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The Preparation and Nuclear Magnetic Resonance Study of 5- and 7-Nitrocoumarans

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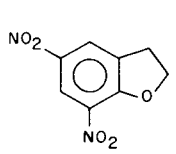
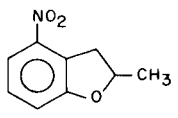
Mononitration of coumaran has been achieved by the use of acetyl chloride and silver nitrate in acetonitrile solution. Nmr decoupling experiments have served to establish the structures of the two products as the 5- and 7-nitrocoumarans. Attempted nitration with nitronium tetrafluoroborate resulted in extensive ring opening.

Although many of the reactions of coumaran (benzodihydrofuran) and its derivatives have been thoroughly studied, nitration has received only limited attention. In his extensive review of the preparation and reactions of heterocyclic oxygen compounds Chatelus (2) reported as the only coumaran nitration product, the 5,7-dinitro



I



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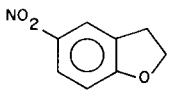

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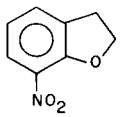


IV

derivative, I, obtained in a reaction with concentrated nitric acid. Arnold and McCool (3) obtained compound II in the course of their studies on orientation effects in a series of alkyl coumarans. More recently, Hurd and Dowbenko (4) have proposed that di- and tri-nitration products of alkylated coumarans formed in the reaction with cold mixed nitric and sulfuric acids may serve as useful solid derivatives of these substituted coumarans.

In connection with other studies in progress in our laboratories certain mononitrocoumarans were required. This investigation was undertaken in order to develop a practical method for the preparation of these compounds. In the course of this work two aromatic nitration systems were examined, acetyl chloride-silver nitrate and nitronium tetrafluoroborate.

RESULTS AND DISCUSSION

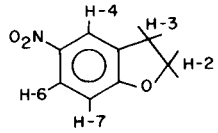
Acetyl Nitrate Nitration.

The successful nitration of β-phenylethyl acetate with silver nitrate and acetyl chloride (5) prompted us to investigate this source of nitronium ions for the coumaran system. The reactions were carried out by the dropwise addition of acetyl chloride to cold dilute solutions of coumaran and silver nitrate in acetonitrile. A gas chromatographic analysis of the solid organic product isolated from the reaction mixture showed the presence of about 3% of unreacted coumaran and 4% of unidentified impurities. The remainder of the material consisted of mononitrocoumarans, III and IV, in approximately equal proportions. Separation and purification of these isomers were accomplished by repetitive glpc trapping procedures followed by selective dissolution and recrystallization.

TABLE I

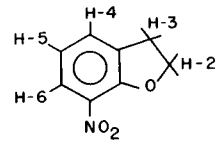
NMR and Decoupling Data (a) for 5- and 7-Nitrocoumarans

5-Nitrocoumaran



Signal	δ c/s	Area	Jc/s (b)	Appearance before irradiation	Appearance after irradiation: Proton irradiated	Effect
H-2	470	2	9	Sharp triplet, W_h = 2 c/s (c)	H-4,6	No change
H-3	325	2	9	Broadened triplet, W_h = 4 c/s	H-4,6	Sharp triplet, W_h = 2 c/s
H-4, H-6	805	2	— (d)	Complex multiplet, partially resolved, W_h = 10 c/s	H-7	Broad singlet, W_h = 3 c/s
H-7	677	1	10	Broadened doublet	H-4,6	Singlet

7-Nitrocoumaran



Signal	δ c/s	Area	Jc/s (b)	Appearance before irradiation	Appearance after irradiation at H-4
H-2	478	2	9	Sharp triplet, W_h = 2 c/s (c)	No change
H-3	328	2	9	Broadened triplet, W_h = 3.5 c/s	Sharp triplet, W_h = 2 c/s
H-4	740	1	~8	Broadened doublet	
H-5	687	1	~8	Doublet of doublets, incompletely resolved	Doublet
H-6	786	1	~9	Broadened doublet	Sharper doublet

(a) Data from Varian HA-100 spectra. Spectra were run in deuteriochloroform; chemical shift values are measured from TMS = 0. (b) Measured for major couplings. (c) W_h, width of line or signal at half-height. (d) Not measurable.

