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SYNTHESIS OF 1,1-BIS(ALKOXYARYL)-2-NITROALKANES FOR INSECTICIDAL EVALUATION[1]

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Müller (1), Neher (2), and Blickenstaff (3) have prepared a series of 1,1-diaryl-2-nitroalkanes which show marked insecticidal activity, especially against the Mexican bean beetle. The series has been extended by us to include a number of 1,1-diaryl-2-nitroalkanes in which each of the aromatic nuclei contains one or more alkoxy substituents. This particular series of compounds which contain no chlorine atoms was chosen in an attempt to avoid some of the animal toxicity which is frequently associated with insecticides containing this element.

The diarylnitroalkanes are usually prepared by reacting an aromatic aldehyde with the salt of a nitroparaffin to form a salt of a 1-aryl-2-nitro-1-alkanol. This is acidified to obtain the intermediate nitro alcohol, which is then condensed with an aromatic compound in the presence of an acidic condensing agent such as sulfuric acid, aluminum chloride, or zinc chloride.

$$\text{(a)}\ \mathrm{ArCHO} + \mathrm{RCH{=}NO_2Na} \rightarrow \mathrm{ArCHOHC(R){=}NO_2Na}$$

$$\text{(b)}\ \mathrm{ArCHOHC(R){=}NO_2Na} \xrightarrow{H^+} \mathrm{ArCHOHCH(R)NO_2}$$

$$\text{(c)}\ \mathrm{ArCHOHCH(R)NO_2} + \mathrm{ArH} \xrightarrow{H_2SO_4} \mathrm{Ar_2CHCH(R)NO_2}$$

The principal difficulty encountered with this synthesis is the formation of nitroölefins (d) instead of nitro alcohols in the acidification step (b).

$$\text{(d)}\ \mathrm{ArCHOHC(R){=}NO_2Na} \xrightarrow{H^+} \mathrm{ArCH{=}C(R)NO_2}$$

With each of the aldehydes studied in this investigation some nitroölefin was formed and with most of them the nitroölefin was the sole isolatable product. All attempts to use the nitroölefins formed in place of nitro alcohols in reaction (c) were unsuccessful. Intractable oils always resulted and the desired product could not be isolated as such, although oxidations leading to the corresponding benzophenone indicate that it may have been formed in small amounts. Attempts to influence the amounts of nitroölefins formed by using acids of different strengths (H_2SO_4, CH_3CO_2H, H_2CO_3) in the acidification step led to no improvement in the yields of nitro alcohols.

It was finally discovered that nitroölefin formation could be avoided and very much better yields of nitro alcohols obtained by isolating and drying the salts produced in reaction (a) and then acidifying them under anhydrous con-

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[1] An abstract of a thesis submitted to the faculty of Purdue University by Theodore August Jacob in partial fulfilment of the requirements for the degree of Doctor of Philosophy in February, 1950.

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ditions, as, for example with glacial acetic acid in dry ether. This procedure also prevents reversal of reaction (a) which usually occurs to some extent when aqueous acids are used. Unfortunately the new method can be applied readily only when the necessary salt of the nitro alcohol can be isolated and dried. This is possible in most syntheses involving nitromethane but often does not work for the homologs of nitromethane. Under the conditions here employed (reaction in methanol or ethanol) the salts do not precipitate except for those from nitromethane.

A number of different procedures have been reported for the reaction of the nitromethane homologs with aromatic aldehydes using condensing agents such as sodium bicarbonate (4), sodium hydroxide (5), and triethylamine (6). However, in each of these procedures the nitro alcohol rather than its salt is isolated from the reaction product. An attempt was made to react nitroethane and nitropropane with the alkoxybenzaldehydes in the presence of sodium methoxide but the sodium salt of the corresponding nitro alcohol did not form. A reaction took place when the bisulfite addition complex of anisaldehyde was treated with the sodium salt of nitroethane or nitropropane according to the procedure reported by Kamlet (7). Under these conditions the nitro alcohol was formed directly and recovered as a crude oil contaminated with the free aldehyde and nitroparaffin. Since these contaminants were difficult to remove completely, the nitro alcohol could not be crystallized. However, the reaction of the bisulfite addition complex of *o*-methoxybenzaldehyde and *o*-ethoxybenzaldehyde with the sodium salt of nitroethane took place readily, and the resulting nitro alcohol could be isolated in a sufficiently pure state to permit crystallization.

