with J = 1 c.p.s. This proton (labeled D) is in turn coupled to a second proton whose resonance appears at about 5.02 p.p.m. with J = 3 c.p.s. The group C at 5.02 p.p.m. is subsequently coupled to a proton whose signal appears at 5.38 p.p.m. (labeled B) with J = 9 c.p.s. The signal at 5.54 p.p.m. may be assigned to the proton geminal to both a chlorine and oxygen. Based on the magnitude of the coupling constants and going around the ring (structure II) protons 1 and 2 are equatorial, protons 3, 4, and 5 are axial.

This corresponds to an α-D-*manno* configuration. The material which both Fischer and Danilov obtained, therefore, was a mixture of tri-*O*-acetyl-2-chloro-2-deoxy-α-D-gluco and α-D-mannopyranosyl chlorides.

Experimental[5]

Reaction Procedure.—Triacetyl-D-glucal[6] was chlorinated in chloroform as described by Fischer, Bergmann, and Schotte except that a stoichiometric amount[7] of chlorine was used. The colorless oil obtained after removal of the solvent *in vacuo* was left in the refrigerator (4–5°) for 24 hr. A sample of the crystalline material (m.p. 59–70°) which had formed was subjected to t.l.c. The plate indicated that the material was a mixture of two major components of R_f 0.51 (III) and R_f 0.36 (II), and several trace components[8] of R_f 0.0–0.30. A densitometric scan[9] indicated that II and III had been formed in 58% yield in a ratio of *ca.* 1:4. Recrystallization twice from anhydrous ethyl ether afforded a material of m.p. 89–93° which consisted of only II and III (t.l.c.).

Isolation of II and III.—A slurry of 30 g. of silica gel containing 5% calcium sulfate (Brinkmann Instrument Co., Westbury, N.Y.) in 65 ml. of water was applied to the 20 × 20 cm. plates using a commercial spreader. The layer was about 250 μ thick. After air drying for 10 min. the plates were placed in the oven at 100–105° for 30 min. They were then stored in a desiccator containing anhydrous calcium chloride for at least 12 hr. before use.

The dichlorotriacetylglycal mixture (25 mg.) of m.p. 89–93° was applied to a plate with a micropipet so that 25 small spots were obtained.[10] The plate was allowed to develop (toluene–anhydrous ethyl ether, 2:1) without prior equilibration until the solvent was 16 cm. past the spotting point, and then air dried in a horizontal position. A strip 1.5 cm. wide was then removed from the plate by means of a good glass cutter. The spots on this strip could then be developed by spraying with a 5% solution of concentrated H_2SO_4 dissolved in 95% ethyl alcohol. The observed R_f values were found to vary somewhat from plate to plate, but the separation of spots was always reproducible and reliable. The developed strip showing only two spots was placed alongside the undeveloped plate and the appropriate areas scraped onto a glassine weighing paper by means of a spatula. The two fractions so obtained (from several plates) were extracted with hot chloroform. Separation of the silica gel by filtration and removal of the solvent *in vacuo* afforded 19.8 mg. of III, m.p. 95–95.5°, and 3.7 mg. of II, m.p. 139–140° (crystallization occurred after several hours in the refrigerator at 5°).

(5) Melting points were determined on a Fisher-Johns block and are uncorrected. Compounds II and III gave satisfactory carbon, hydrogen, and chlorine analysis which were performed by Drs. Weiler and Strauss, Microanalytical Laboratory, Oxford, England.

(6) P. T. Manolopoulous, M. Mednick, and N. N. Lichtin, *J. Am. Chem. Soc.*, **84**, 2203 (1962).

(7) We found that, if an excess of chlorine was used, the product which was obtained when analyzed by t.l.c. showed the presence of materials of low R_f. This is possibly the result of chlorination (of the acetyl groups) or partial deacetylation of the triacetyl-D-glucal. Immediately before use, 1 ml. of the chlorine solution was added to a solution of 2 g. of KI in 10 ml. of water. Ten milliliters of 0.2 *N* HCl was added and the mixture was titrated with 0.1000 *N* thiosulfate using 1 drop of starch solution as an indicator.

(8) If the β-*gluco* or β-*manno* isomers were present in the reaction mixture then their R_f's would have been identical with those of the α-*gluco* and α-*manno* dichlorides. The n.m.r. spectra eliminated this possibility.

(9) Concentrations were determined by means of a Photovolt recording densitometer and the appropriate areas were integrated planimetrically.

(10) The best separations were obtained under these conditions. A thicker layer of gel or more than 1.5 mg./spot gave considerable smearing.