Compounds III and IV are yellow crystalline solids of melting points, 122° and 95°, respectively. The mass spectra for both substances and a quantitative analysis of one isomer support the correctness of the molecular formula assigned for a mononitrocoumaran. Their infrared spectra show characteristic N-O stretching bands (6) as well as the aromatic vibrations, alkyl-aryl ether and ring substitution effects attributed to coumarans (7). The mononitrocoumaran structures are further confirmed by their nmr spectra (*vide infra*).

Nitronium Tetrafluoroborate Nitration.

The report (8) of the extensive decomposition which had accompanied furan nitration with nitronium tetrafluoroborate suggested the need for careful handling in the coumaran nitration in order to avoid cleavage of the ether bond. Accordingly, a dilute solution of nitronium tetrafluoroborate in sulfolane (9) was added to a cooled, stirring sulfolane solution of coumaran. Despite all precautions taken to ensure mild reaction and quenching conditions, tars appeared in the reaction mixture. The

TABLE II

	5-Nitrocoumaran	7-Nitrocoumaran
Melting Point	122.1-122.5° (a)	94.6-95.4° (a)
Mass Spectrum m/e (relative intensity)	165(100) 135(57) 119(29) 91(50)	165(100) 135(31) 119(35) 91(58)
Ultraviolet Spectrum λ max (95% EtOH) (log ϵ)	234 mμ(3.83) 323 mμ(3.93)	221 mμ(4.18) 2.66 mμ(3.92) 3.43 mμ(3.66)
Infrared Spectrum ν max (carbon tetrachloride)	2982, 2902, 1519, 1484, 1466, 1422, 1365, 1340, 1246, 1116, 1073, 975, 939, 918, 899 cm^{-1}	ν max (melt) 3090, 2937, 1614, 1595, 1521, 1480, 1455, 1443, 1355, 1334, 1266, 1241, 1197, 1060, 993, 921, 842, 799, 736 cm^{-1}

(a) Melting point is corrected.

