Experimental[8]

6-Methoxy-7-deuteriomethoxycoumarin (V).—To a solution of 23 mg. of scopoletin (III) in 1.5 ml. of O-deuteriomethyl alcohol was added 8 drops of deuterium oxide, and the solvent was removed under reduced pressure in an apparatus protected from atmospheric moisture. After repeating the above equilibration twice more, the O-d_1-scopoletin (IV) was dissolved in 2 ml. of deuteriomethyl alcohol and treated with an excess of freshly prepared solution of diazomethane in ether (1 hr., room temperature). The solvents were removed on the steam bath and the residue was recrystallized from methanol to yield 17.5 mg. of fine needles, melting at 145.5–146° [lit.,[6] for 6,7-dimethoxycoumarin (I), m.p. 144–145°]. The isotopic composition, as judged from the mass spectrum (Figure 2) was 3% d_0, 22% d_1, 29% d_2, and 46% d_3 (V). More complete deuterium incorporation could probably have been accomplished by a recently recorded procedure.[7]

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(8) We are indebted to Dr. H. Budzikiewicz for the mass spectrum (Figure 2) of the deuteriated 6,7-dimethoxycoumarin which was obtained with a CEC Model 21-103C mass spectrometer equipped with a glass inlet system heated to 200° (ionization energy 70 e.v., ionizing current 50 μa.).

The Chemistry of Benzenesulfonyl Isocyanate. I. Identification of Hindered Phenols and Alcohols[1]

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The reactions of benzenesulfonyl isocyanate (I) with ethanol and phenol were reported by Billeter to afford the normal urethan products.[2] Amines and mercaptans have also been shown to react with sulfonyl isocyanates to produce ureas and thiourethans.[2,3] The use of I in preparing derivatives of phenols and alcohols, some of which are extremely sterically hindered and for which derivative formation is difficult by other means, is reported herein.

$$C_6H_5SO_2NCO + HOR \longrightarrow C_6H_5SO_2NHCO_2R$$

The reaction of I with the tertiary alcohols, 2-methyl-2-propanol and 3-ethyl-3-pentanol, occurred almost instantaneously even at 0° in toluene. For example, when I and 2-methyl-2-propanol were mixed (0.01 M each) in toluene at 0°, titration of an aliquot after 1 min. indicated a negligible amount of isocyanate remaining. This is in marked contrast to the reaction between phenyl isocyanate and 2-methyl-2-propanol which at the same concentrations in toluene was only 50% completed after 19 days at 100°.

The reaction of I with the phenols took place in toluene at 80–100° in the absence of a catalyst. The high temperatures are undoubtedly unnecessary for most of the phenols but for the sake of standardization uniform temperatures were employed. The reaction proceeded readily in cases where large bulky groups occupied the 2- and 6-positions of the phenol, examples being 2,6-di-*t*-butylphenol, 2,6-diisopropylphenol, 2,6-dimethoxyphenol, 2,6-dimethylphenol, and pentachlorophenol.

