 27 g (0.24 mol) of 30% hydrogen peroxide over 10 min with stirring and cooling at 25–40°. After the solution had stirred for 2 hr at ambient temperature, the solvent was removed *in vacuo*, yielding an oil which solidified in quantitative yield, 21 g. Crystallization from 1-butanol gave the analytical sample: mp 90–94°; ir (Nujol) 1780 and 1920 (*para* aromatic substitution overtones) and 1150 and 1300 cm^{-1} (CSO_2).

Anal. Calcd for $C_{11}H_{16}O_2S$: C, 62.3; H, 7.5. Found: C, 62.1; H, 7.3.

Bis(4-*t*-butylphenyl) Sulfone (Ie).—Chlorosulfuric acid (4.3 g, 0.03 mol) was added rapidly with stirring to 10 g (0.075 mol) of *t*-butylbenzene precooled to 5°. Chlorodifluoroacetic anhydride (18 g, 0.075 mol) was added and the mixture was refluxed for 8 hr. Volatile materials were then removed by distillation *in vacuo*, and the residual oil was triturated with 200 ml of boiling water. The solid product was filtered and air dried; the yield was 9 g (75%). Two crystallizations from 1-butanol gave the analytical sample: mp 213–215° (lit.[21] mp 213–215°); ir (Nujol) 1780 and 1920 (*para* aromatic substitution overtones) and 1310 and 1160 cm^{-1} (CSO_2).

4-*t*-Butyl(hexafluoro-2-hydroxy-2-propyl)benzene (Ig).[22]—Hexafluoroacetone (390 g, 2.35 mol) was bubbled into a stirred mixture of 400 g (3.0 mol) of *t*-butylbenzene and 1 g of aluminum chloride over a 2.5-hr period at 25–35°; an additional 0.5 g of aluminum chloride was added after 1.5 hr.[23] The reaction product (791 g, 100%) was washed with water, dried (Na_2SO_4), and distilled through a 2 ft × 0.75 in. helix-packed column, giving 344 g of Ig: bp 80° (4 mm); purity 97% (glpc); ir (neat) 1730, 1800, and 1900 (*para* aromatic substitution overtones), 705, 750, and 925 (*para* aromatic substitution), and 3650 cm^{-1} (OH); nmr ($CDCl_3$) δ 1.30 [s, 9, $(CH_3)_3C$], 3.2 (s, 1, OH), 7.48 (d, J = 8 Hz, H-2, -3, -5), and 7.75 (br d, J = 8 Hz, H-2, -2′, -6).

Anal. Calcd for $C_{13}H_{14}F_6O$: C, 52.0; H, 4.7. Found: C, 51.8; H, 4.8.

4-*t*-Butyl(heptafluoro-2-propyl)benzene (Ih).[22]—To a stainless steel pressure vessel at −80° were charged 30 g (0.1 mol) of Ig and 23 g (0.2 mol) of sulfur tetrafluoride. The sealed vessel was allowed to warm to room temperature, and was finally held for 1 hr at 45° (170 psi). The reactor was vented at room temperature and crude Ih (30.5 g, 100%) was recovered as a semisolid. It was dissolved in methylene chloride, washed with water, dried (Na_2SO_4), and distilled: yield 25 g; bp 58–61° (45 mm); ir (neat) 1730, 1800, and 1920 cm^{-1} (*para* aromatic substitution overtones).

Anal. Calcd for $C_{13}H_{13}F_7$: C, 51.7; H, 4.3. Found: C, 51.6; H, 4.5.

Monosodium 3-Sulfo-4-isopropylbenzoate (IIb).—Purchased 4-isopropylbenzoic acid (6 g, 37 mmol), 75 ml of tetrachloroethylene, and stabilized sulfur trioxide (6 g, 75 mmol) were mixed in the order given and stirred for 8 hr at 65°. The solvent layer was decanted and the lower layer was dissolved in 25 ml of water. The solution was mixed with 35 ml of saturated sodium chloride solution to precipitate the monosodium salt (IIb), which was filtered and dried to constant weight at 50°. The yield was 7 g (72%); unreacted acid was recovered from the solvent layer. The salt was recrystallized from 90% isopropyl alcohol: mp >390°; nmr (D_2O) δ 6.5 [d, J = 6.5 Hz, 6, $(CH_3)_2C$], 4.0 [m, J = 6.5 Hz, 1, HC $(CH_3)_2$], 7.7 (d, $J_{5,6}$ = 8.1 Hz, 1, H-5), 8.1 (d of d, $J_{2,6}$ = 2.0 Hz, $J_{5,6}$ = 8.1 Hz, 1, H-6), and 8.5 (d, $J_{2,6}$ = 2.0 Hz, 1, H-2); ir (KBr) 1700 (C=O), 1600 (phenyl mode), and 1300–1100 cm^{-1} (complex pattern, SO_3).