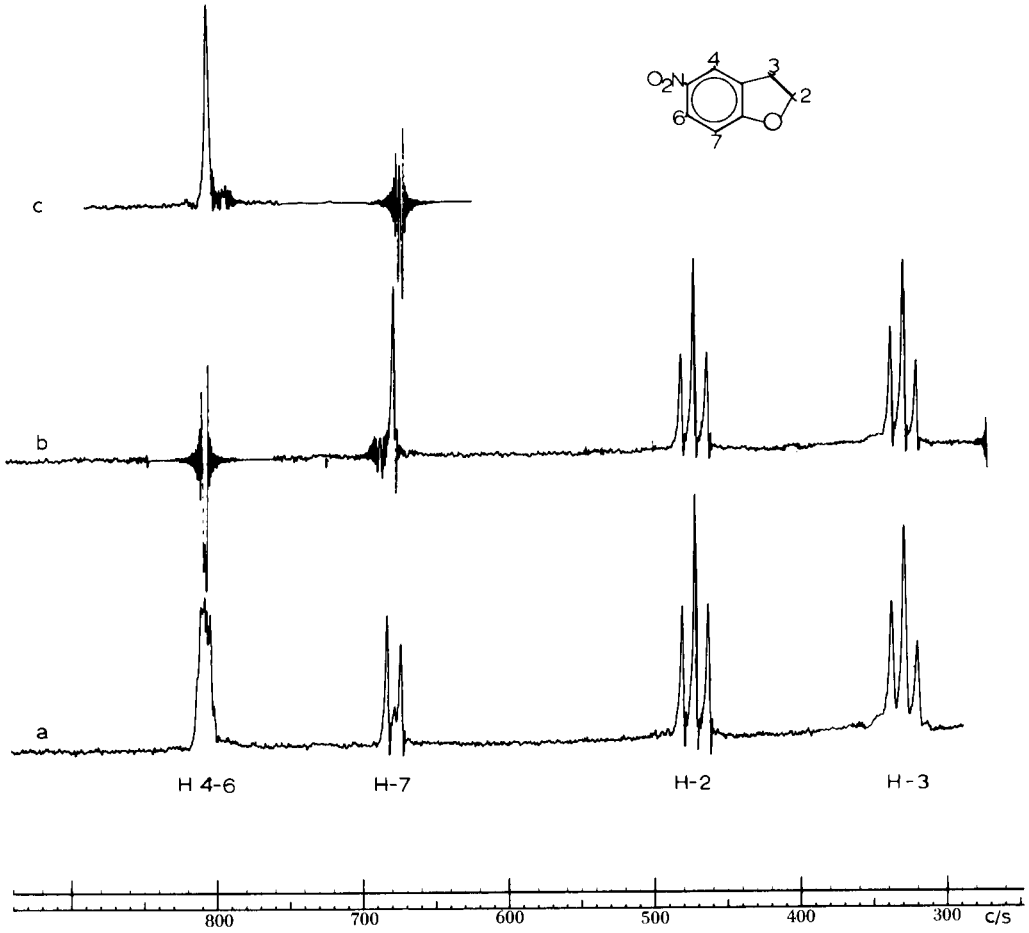


Figure 1. The 100 Mc/sec nmr spectrum of III. (a) Normal spectrum. (b) After irradiation at 805 c/s. (c) After irradiation at 677 c/s.

