The Addition of Nitroparaffins to (N-Ethyl)-ethylenesulfonanilide

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Received January 16, 1954

The present investigation was undertaken in an effort to determine to what extent unsaturated sulfonamides undergo base-catalyzed, Michael-type addition reactions. Examples of compounds with the structure —CH=CHSO$_2$— which have previously been employed successfully as acceptors in analogous reactions are vinyl sulfones[1] and unsaturated sulfonic esters.[2] Concerning related reactions using α,β-unsaturated sulfonamides, the published literature records the addition of alkyl or aryl amines to ethylenesulfonanilides at elevated temperatures preferably in the presence of copper powder.[3] Goldberg[3] also found that an addition product was obtained by causing the sodium salt of acetylsulfanilamide to react with ethylenesulfonanilide.

In the course of experiments in this Laboratory, a series of γ-substituted sulfonamides was desired. The addition of ethyl malonate, ketones, nitroparaffins, etc., in the presence of bases might be expected to yield such compounds. But attempts to apply the base-promoted reactions to unsaturated sulfonamides from primary amines (*e.g.*, $CH_2=CHSO_2NHR$) meets with difficulty if the sulfonamide is a stronger acid than the addend. In order to prevent any reaction of the base with the acceptor in the present work, the sulfonamide from a secondary amine was studied. The new (N-ethyl)-ethylenesulfonanilide was prepared and found to enter into addition reactions with nitroparaffins in the presence of traces of methanolic potassium hydroxide. Attempts to find conditions under which sulfonamides from primary amines react are in progress in this Laboratory.

A tendency for the substitution of all the active hydrogen atoms of the nitroparaffins was observed. Even when the unfavorable ratio of almost six moles of nitromethane per mole of (N-ethyl)-ethylenesulfonanilide was employed, a 38% yield of the tris-substituted nitro compound, $O_2NC(CH_2CH_2SO_2NC_2H_5C_6H_5)_3$, was isolated. When large quantities of potassium hydroxide were used (resulting in higher concentrations of the salts of the nitroparaffins), the formation of lower substituted products was facilitated. Thus, although N-ethyl-3-nitropropanesulfonanilide was not isolated as a product from nitromethane in the course of this work, the 2:1 adduct, N,N′-diethyl-3-nitropentane-1,5-disulfonanilide, was. This was accomplished in 18% yield (along with some of the 3:1 adduct) through the use of nearly equivalent quantities of nitromethane, (N-ethyl)-ethylenesulfonanilide and potassium hydroxide. The yields of the 1:1 adducts to nitroethane and 1-nitropropane also were raised to 44 and 40%, respectively, by the use of equivalent quantities of potassium hydroxide.

The procedures reported in the literature[4] for the preparation of ethane-1,2-disulfonyl chloride from sodium ethane-1,2-disulfonate were improved through the use of small amounts of phosphorus oxychloride to liquefy the reaction mixture.

Experimental

Melting points reported herein are uncorrected.

(N-Ethyl)-ethylenesulfonanilide (I).—A solution of 12.9 g. of N-ethylaniline in 15 ml. of freshly dried ether was added dropwise to an ice-cold solution of 10.0 g. of ethane-1,2-disulfonyl chloride[4] in 200 ml. of anhydrous ether. During the addition, a colorless precipitate of N-ethylaniline hydrochloride separated and sulfur dioxide was evolved. After the mixture was allowed to stand at room temperature for two hours, the precipitate was removed by filtration and the filtrate was washed with three 20-ml. portions of 3 *N* hydrochloric acid. The ethereal solution was then dried over calcium chloride and the solvent was evaporated in a vacuum desiccator. The solid, which was obtained by chilling the resulting brown oil, was recrystallized from absolute ethanol using a Dry Ice–acetone-bath. There was thus obtained 4.4 g. (60% based on N-ethylaniline) of I as colorless crystals, m.p. 37–39°.