TABLE I

DERIVATIVES FROM BENZENESULFONYL ISOCYANATE

Parent compd.	Derivative, m.p. °C.	% N	
		Calcd.	Found
2,6-Di-*t*-butylphenol	165–166	3.54	3.57
2,6-Diisopropylphenol	120–121.5	3.88	3.62
2,6-Dimethoxyphenol	166.5–168.5	4.16	3.99
2,6-Dimethylphenol	159–160	4.58	4.50
2,5-Dimethylphenol	110–111	4.58	4.81
3,4-Dimethylphenol	135–136.5	4.58	4.72
3,5-Dimethylphenol	148.5–150	4.58	4.37
2-Methyl-4-(2-propenyl)-phenol (eugenol)	96–98	4.04	3.91
3-Methyl-4-chlorophenol	94–96	4.30	4.66
Pentachlorophenol	146–148	2.55	2.46
2,4-Dichlorophenol	138–140	4.06	4.01
2,4-Dibromophenol	121.5–123	3.20	3.40
2,4,6-Trinitrophenol (picric acid)	109–110	13.56	13.80
2-Phenylphenol	64–65	3.96	3.82
4-Phenylphenol	166–167.5	3.96	4.02
2-Ethoxyphenol	113–115	4.43	4.31
2-Methoxyphenol	128–130	4.56	4.44
4-Methylphenol	126–127	4.81	4.96
4-*t*-Amylphenol	135–137	4.03	4.10
4-*t*-Butylphenol	155–157	4.20	4.16
2-Chlorophenol	112–114	4.50	4.38
4-Chlorophenol	110–112	4.50	4.28
4-Bromophenol	108–110	3.92	4.08
2-Nitrophenol	108–110	8.69	8.50
4-Hydroxyphenol (hydroquinone)	208–210 (Diurethan)	5.88	5.79
2-Naphthol	133–135	4.28	4.09
Phenol	123	Previously reported[a]	
2-Methyl-2-propanol	128–128.5	5.45	5.71
3-Ethyl-3-pentanol	94–95 dec.	4.68	4.72
Diphenylmethanol	149–151	3.83	3.93
Ethanol	109	Previously reported[a]	

[a] See ref. 2.

Monohalophenols and polyhalophenols reacted without difficulty. This was equally true of mono- and polynitrophenols. Picric acid formed the normal urethan with I. Such a result is of great interest in view of the fact that β-bromopropionyl isocyanate has been reported not to react with picric acid under somewhat milder conditions.[4]

Hydroquinone reacted with I giving a mixture of products. The diurethan (product from 2 moles of I and 1 mole of hydroquinone) was separated from other products since it was the only toluene-insoluble product. The diurethan was then recrystallized from acetone. The monourethan was not obtained in pure form but was indicated by infrared absorption and appeared to melt at approximately 165°. The production of diurethan was probably due in part to the limited solubility of hydroquinone under the conditions of the reaction.

The derivatives prepared from phenols and alcohols were stable under ordinary storage conditions, some having undergone no change after 2 years in the laboratory.

I is readily available by either the reaction between benzenesulfonyl chloride and silver cyanate[2] or by the

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(1) This work was supported in part by National Science Foundation Grant No. GE-1931 (Undergraduate Research Participation Program). Grateful acknowledgment is made of such support.

(2) O. C. Billeter, *Ber.*, **37**, 690 (1904).

(3) C. King, *J. Org. Chem.*, **25**, 352 (1960).

(4) H. W. Johnson, Jr., R. J. Day, and D. S. Tinti, *ibid.*, **28**, 1416 (1963).

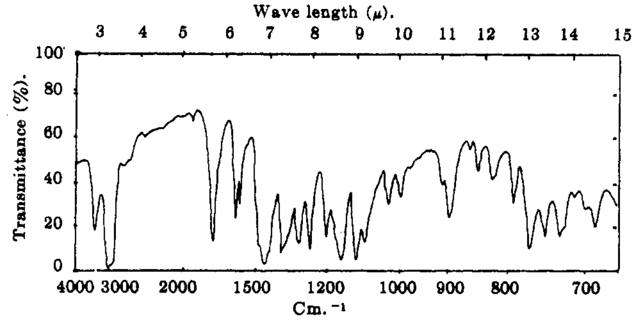

Figure 1.—Infrared spectrum of 2,6-di-*t*-butylphenol derivative (Nujol mull).

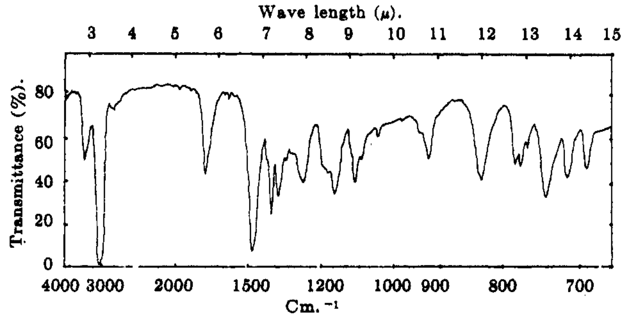

Figure 2.—Infrared spectrum of 2-methyl-2-propanol (*t*-butyl alcohol) derivative (Nujol mull).