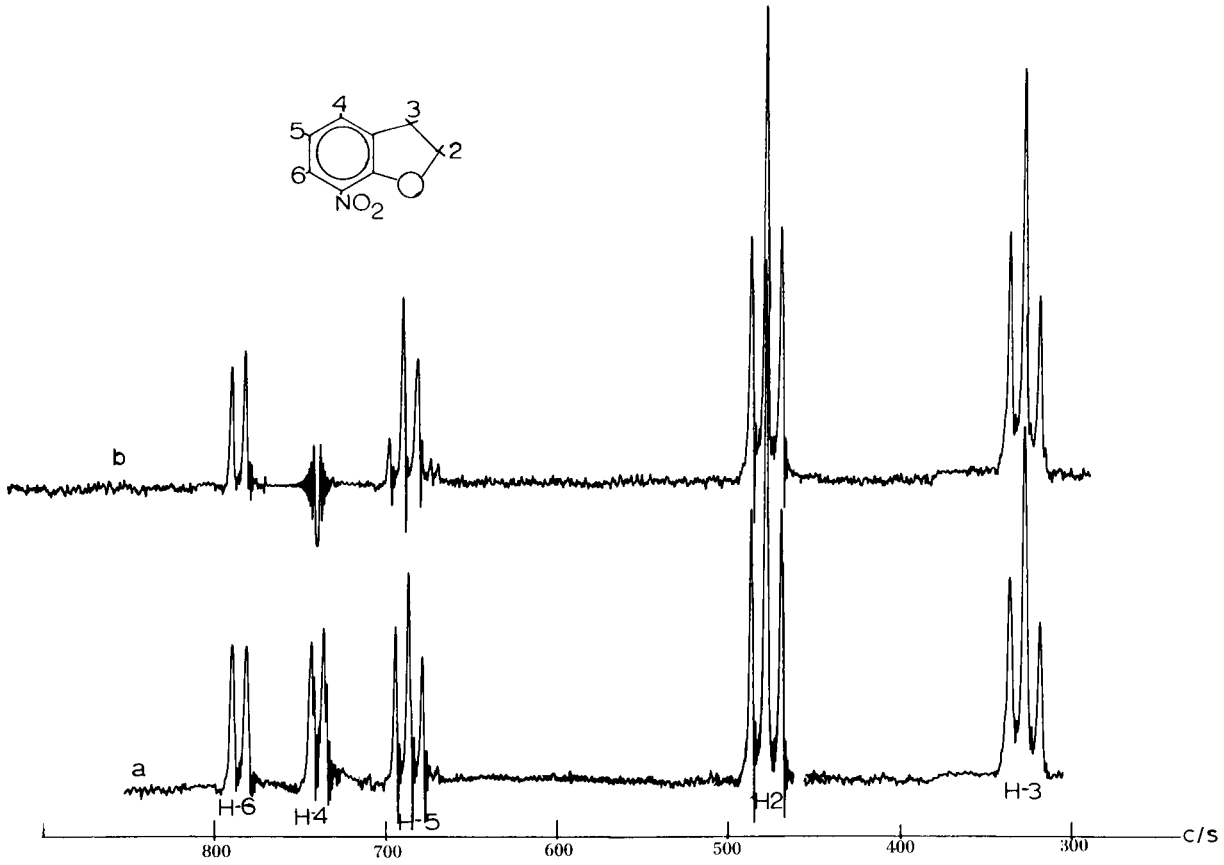


Figure 2. The 100 Mc/sec nmr spectrum of IV. (a) Normal spectrum. (b) After irradiation at 740 c/s.

glpc analysis of the semiliquid crude residue revealed four products in the proportions 8.5:2:2.5:1. The major component of this mixture was an almost colorless liquid which darkened and thickened rapidly on standing. Spectral and chemical evidence (see Experimental) strongly suggest that this product was *o*-vinyl phenol, produced by ring opening of the original coumaran. The second and third components eluted were trapped as yellow crystalline solids. Comparison of melting points and ir spectra showed that they were identical with components III and IV from the silver nitrate-acetyl chloride nitration. The fourth product, isolated in minute amounts, was a deep yellow solid whose melting point and ir spectrum were suggestive of the 5,7-dinitrocoumaran, (I), reported by Chatelus (2). It has not been investigated further.

Evidence for Structures of Mononitrocoumarans.

The assignment of position to the nitro group in III and IV presents a problem. Certainly, the "logical" positions are those shown, *ortho* and *para* to the oxygen function. Yet the importance of the methylene C-3 as a competing orienting influence cannot be dismissed. It is necessary, then, to established that the nitro groups are at carbons 5 and 7 and not at C-4 and C-6.

The overtone and combination band patterns in the infrared are in agreement with 1,2,4- and 1,2,3- substitutions of an aromatic ring (10), but these obviously argue just as well for C-4 and C-6 substituents.

The comparison of the uv spectra of these coumarans with those of the nitroanisoles (11) as the most closely related structures available is inconclusive. The spectrum for the compound assigned the 5-nitro structure is in close agreement with that of *p*-nitroanisole (11) with the predicted small bathochromic shifts associated with ring closure. However, the uv spectrum of the compound assigned as 7-nitrocoumaran agrees almost as well with the spectrum for *m*-nitroanisole as with that for *o*-nitroanisole (11).

The nuclear magnetic resonance spectra and decoupling experiments furnish conclusive proof of the positions of

the nitro substituents in the 5- and 7- positions. The nmr data are recorded in Table I and the spectra are shown in Figures 1 and 2. Of major importance is the evidence provided by the C-3 benzylic protons for the presence of a C-4 proton which is a requirement for structures assigned. Although this C-3 triplet does not exhibit the measurable splitting reported by Rottendorf and Sternhell (12) for *ortho* side chain coupling when a free methyl group is spin-coupled with a ring proton, it is distinctly broadened and shortened due to some interaction with the proton at C-4. Further, for both compounds, irradiation with the frequency corresponding to the chemical shift assigned to the H-4 signal results in the sharpening and heightening of the triplet to match that of the C-2 protons.