Anal. Calcd. for $C_{10}H_{13}NO_2S$: C, 56.84; H, 6.20. Found: C, 56.80; H, 6.15.

Condensation of I with Nitromethane. *Experiment A.*—To a mixture of 0.023 g. of nitromethane and 0.290 g. of I was added one drop of 5% methanolic potassium hydroxide. This was mixed as thoroughly as possible in a stoppered flask and allowed to stand for ten minutes. Methanol (approximately 2 ml.) was then added and the mixture was stirred. After one hour, the mixture was acidified with acetic acid. The resulting solid was then washed with small portions of water. The solid residue was crystallized from absolute ethanol, yielding 0.126 g. of nitromethylidyne-tris-(N-ethyl)ethanesulfonanilide (48%, m.p. 143–145°). The melting point of the product was raised to 146–147° by further recrystallization from absolute ethanol.

Anal. Calcd. for $C_{31}H_{42}N_4O_8S_3$: C, 53.58; H, 6.09. Found: C, 53.73; H, 6.17.

Experiment B.—When 0.500 g. of I, 0.870 g. of nitromethane and one drop of saturated potassium hydroxide–methanol solution were treated according to the procedure of the previous experiment, 0.207 g. (38%) of the 3:1 adduct (m.p. 137–140°) was obtained. Crystallization of the product from absolute ethanol again afforded a sample melting at 146–147°. On dilution of the filtrate, an oil which could not be induced to crystallize separated.

Experiment C.—When 0.500 g. of I was added to 0.150 g. of nitromethane and to this solution was added a solution of 0.140 g. of potassium hydroxide in 0.84 ml. of methanol with vigorous shaking and the resulting solution was worked up as in the previous experiments, a heavy oil resulted. This oil was crystallized and recrystallized several times from very small quantities of absolute ethanol, yielding 0.100 g. (18%) of N,N′-diethyl-3-nitropentane-1,5-disulfonanilide, m.p. 105–106°.

Anal. Calcd. for $C_{21}H_{29}N_3O_6S_2$: C, 52.15; H, 6.04. Found: C, 52.25; H, 6.32.

With Nitroethane. Experiment A.—To a mixture of 0.500 g. of I and 0.585 g. of nitroethane was added a drop of saturated potassium hydroxide–methanol solution. After 12 hours, the base was neutralized with 3 *N* acetic acid and the mixture was evaporated to dryness in a stream of air. The remaining solid was triturated with water, separated and then crystallized from approximately 20 ml. of hot, absolute ethanol, yielding 0.360 g. (61%) of N,N′-diethyl-3-nitro-3-methylpentane-1,5-disulfonanilide, m.p. 174–176°. By repeated recrystallization from absolute ethanol, the melting point was raised to 179–180°.

Anal. Calcd. for $C_{22}H_{31}N_3O_6S_2$: C, 53.10; H, 6.28. Found: C, 52.90; H, 6.31.

The filtrate from the initial crystallization above was diluted with about three volumes of water and cooled to 0°. Colorless crystals of N-ethyl-3-nitrobutanesulfonanilide (0.208 g., 31%, m.p. 60–63°) separated. The melting

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[1] *E.g.*, E. P. Kohler and H. Potter, This Journal, **57**, 1316 (1935).

[2] A. Lambert and J. D. Rose, *J. Chem. Soc.*, 46 (1949).

[3] A. A. Goldberg, *ibid.*, 464 (1945).

[4] (a) E. P. Kohler, *Am. Chem. J.*, **19**, 733 (1897); (b) P. W. Clutterbuck and J. B. Cohen, *J. Chem. Soc.*, **121**, 120 (1922).

point was raised to 70–71° by recrystallization from dilute ethanol with the removal of small amounts of the least soluble material by filtration before dilution and cooling.

Anal. Calcd. for $C_{12}H_{18}N_2O_4S$: C, 50.33; H, 6.34. Found: C, 50.43; H, 6.25.