This procedure is more convenient than the published method.[5]

2-Sulfo-4-*t*-butylbenzoic Acid (IIa). A. From 4-*t*-Butylbenzoic Acid (Ic).—The method detailed above for IIb was followed, starting from purchased acid. Sulfonation was also effected using 4 molar equiv of chlorosulfuric acid at gentle reflux for 8 hr with tetrachloroethylene as solvent. The analytical sample was obtained: mp >390°; nmr (DMSO-d_6) δ 1.31 [s, 9, $(CH_3)_3C$], 7.61 (d of d, $J_{3,5}$ = 1.8 Hz, $J_{5,6}$ = 8.0 Hz, 1, H-5), 7.82 (d, $J_{5,6}$ = 8.0 Hz, 1, H-6), and 7.98 (d, $J_{3,5}$ = 1.8 Hz, 1, H-3); ir (KBr) 1730 (C=O), 1595 (phenyl mode), and 1220, 1160, and 1120 cm^{-1} (three distinct bands, SO_3).

Anal. Calcd for $C_{11}H_{13}NaO_5S$: C, 47.1; H, 4.7. Found: C, 47.2; H, 4.9.

B. From 4-*t*-Butyltoluene.—2-Methyl-5-*t*-butylbenzenesulfonamide was prepared by a published procedure[24] from purchased 4-*t*-butyltoluene, mp 139–142° (lit.[24] mp 138–140°).

To a suspension of 11 g of the sulfonamide in a mixture of 73 g of 98% sulfuric acid, 12 ml of water, and 100 ml of acetic acid, 20 g of sodium dichromate was added portionwise with stirring over 45 min at 30–40°. After stirring for 2 hr, the mixture was added to four volumes of water to precipitate 8 g (69%) of 6-*t*-butyl-1,2-benzothiazolin-3-one 1,1-dioxide (6-*t*-butylsaccharin): mp 238–240° from benzene; ir (KBr) 1160 (symmetric SO_2 stretch), 1320 (asymmetric SO_2 stretch), and 1690 cm^{-1} (amide C=O). This procedure is a modification of a published method[25] for preparing saccharin. The *t*-butyl derivative has a bitter taste.

Anal. Calcd for $C_{11}H_{13}O_3NS$: C, 55.2; H, 5.5. Found: C, 55.5; H, 5.3.

6-*t*-Butylsaccharin was hydrolyzed to monoammonium 2-sulfo-4-*t*-butylbenzoic acid by refluxing with hydrochloric acid. A published procedure for the similar hydrolysis of saccharin[26] was followed, except that twice the amount of acid was used and a much longer heating time (18 hr) was required to achieve solution. Evaporation to half volume and cooling gave the ammonium salt. The nmr spectrum showed the same aromatic substitution pattern as the sodium salt of IIa. The ir spectra were identical, except for the addition of a broad NH_4^+ peak at 1450–1380 cm^{-1}.

Sodium 2-Sulfo-4,4′-*t*-butylbenzophenone (IIIb).—Compound IIIa was sulfonated by refluxing with 2 molar equiv of chlorosulfuric acid for 4 hr in tetrachloroethylene. The sodium salt was isolated as described above; it was purified by recrystallization from toluene–isopropyl alcohol (85:15, v/v): mp 346–348°; nmr (D_2O) δ 1.13 [s, 9, $(CH_3)_3C$], 1.27 [s, 9, $(CH_3)_3C$], 6.82 (d, J = 9 Hz, H-1, -5), 7.2–7.35 (m, 3, H-6, -3′, -5′), 7.72 (d, J = 9 Hz, H-2, -2′, -6′), and 8.15 (s, 1, H-3).

Anal. Calcd for $C_{21}H_{25}NaO_4S$: C, 63.6; H, 6.3. Found: C, 63.8; H, 6.4.

Compound Id was sulfonated with sulfur trioxide as described above for IIb. The sodium salt (78% crude yield) was identified as that of Ib by comparison of the nmr and ir spectra with those of a sample made by the sulfonation of *t*-butylbenzene.[27]

Compound Ie was sulfonated with 3 molar equiv of chlorosulfuric acid by refluxing in tetrachloroethylene for 8 hr. The solvent layer gave a 73% yield of 4-*t*-butylbenzenesulfonyl chloride, mp 79–81° (lit.[3] mp 79.9–81.2°). It was found to be identical, by mixture melting point and ir spectrum, with a sample made by chlorosulfonation of *t*-butylbenzene; the sulfonamides were also identical.

Procedures similar to those described above were employed for the attempted sulfonation of If–h. Decomposition was extensive, as indicated by darkening and the evolution of sulfur dioxide. No definite water-soluble products could be isolated.

Registry No.—Id, 22796-14-1; Ig, 22796-15-2; Ih, 22796-16-3; IIa, 22796-17-4; IIb, 22796-18-5; 6-*t*-butyl-1,2-benzothiazolin-3-one 1,1-dioxide, 22796-19-6; IIIb, 22796-20-9.

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