For the aromatic protons of the 5-nitrocoumaran, the least deshielded one, H-7, appears as a broadened doublet, predicted, by a first order treatment, for the *ortho* coupling to H-6 and *para* coupling to H-4. Apparently, the H-4 and H-6 are sufficiently similarly deshielded by the nitro group that, despite other influences, they appear as the unresolved complexity at 805 c/s. (For a 6-nitro substituent, this *ortho* hydrogen similarity would certainly have been unlikely.) Irradiation at the frequency of the H-4,6 signal removes the *ortho* coupling of H-6 to H-7 so that H-7 becomes an apparent singlet. In like manner, irradiation at 677 c/s, the frequency of H-7, leads to the simplification of the 805 c/s signal to a broad singlet due to the removal of an *ortho* coupling.

The positions of the aromatic proton signals in the 7-nitro isomer reflect the deshielding influence of the nitro group as expected: H-6 > H-4 > H-5. The H-6 signal shows a major *ortho* coupling with H-5, broadened by *meta* coupling with H-4. The proton, H-5, is a poorly resolved pair of doublets due to its *ortho* couplings with H-4 and H-6. The shape of the H-4 signal suggests *ortho* coupling with H-5 and *meta* coupling with H-6. Irradiation at the frequency of the H-4 signal sharpens the H-6 signal and simplifies the H-5 signal to a doublet due to the removal of one *ortho* coupling. This is illustrated in Fig. 2.

To the extent that such a comparison if valid here, it can be seen that the estimated coupling constants J_{67} (*ortho* to oxygen), J_{56} (*ortho* to nitrogen), and J_{45} (*ortho* to carbon) show the decreasing values predicted for the decrease in electronegativity of the *ortho* atom (13).

EXPERIMENTAL

Melting points were determined in open capillaries with a Mel-temp device and with a Hershberg melting point apparatus. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Infrared spectra were recorded on Beckman IR-10 and Perkin-Elmer, Model 21 spectrophotometers. Ultraviolet spectral records were determined on Beckman DB and Cary Model 11 spectrophotometers. NMR spectra were recorded on Varian A-60 and Varian HA-100 instruments using deuteriochloroform as the solvent and tetramethylsilane as an internal standard. The mass spectra were recorded with a Consolidated Engineering 21-102 mass spectrometer operating with an ionization energy of 70 ev. Gas chromatography was carried out on a Wilkens Aerograph A-90P and on an Aerograph 1520 equipped with a 1/8" x 5' column packed with 5% SE-30 on GasChrom P.

Materials.

Nitronium tetrafluoroborate was prepared from fuming nitric acid, anhydrous hydrogen fluoride and boron trifluoride according to the method of Kuhn and Olah (9a). Sulfolane (Aldrich) was purified by vacuum distillation, b.p. 87-88° (0.3 mm). Acetonitrile (Baker Analyzed) and acetyl chloride (Eastman) were redistilled before use. Silver nitrate was used as received. Coumaran was synthesized from *o*-anisidine by the method used by Chatelus (2). Its b.p., 79° (17 mm), n_D^{25} 1.5480, and picrate, m.p. 75-75.7°, were in agreement with values reported there (2). Its infrared spectrum gave the characteristic coumaran absorptions at 1488, 1442, 1230, 986, 945 and 748 cm^{-1} (7).

Nitration with Acetyl Nitrate (5).

In a representative experiment, 3.7 g. (22 mmoles) of silver nitrate and 2.4 g. (20 mmoles) of coumaran dissolved in 10 ml. acetonitrile were placed in a 100 ml. three-necked flask equipped with a dropping funnel, condenser and drying tube, and thermometer. To this were added 1.7 g. (22 mmoles) of acetyl chloride in 2 ml. of acetonitrile. As the quantity of silver chloride increased, further dilution with acetonitrile and more vigorous stirring were used to help maintain reactant contact for one hour at 5-10° and four hours at room temperature. To the reaction flask cooled to 5° were added 20 ml. of water, then an additional 10 ml. when the mixture was at room temperature. Exhaustive treatment of solid and liquid materials with small portions of ether was used to extract products. The solvent-free crude solid weighed 3.5 g. Peak area measurements on the chromatogram for this mixture (in acetonitrile) indicated that it consisted of 3% unreacted coumaran, 48% compound III, 45% compound IV, and 4% unidentified impurities.