N.m.r. Measurements.—The spectra were obtained using the Varian HA-60 spectrometer which is the HR-60 with a proton stabilization control added. The relative sensitivity of this instrument is slightly in excess of 20 to 1 for the HA-60 compared with a normal 6 or 7 for an A-60. Spectra of compound II were taken of a $CDCl_3$ solution contained in closed microcell plugs. Spectra were obtained on compound III dissolved in $CDCl_3$ contained in microcell tubes using the microcells gapped at approximately 7 mm. Data are reported in terms of the frequency-independent unit δ, using tetramethylsilane as an internal standard.

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Mass Spectrometry in Structural and Stereochemical Problems. LXVI.[1] Mass Spectral Fragmentation of 6,7-Dimethoxycoumarin[2]

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In a recent significant paper, Barnes and Occolowitz[3] recorded the mass spectra of numerous oxygen-containing heterocyclic systems and pointed out the potential utility of mass spectrometry in that field. Particular attention was paid[3,4] to coumarins, where the loss of the lactonic carbonyl function as carbon monoxide represents one of the most important processes. Methoxylated coumarins display a somewhat more complicated pattern, as is illustrated in Figure 1 by the mass spectrum[3] of 6,7-dimethoxycoumarin (I). The characteristic peaks at m/e 191 (M − CH_3), m/e 178 (M − CO), and m/e 163 (M − [CO + CH_3]) were interpreted[3] in terms of species *a*, *b*, and *c*.

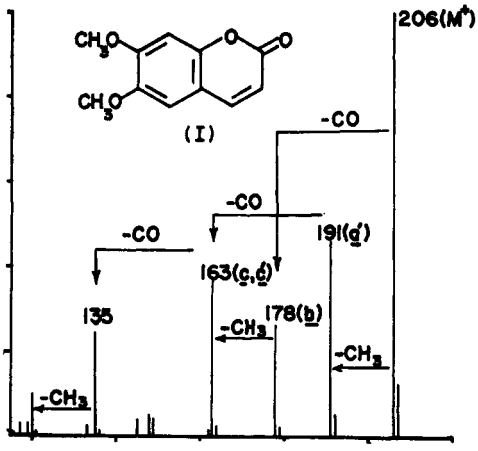


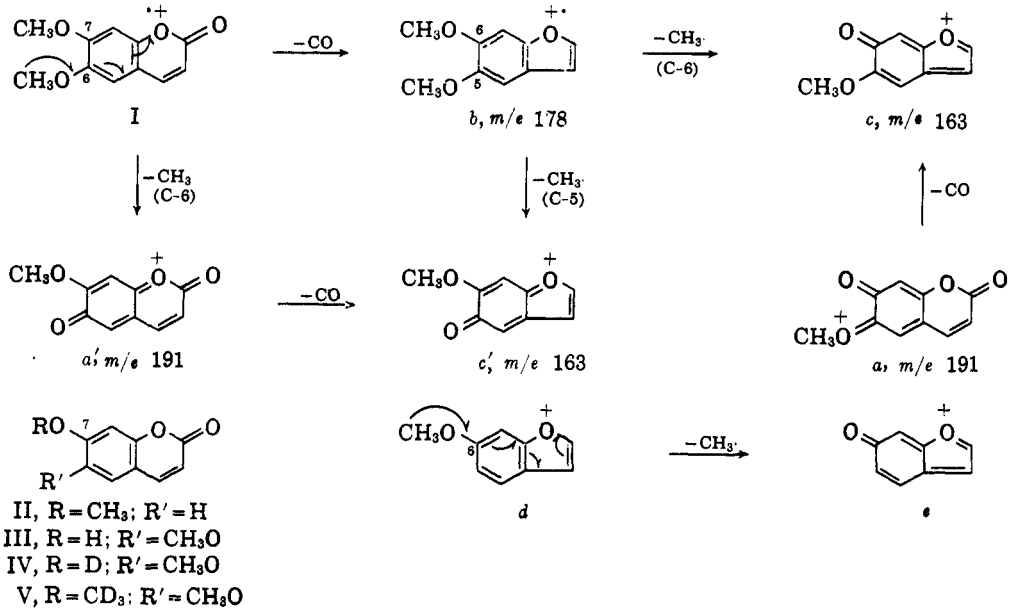
Figure 1.—Partial mass spectrum of 6,7-dimethoxycoumarin (I) (see ref. 3).

(1) For paper LXV, see C. Djerassi, G. von Mutzenbecher, J. Fajkos, D. H. Williams, and H. Budzikiewicz, *J. Am. Chem. Soc.*, **87**, 817 (1965).

(2) Supported by the National Institutes of Health of the U. S. Public Health Service (Grant No. GM 11309).