TABLE I

1-ARYL-2-NITRO-1-ALKANOLS

COMPOUND[a]	M.P., °C.[b]	ANALYSES NITROGEN	
		Calc'd	Found
1-Anisyl-2-nitroethanol	37–41	7.10	7.28
1-(*p*-Ethoxyphenyl)-2-nitroethanol	67–68	6.63	6.69
1-(*p*-Propoxyphenyl)-2-nitroethanol	65–67	6.22	6.15
1-(3′,4′-Dimethoxyphenyl)-2-nitroethanol	92–93.5	6.17	6.21
1-(3′,4′-Methylenedioxyphenyl)-2-nitroethanol	95–96	6.63	6.54
1-(*p*-Chlorophenyl)-2-nitroethanol	35–37	6.95	6.88
1-(*o*-Methoxyphenyl)-2-nitro-1-propanol	83–86	6.63	6.55
1-(*o*-Ethoxyphenyl)-2-nitro-1-propanol	64.5–66.0	6.22	6.23

[a] 1-(*o*-Methoxyphenyl)-2-nitroethanol and 1-anisyl-2-nitro-1-propanol were also prepared but could not be crystallized. [b] All melting points are corrected.

The nitro alcohols which were isolated as solid compounds are given in Table I.

The 1,1-diaryl-2-nitroalkanes were prepared by reacting the 1-aryl-2-nitro-1-alkanol with the desired aromatic compound in the presence of sulfuric acid. The reaction mixture was poured into ice-water, neutralized with base, and steam-distilled. The residual product usually crystallized but in some cases remained as an oil. Both the yield and ease of crystallization of the 1,1-diaryl-2-nitroalkanes depend to a large extent on the purity of the nitro alcohol employed in the reaction. When the alcohol is added as a crude oil, the condensation product is often exceptionally difficult to crystallize, and the yield of the crude solid product lies in the range of 20–50%. However, when a relatively pure nitro alcohol is used, the product crystallizes much more easily and the yield of crude solid is increased to 70–95%.

The 1,1-diaryl-2-nitroalkanes which were prepared are shown in Table II.

TABLE II

1,1-DIARYL-2-NITROALKANES

COMPOUND	M.P., °C.[a]	ANALYSES		
		Yield,[b]%	Nitrogen	
			Calc'd	Found
1,1-Bis(*p*-ethoxyphenyl)-2-nitroethane	79–80	95	4.44	4.50
1-Anisyl-1-(*p*-ethoxyphenyl)-2-nitroethane	75–76	98	4.65	4.65
1-Anisyl-1-(*o*-methoxyphenyl)-2-nitroethane	88–90	96	4.88	4.87
1,1-Bis(*p*-propoxyphenyl)-2-nitroethane	48–49	92	4.08	4.12
1-(*p*-Chlorophenyl)-1-(*p*-ethoxyphenyl)-2-nitroethane	89–90	82	4.58	4.58
1,1-Dianisyl-2-nitropropane	102.0–102.5	40	4.65	4.61
1-Anisyl-1-(*o*-methoxyphenyl)-2-nitropropane	83–84	60	4.65	4.65
1-(*p*-Ethoxyphenyl-1-(*o*-ethoxyphenyl)-2-nitropropane	85–87	69	4.25	4.23

[a] All melting points are corrected. [b] Based on weight of crude solid.

Insecticidal evaluation. The authors are indebted to the Commercial Solvents Co. for a preliminary evaluation of these compounds as insecticides. All of them are active, but no one is quite as active as 1,1-bis-(*p*-chlorophenyl)-2-nitropropane against Mexican bean beetle larvae, house flies, and red spider mites. None shows activity against southern army worm. A dust containing 0.0625% of 1,1-dianisyl-2-nitropropane gave 100% kill of the bean beetle larvae.

EXPERIMENTAL

1-(p-Ethoxyphenyl)-2-nitroethanol. A 500-ml. three-necked flask was fitted with a stirrer, thermometer, and dropping-funnel and immersed in an ice-bath. Nitromethane (24.4 g., 0.4 mole), *p*-ethoxybenzaldehyde (30.0 g., 0.2 mole), and absolute ethanol (130 ml.) were added to the flask and cooled. A solution of sodium (9.2 g., 0.4 g.-atom) in methanol (110 ml.) was added with stirring over 1.5 hours at 2–4°, and the stirring was then continued for 2 hours at 3°. The precipitate which formed was filtered, suspended in ether, filtered again, and then added to a cold solution of glacial acetic acid (48.0 g., 0.8 mole) in 700 ml. of ether (water content not over 0.2%). After standing for 12 hours at room temperature, the ether solution was mixed with ice-water, washed with a cold, 5% sodium bicarbonate solution, and dried with sodium sulfate. Removal of the ether at reduced pressure left an oil which weighed 40 g. This oil was crystallized from a solution of 1 part of benzene and 2 parts of petroleum ether (60–70°) to give 29 g. (69%) of 1-(*p*-ethoxyphenyl)-2-nitroethanol, m.p.