Nitronium Tetrafluoroborate Nitration (9).

A reagent solution was prepared by magnetically stirring for several hours 37 ml. of freshly distilled sulfolane to which 2.45 g. (18.4 mmoles) of nitronium tetrafluoroborate had been added. This solution was then introduced via a dropping funnel into a 125 ml. suction flask-reaction vessel containing 2.00 g. (16.7 mmoles) of coumaran in 3.5 ml. of sulfolane. Throughout the 30 minute addition period, the stirring solution was maintained at a temperature of 8-10° by means of an ice-water bath. Acidic vapors were trapped by a sodium hydroxide solution. After the reaction solution had stirred for 5.5 hours at room temperature, 80 ml. of water were added. Five 15 ml. portions of ether were used to extract organic products. Tarry material and ether solution were dried over anhydrous magnesium sulfate. Flash distillation of the ether solution left 2.10 g. of semiliquid products. Estimates from peak area measurements and tests on trapped materials showed the four components of the product mixture to be (1) 59%, (retention time, 4.5 minutes), of a colorless liquid which darkened and thickened readily on standing, gave a positive ferric chloride test, and had an infrared spectrum showing absorptions characteristic of a vinyl phenol at 3630, 3550, 1635, 1430, 1305, 1148, 910, and 735 cm^{-1}, but lacking the characteristic bands of nitro at 1520 and 1360 cm^{-1} (6) and the coumaran structure at 1480, 1240, 986 and 945 cm^{-1} (7); (2) 15%

(retention time, 15 minutes), yellow, needle-like crystals, m.p. 117.3-117.9° (14), ν max 2914, 1604, 1514, 1487, 1444, 1342 cm^{-1}; (3) 19% (retention time, 18 minutes), light yellow crystals, m.p. 86.6-87.1° (14).

Anal. Calcd. for $C_8H_7NO_3$: C, 58.18; H, 4.27; N, 8.49. Found: C, 58.06; H, 4.45; N, 8.29.

(4) Seven Percent (retention time, 78 minutes), was dark yellow needles, m.p. 137.8-138.2° [lit. (2) m.p. for 5,7-dinitrocoumaran, 141°]. In carbon tetrachloride solution, the infrared spectrum showed bands at 1528 and 1342 cm^{-1} [nitro (6)]; 1242, 990, 930 cm^{-1} [coumaran (7)].

Separation and Purification of Mononitration Products.

The 5-nitrocoumaran (III) and 7-nitrocoumaran (IV) were separated from each other and from impurities by trapping in capillary tubes inserted directly into the collector port of the Aerograph instrument. Column and conditions used were: 1/4" x 2.5 m 25% SE-52 on Gas Chrom P, 205°, 88 ml./minute of helium. From the 20 μl. injection of the acetonitrile solution of the crude product mixture yellow crystals of III, retention time 17 minutes, m.p. 117.5-118.0° and pale yellow crystals of IV, retention time 23 minutes, m.p. 87-88°, were condensed in the trapping tubes.

Solubility tests on the mixture, checked by their gas chromatograms, revealed similar solubility in benzene, acetone, acetonitrile, ethyl acetate; similar insolubility in water and pentane; and similar partial solubility in carbon disulfide and carbon tetrachloride. Because methanol dissolved compound IV and impurities readily at 57° while compound III remained largely undissolved, isolation of compound III in quantity, 0.35 g., was achieved by stirring the crude mixture, 1.31 g., with 9 ml. of methanol maintained at a temperature of 57°. The methanol-insoluble residue was removed by filtration. Repetition of this treatment three times left a residue of 96% purity, which, after a recrystallization from methanol, melted at 122.1-122.5° (14). Pertinent physical data on the purest samples (retrapped or recrystallized) of these isomeric mononitrocoumarans are summarized in Table II.

Acknowledgments.

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