reaction of benzenesulfonamide with phosgene.[5] Our experience with I leads us to recommend it as a reagent for the preparation of crystalline derivatives of all types of phenols and alcohols (see Table I). It is especially useful with highly hindered phenols and alcohols. The only exception to the formation of normal urethans was with I and triphenylmethanol. As is shown in a forthcoming publication from this laboratory, I reacted facilely with $(C_6H_5)_3COH$. The products, however, did not include the urethan but rather the decarboxylated product, $(C_6H_5)_3CNHSO_2C_6H_5$, plus carbon dioxide.

Another advantage of I over traditional isocyanates used to prepare derivatives is that I reacts with moisture to give benzenesulfonamide rather than the urea. Benzenesulfonamide could usually be removed from the desired urethan by crystallization. When this technique was ineffective, it was found possible to wash out the benzenesulfonamide with water leaving pure urethan.

Although other solvents should be effective, toluene has the advantage that most of the phenol and alcohol derivatives precipitate either during the reaction or upon cooling. The more soluble derivatives were easily precipitated by adding petroleum ether to the cooled toluene solution.

Whether or not the derivatives from 2,6-disubstituted phenols are urethans or *para*-substituted amides has not been settled. The similarity of the infrared spectra with those of derivatives from alcohols leads us to favor the urethan structure. The spectrum of the derivative from 2,6-di-*t*-butylphenol has single bands at 3400 and 1750 cm.⁻¹. Absorption bands occur at identical positions in the spectrum of the 2-methyl-2-propanol derivative (see Figures 1 and 2). Work is proceeding in this laboratory with the objective of elucidating the structures of the phenol derivatives.

Experimental

Benzenesulfonyl isocyanate (I) was prepared according to the method of Billeter from benzenesulfonyl chloride and silver cyanate.[2] The isocyanate was purified by distillation through a 30-in. spinning-band column, b.p. 69–72° (0.15 mm.). The isocyanate could be stored for several months if moisture was scrupulously excluded. The phenols and alcohols were obtained from commercial sources and used without further purification. Toluene and benzene were dried over sodium prior to use.

Preparation of Derivatives. A. From Phenols.—I (0.915 g., 0.005 mole) was added to 7 ml. of toluene in a dry test tube. To the solution was added 0.0063 mole (25% excess) of the phenol and the test tube was closed with a cork stopper. The test tube was placed in a 100° oil bath or steam bath and heated for 6 hr. A repeat of many of the reactions showed that heating for 1 hr. at 80° was sufficient to give good yields of derivatives. The solution was cooled to 0° and if solid had precipitated it was collected and recrystallized from toluene or benzene. If no solid precipitated on cooling the toluene solution, petroleum ether was added. The white solid was collected and recrystallized from benzene–petroleum ether. In those instances where recrystallization failed to produce purity, the derivative was slurried with water to remove benzenesulfonamide impurity, dried, and then recrystallized.

B. From Alcohols.—To a solution of 0.01 mole of I in 10 ml. of toluene or benzene was added 0.01 mole of alcohol. After the heat of reaction had subsided (approximately 5 min.) the solution was cooled to 0° and the precipitate was collected by filtration. A second crop of crystals could be obtained by diluting the toluene filtrate with petroleum ether. The derivative was recrystallized from benzene or toluene.

Alternatively, the preparation of derivatives could be carried out without solvent by mixing the reagents at room temperature or by mixing at 0°. Five drops of isocyanate was placed in a dry test tube and alcohol was added dropwise until no further heat of reaction was observed (6–9 drops). The resultant solid was recrystallized from benzene or toluene.

The infrared spectra of the urethan derivatives exhibited characteristic N-H absorption in the 3300–3400-cm.⁻¹ region and carbonyl absorption in the 1725–1775-cm.⁻¹ region (see Figures 1 and 2).

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[5] H. Krzikalla, German Patent 817,602; *Chem. Abstr.*, **47**, 2206e (1953).