(3) C. S. Barnes and J. L. Occolowitz, *Australian J. Chem.*, **17**, 975 (1964).

(4) N. S. Wulfson, V. I. Zaretskii, and V. G. Zyakoon, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2215 (1963).



The postulated loss of a methyl radical from the 7-methoxyl function in the formation of the first fragment ion (*a*, *m/e* 191) is somewhat surprising, especially since 7-methoxycoumarin (herniarin) (II) does not display[3] any detectable M − CH_3 peak in its mass spectrum. In our hands, localization of the positive charge,[5a] where possible, has proved to be a very useful approach to the rationalization of many mass spectrometric fragmentation processes and, when applied to 6,7-dimethoxycoumarin (I), leads to the prediction[5b] that it is the methyl radical from the C-6 methoxyl group that is lost preferentially. The resulting M − CH_3 species would then be formulated as *a′* rather than as *a*.[3] While the *para*-quinoid system of *a′* would be expected to be preferred energetically over *a*, thus favoring the loss of a methyl radical from C-6, no such clear-cut distinction seems possible in the expulsion of a methyl radical from the M − CO ion (*b*, *m/e* 178), a process which is known[3] to occur through recognition of the appropriate metastable ion. The resulting fragment could be either *c* (loss of methyl from C-6 of *b*) or *c′* (loss of methyl from C-5 of *b*), especially as the M − CO ion *d* of herniarin (II) shows[3] a pronounced loss of the single methyl function (*e*). It seemed of interest to settle these questions, especially since a definite answer may be of some general applicability to other related natural products possessing this very common oxygenation pattern.

A firm distinction among all these alternatives can be reached by labeling one of the aromatic methoxyl groups. For this purpose, scopoletin (III)[6] was converted into O-d_1-scopoletin (IV) by equilibration in O-deuteriomethyl alcohol–deuterium oxide and methylated with diazomethane by the general procedure of van der Merwe,[7] which constitutes the simplest and cheapest way of labeling methyl esters or methyl ethers in the methyl group. Since the diazomethane in our experiment had not been equilibrated previously with deuterium oxide, a mixture of 6-methoxy-7-d_1-, -d_2-, and -d_3-methoxycoumarin (V) was obtained as seen from an inspection of the molecular ion region in its mass spectrum (Figure 2). The lack of isotopic homogeneity was of no consequence for our purposes, since all of the label resided in the methyl group attached to C-7.

By comparing the relevent regions in Figures 1 and 2, it will be seen that in the genesis of the M − CH_3 ion, only the C-6 methoxyl group is implicated, thus demonstrating that structure *a′* rather than *a*[3] is the correct formulation for this ion. On the other hand, inspection of the *m/e* 163–166 region in Figure 2 shows quite clearly that the loss of a methyl radical from the M − CO fragment (*m/e* 178 → *m/e* 163) can occur from either C-5 or C-6 in *b*. Hence, both species *c* and *c′* contribute to the *m/e* 163 peak.

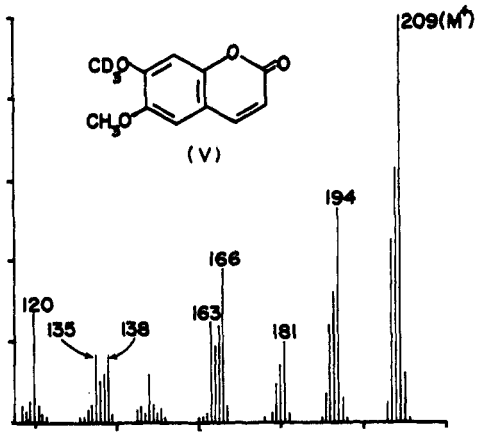


Figure 2.—Partial mass spectrum of 6-methoxy-7-deuteriomethoxycoumarin (V).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, (a) pp. 1–3; (b) pp. 256–257.

(6) See for instance W. Rittel, A. Hunger, and T. Reichstein, *Helv. Chim. Acta*, **36**, 434 (1953); J. Iriarte, F. A. Kincl, G. Rosenkranz, and F. Sondheimer, *J. Chem. Soc.*, 4170 (1956). We are indebted to Professor Reichstein (University of Basel) and Dr. Iriarte (Syntex, S.A., Mexico City) for samples of scopoletin.

(7) We are grateful to Dr. K. J. van der Merwe (Council for Scientific and Industrial Research, Pretoria, South Africa) for advance information on this procedure (K. J. van der Merwe, P. S. Steyn, and S. H. Eggers, *Tetrahedron letters*, in press). See also N. Dinh-Nguyen, *Arkiv Kemi*, **22**, 151 (1964).

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]

(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.	% N 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

(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).