Experiment B.—When 0.58 g. of I, 0.33 g. of nitroethane and 0.34 g. of potassium hydroxide in a small amount of methanol were employed according to the procedure of the preceding experiment, 0.12 g. (18%) of the adduct containing two sulfonanilide units (m.p. 175–176°) and 0.35 g. (44%) of the 1:1 adduct were obtained.

With 1-Nitropropane. Experiment A.—Following the procedure described under experiment A of nitroethane, 0.500 g. of I was caused to react with 0.695 g. of 1-nitropropane in the presence of one drop of saturated potassium hydroxide–methanol solution. The less soluble product was N,N′,3-triethyl-3-nitropentane-1,5-disulfonanilide obtained in 0.187 g. yield (31%, m.p. 124–126°, raised to 130–131° by recrystallization from absolute ethanol).

Anal. Calcd. for $C_{22}H_{33}N_3O_6S_2$: C, 53.98; H, 6.50. Found: C, 53.50; H, 6.26.

When the filtrate from the initial crystallization was concentrated to approximately 5 ml. and cooled to 0°, 0.250 g. (35%) of N-ethyl-3-nitropentanesulfonanilide (m.p. 50–54°, raised to 59–60° by recrystallization from small portions of absolute ethanol) was obtained.

Anal. Calcd. for $C_{13}H_{20}N_2O_4S$: C, 51.98; H, 6.71. Found: C, 52.46; H, 6.68.

Experiment B.—Using 0.37 g. of 1-nitropropane, 0.57 g. of I and 0.45 g. of potassium hydroxide in approximately 4 ml. of methanol according to the procedure of the previous experiment, only a trace of the 2:1 adduct was obtained. A 0.32-g. quantity (40%, m.p. 47–50°) of the 1:1 adduct was obtained.

With 2-Nitropropane.—To 0.100 g. of I was added 0.045 g. of 2-nitropropane and one drop of saturated potassium hydroxide–methanol solution. The resulting solution was allowed to remain at room temperature for 12 hours and then acidified with 3 *N* acetic acid. The solid which precipitated was separated, washed with small portions of water and dried. The yield of N-ethyl-3-methyl-3-nitrobutanesulfonanilide obtained was 0.120 g. (83%, m.p. 89–90°). The analytical sample was recrystallized from absolute ethanol, but the melting point was not changed.

Anal. Calcd. for $C_{13}H_{20}N_2O_4S$: C, 51.98; H, 6.71. Found: C, 52.04; H, 6.68.

Acknowledgment.—Some of the analyses reported herein were carried out by Miss Peggie Garrison.

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Flavonoids of Various Prunus Species. II. The Flavonoids in the Wood of *Prunus speciosa*

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RECEIVED MARCH 3, 1954

In a previous paper,[1] we reported the presence in the wood of *Prunus yedoensis* of four flavonoid constituents (prunin, genkwanin, naringenin and *d*-catechin). We have now obtained two flavonoid compounds from the wood of *Prunus speciosa* (Ohshimazakura in Japanese), cultivated in the Akanuma Experimental Nursery in Saitama Prefecture. No crystalline substance was obtained from the ethereal fraction, but two glycosides of a flavanone and a flavone, respectively, were isolated from the ethyl acetate fraction.

On the basis of its melting point, elementary analysis and hydrolysis products (one mole each of sakuranetin and glucose), the flavanone glycoside was identified as sakuranin, which was first isolated by Asahina[2] from the bark of *Prunus yedoensis* and *P. donarium*.

The flavone glycoside consisted of one mole each of glucose and of aglycone which showed the properties of genkwanin. Ohta and Nishikawa[3] isolated a genkwanin glucoside from the bark of *Prunus serrulata*. Ohta[4] showed it to be a 5-glucoside, which he named glucogenkwanin. The flavone glucoside and glucogenkwanin have the same melting point which was not depressed by admixture of the two.

