463. *Organic Fluoro-compounds. Part II. The Preparation of Alkyl 2 : 4-Dinitrophenyl Ethers from* 1-*Fluoro*-2 : 4-*dinitrobenzene.*

By W. B. WHALLEY.

The interaction of 1-fluoro-2 : 4-dinitrobenzene with alcohols in the presence of triethylamine readily furnishes the corresponding 2 : 4-dinitrophenyl ethers, which are suitable in many instances for the characterisation of the alcohols.

THE 2 : 4-dinitrophenyl ethers of phenols are readily preparable by the interaction of an alcoholic solution of 1-chloro-2 : 4-dinitrobenzene and a solution of the phenol in aqueous sodium hydroxide (Bost and Nicholson, *J. Amer. Chem. Soc.*, 1935, **57**, 2368). In general 1-chloro-2 : 4-dinitrobenzene does not react readily wth alcohols and those 2 : 4-dinitrophenyl ethers of alcohols reported have usually been formed by the interaction at an elevated temperature, of the appropriate sodium alkoxide and the reagent (*e.g.*, Blanksma and Van der Weyden, *Rec. Trav. chim.*, 1940, **39**, 629), or by indirect methods such as ether exchange (Ogata and Okano, *J. Amer. Chem. Soc.*, 1949, **71**, 3211, 3212).

The easy replacement of a fluorine atom, located in the *ortho*- or *para*-position to a nitro-group, by an alkoxyl group under the influence of methyl or ethyl alcoholic potassium hydroxide (Schiemann, *Ber.*, 1929, **62**, 1794; Brown, Suckling, and Whalley, *J.*, 1949, S95) suggested the use of 1-fluoro-2 : 4-dinitrobenzene for the general production of the 2 : 4-dinitrophenyl ethers of alcohols. The present communication records that alcohols and 1-fluoro-2 : 4-dinitro-

2 : 4-*Dinitrophenyl ethers.*

				Found, %.			Required, %.		
Alcohol.	M. p.	Crystalline form.	Formula.	C.	H.	N.	C.	H.	N.
Methyl alcohol	87° [8]	Glistening plates [1]	$C_7H_6O_5N_2$	42·6	3·2	14·3	42·4	3·0	14·2
*iso*Propyl alcohol	56 [4]	Needles [1]	$C_9H_{10}O_5N_2$	47·8	4·5	12·2	47·8	4·4	12·4
*iso*Butyl alcohol	35 [3]	Plates [1]	$C_{10}H_{12}O_5N_2$	50·1	5·1	11·9	50·0	5·0	11·7
Allyl alcohol	45 [5]	Very pale yellow needles [1]	$C_9H_8O_5N_2$	48·5	3·5	13·2	48·2	3·6	12·5
2-Phenylethyl alcohol	88	Massive long slender prisms [1]	$C_{14}H_{12}O_5N_2$	58·3	4·3	9·8	58·3	4·2	9·7
Cinnamyl alcohol	135	Pale greenish-yellow long slender needles [1]	$C_{15}H_{12}O_5N_2$	60·2	4·2	9·9	60·0	4·0	9·3
Benzyl alcohol	150 [7]	Plates [2]	$C_{13}H_{10}O_5N_2$	57·1	3·5	10·3	56·9	3·7	10·2
m-Nitrobenzyl alcohol	168	Slender prisms [2]	$C_{13}H_9O_7N_3$	48·7	3·0	13·4	48·9	2·8	13·2
p-Nitrobenzyl alcohol	207 [6]	Shimmering flat prisms [2]	$C_{13}H_9O_7N_3$	48·9	2·9	13·1	48·9	2·8	13·2
(−)-3-(4 : 6-Dimethoxy-*o*-tolyl)butan-2-ol	124	Pale lemon-yellow glistening plates [1]	$C_{19}H_{22}O_7N_2$	58·6	5·7	7·2	58·5	5·6	7·2
Benzoin	226	Slender flat prisms [2]	$C_{20}H_{14}O_6N_4$	63·3	3·9	7·6	63·5	3·7	7·4
Ethylene glycol	212	Pale yellow plates [2]	$C_{14}H_{10}O_{10}N_4$	42·7	2·7	14·3	42·6	2·5	14·2
Ethylene glycol monomethyl ether	38	Needles [1]	$C_9H_{10}O_6N_2$	44·8	4·2	11·9	44·6	4·1	11·6
Propylene glycol	157	Clusters of very small needles [2]	$C_{15}H_{12}O_{10}N_4$	44·4	3·2	13·9	44·1	2·9	13·7
Trimethylene glycol	187	Glistening prisms [2]	$C_{15}H_{12}O_{10}N_4$	44·3	3·0	14·0	44·1	2·9	13·7
Cetyl alcohol	60	Feathery needles [1]	$C_{22}H_{36}O_5N_2$	64·7	9·2	6·6	64·7	8·8	6·9
Borneol	128	Needles [1]	$C_{16}H_{20}O_5N_2$	60·2	6·3	9·1	60·0	6·3	8·8
Ergosterol	180	Long slender glistening very pale yellow needles [2]	$C_{34}H_{46}N_2O_5$	72·7	8·3	5·0	72·6	8·2	5·0