64–67°. Three more recrystallizations from petroleum ether gave a white solid melting at 67–68°.

Anal. Calc'd for $C_{10}H_{13}NO_4$: N, 6.63. Found: N, 6.69.

1-(p-Ethoxyphenyl)-2-nitroethylene. A small amount of 1-(*p*-ethoxyphenyl)-2-nitroethanol was dissolved in ethanol, cooled, and mixed with an ethanolic solution of sodium ethoxide. The precipitate which formed was filtered, washed with ether, and dried. Acidification of the solid with dilute acetic acid formed a yellow precipitate of 1-(*p*-ethoxyphenyl)-2-nitroethylene, m.p. 115–116°.

Anal. Calc'd for $C_{10}H_{11}NO_3$: N, 7.25. Found: N, 7.23.

Formation of this olefin is taken as proof of the structure of the nitro alcohol.

1-(o-Ethoxyphenyl)-2-nitro-1-propanol. In the usual apparatus, sodium pyrosulfite (13.3 g., 0.07 mole), *o*-ethoxybenzaldehyde (15.0 g., 0.1 mole), and water (100 ml.) were stirred for 2 hours. Nitroethane (15.0 g., 0.2 mole) was added to a cooled solution of sodium hydroxide (8.0 g., 0.2 mole) in water (100 ml.). After the sodium salt of nitroethane had formed, the solution was dropped into the previous mixture with stirring at 3–5° for 1.5 hours. The temperature of the reaction mixture was permitted to rise to 30° in 1 hour and then maintained at 30° with stirring for 8 hours. The product was extracted with ether, washed with water, and then stirred for 11 hours at room temperature with a saturated aqueous solution of sodium bisulfite. The *o*-ethoxybenzaldehyde-bisulfite addition complex was filtered, washed with ether, and air-dried. It weighed 3.5 g., corresponding to a 14% recovery of unreacted *o*-ethoxybenzaldehyde.

The ether extract was washed with water, sodium bicarbonate, again with water, and dried. The ether was evaporated on a steam-bath, leaving the 1-(*o*-ethoxyphenyl)-2-nitro-1-propanol as an oil weighing 13.0 g., a 67% yield and 58% conversion. The oil was crystallized to a white solid from a solution of 2 parts of petroleum ether (30–60°) and 1 part of benzene; it melted at 64.5–66.0°.

Anal. Calc'd for $C_{11}H_{15}NO_4$: N, 6.22. Found: N, 6.23.

1,1-Bis(p-ethoxyphenyl)-2-nitroethane. In the usual apparatus, immersed in an ice-bath, sulfuric acid (85%, 50 ml.) and phenetole (11.0 g., 0.09 mole) were mixed and cooled. A suspension of solid 1-(*p*-ethoxyphenyl)-2-nitroethanol (16.9 g., 0.08 mole) in phenetole (50 g., 0.41 mole) was added in small portions with stirring for 4 hours at 6–8°. The stirring was continued for 5 hours as the temperature rose gradually to 22°. The gray-colored product was poured into ice-water, extracted with ether, washed with a sodium bicarbonate solution, and steam-distilled for 8 hours. After the water layer had been decanted, the residue was stirred with a small amount of ethanol until the product crystallized. The crude 1,1-bis(*p*-ethoxyphenyl)-2-nitroethane, m.p. 73–77°, weighed 24.0 g. (95% yield). Three recrystallizations from petroleum ether (60–70°) raised the melting point to 79–80°.

Anal. Calc'd for $C_{18}H_{21}NO_4$: N, 4.44. Found: N, 4.50.

The structure of 1,1-bis(*p*-ethoxyphenyl)-2-nitroethane was proved by oxidizing it to *p,p'*-diethoxybenzophenone. The procedure used was an adaptation of that reported by Eaton, Black, and Fuson (8): 1,1-Bis(*p*-ethoxyphenyl)-2-nitroethane (0.5 g.), pyridine (10 ml.), sodium hydroxide (5 g.), potassium permanganate (2.0 g.), and water (90 ml.) were added to a round-bottomed flask and refluxed for 1 hour. After the mixture had cooled, sodium bisulfite was added to reduce the excess potassium permanganate. The product was acidified with dilute sulfuric acid, filtered, washed with water, and dried. The yield of *p,p'*-diethoxybenzophenone, m.p. 128–130°, was quantitative. Recrystallization from absolute ethanol raised the melting point to 131–132°. Gattermann (9) reports m.p. 131°.

SUMMARY

A series of 1-aryl-2-nitro-1-alkanols has been prepared and condensed with aromatic ethers to give the corresponding 1,1-diaryl-2-nitroalkanes for testing as insecticides. All of them show insecticidal activity.

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