The same results were obtained with a sample of *P. speciosa* from Ohshima Island, where this tree grows wild.

Experimental

Isolation of Flavonoids.—Wood chips (400 g.) from living stems (7 cm. diam.) were extracted with 3 l. of boiling methanol for 3 hr., and the extraction repeated. The methanolic filtrate was concentrated to a sirup, mixed with 200 ml. of water, heated on a water-bath and filtered. The filtrate was then repeatedly extracted with ether. After evaporation of the ether, the residue was mixed with an equal volume of ethyl acetate, and allowed to stand overnight. More ethyl acetate was added to dissolve the oily mass which had separated. After a while, white crystals gradually separated. These were filtered off; then yellow crystals appeared. The white crystals were sakuranin (yield of crude substance, 1.0 g.) which were recrystallized from dilute methanol to give white needles, m.p. 212°. The yellow crystals were glucogenkwanin (yield of crude substance, 0.4 g.) which were recrystallized from methanol to give microscopic needles, m.p. 273°.

Sakuranin.—It gave no color with ferric chloride. *Anal.* Calcd. for $C_{22}H_{24}O_{10}\cdot 4H_2O$: H_2O, 13.84. Found: H_2O, 12.93.

Anal. Calcd. for $C_{22}H_{24}O_{10}$: C, 58.92; H, 5.35: OCH_3, 6.91. Found: C, 59.18; H, 5.23; OCH_3, 7.19.

Hydrolysis.—Sakuranin (0.3679 g.) was added to 25 ml. of 2% sulfuric acid and heated for 30 minutes over a direct flame under reflux. The cooled liquor was repeatedly extracted with ether. After evaporation of the ether, the residue was recrystallized from dilute methanol to give white needles of sakuranetin, m.p. 152°.

Anal. Calcd. for $C_{16}H_{11}O_5\cdot H_2O$: H_2O, 5.90. Found: H_2O, 6.24. Calcd. for $C_{15}H_{11}O_4(OCH_3)$: OCH_3, 10.83. Found: OCH_3, 11.23.

The acetate of this aglycone was obtained as colorless plates, m.p. 146°.[5]

The mother liquor freed from aglycone was diluted to 50 ml. with water; the rotation in a 2.2 dm. tube at 18° was 0.25°, from which the amount of glucose was calculated to be 0.12 g.; theoretical amount 0.14 g.

This solution was then carefully neutralized with barium carbonate, evaporated on a boiling water-bath to a small volume and filtered. When the filtrate was heated with phenylhydrazine hydrochloride and sodium acetate, glucosazone was formed, which was filtered and recrystallized from dilute methanol; m.p. 208°, alone and on admixture with an authentic specimen.

Glucogenkwanin, m.p. 273°, was insoluble in benzene, chloroform, petroleum ether and ethyl acetate; sparingly soluble in methanol, ethanol and acetone. It gave an orange color with magnesium powder and concentrated HCl, but no color with ferric chloride.

Anal. Calcd. for $C_{22}H_{22}O_{10}\cdot 2H_2O$: C, 53.77: H, 5.40; OCH_3, 6.95; H_2O, 7.47. Found: C, 53.67; H, 6.17; OCH_3, 7.07; H_2O, 7.25.

Hydrolysis.—Glucogenkwanin (53.3 mg.) was dissolved in 1 ml. of concentrated sulfuric acid; after a while it was added to 15 ml. of cold water, and the solution allowed to

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[1] M. Hasegawa and T. Shirato, THIS JOURNAL, **74**, 6114 (1952).

[2] Y. Asahina, *J. Pharm. Soc. Japan*, **28**, 213 (1908).

[3] T. Ohta and S. Nishikawa, *ibid.*, **62**, 40 (1942).

[4] T. Ohta, *ibid.*, **72**, 456 (1952).

[5] D. Chakravarti, N. Kundo and R. P. Ghosh, *J. Indian Chem. Soc.*, **25**, 329 (1948).