[1] Crystallised from methyl alcohol or aqueous methyl alcohol. [2] Crystallised from acetic acid. [3] Ogata and Okano (*loc. cit.*) give m. p. 34—35°. [4] Blanksma and Van der Weyden (*loc. cit.*) record m. p. 46°. Ogata and Okano (*loc. cit.*) give m. p. 51—53°. [5] Fairbourne and Toms (*J.*, 1921, **119**, 1035) record m. p. 46° for a specimen prepared in low yield by the refluxing of a mixture of allyl alcohol and 1-chloro-2 : 4-dinitrobenzene. [6] Staedel (*Annalen*, 1883, **217**, 177) and Holmes and Ingold (*J.*, 1925, **127**, 1810) describe the product as orange-yellow needles, m. p. 198°. Lyman and Reid (*J. Amer. Chem. Soc.*, 1920, **42**, 616) record m. p. 248° for a substance which was apparently not analysed. [7] Kumpf (*Annalen*, 1884, **224**, 128) records m. p. 149° for a substance prepared by the interaction of benzyl iodide and the silver salt of 2 : 4-dinitrophenol. Raiford and Colbert (*J. Amer. Chem. Soc.*, 1926, **48**, 2659) give m. p. 149·5°. [8] Post and Mehrtens (*Ber.*, 1875, **8**, 1552) record m. p. 87°.

benzene react easily in the presence of triethylamine, as a catalyst, with the production, usually in high yield, of the corresponding ethers which in many cases are highly crystalline solids suitable for the characterisation of the alcohols [cf. the use of 1-fluoro-2 : 4-dinitrobenzene for the characterisation of amino-acids (Sanger, *Biochem. J.*, 1945, **39**, 507)].

Pyridine is not a suitable catalyst; interaction with the reagent produces dark resinous products.

Primary alcohols react very readily and exothermically, whilst secondary and tertiary alcohols react less readily and frequently require warming to complete the reaction. Unsaturated alcohols (*e.g.* allyl alcohol, cinnamyl alcohol, cholesterol, and ergosterol; see table) appear to react normally: the two ketonic alcohols examined (benzoin and diacetone alcohol) appeared to suffer considerable decomposition.

As a reagent for the characterisation of alcohols, 1-fluoro-2 : 4-dinitrobenzene would appear to offer considerable advantages over the conventional reagents which require careful storage under anhydrous conditions and in general necessitate the use of the anhydrous alcohol. In contrast, 1-fluoro-2 : 4-dinitrobenzene is quite stable to atmospheric moisture and may apparently be stored indefinitely without the observance of special precautions designed to prevent the ingress of water. Small amounts of water do not appear seriously to impair the yield of derivative, and any 2 : 4-dinitrophenol produced by the hydrolysis of the reagent is readily removable (contrast, for example, the behaviour of the *iso*cyanates, "Organic Reagents for Organic Analysis," 1944, London, p. 11).

EXPERIMENTAL.

1-*Fluoro*-2 : 4-*dinitrobenzene.*—*p*-Fluoronitrobenzene (Balz and Schiemann, *Ber.*, 1927, **60**, 1186) was nitrated by Holleman and Beekmann's method (*Rec. Trav. chim.*, 1904, **23**, 253).

Alkyl 2 : 4-*Dinitrophenyl Ethers.*—The general method of preparation consists of the interaction of equimolecular quantities of the reagents in the presence of a little triethylamine. Reaction may occur at room temperature, rapidly or during several hours, or when the mixture is heated on the steam-bath for several hours. No solvent is necessary for liquid alcohols, but solids require the use of a solvent; benzene or ether is convenient, benzene being preferable where heating is required to complete the reaction. The product frequently crystallises from the dark reaction mixture which is decomposed by the addition of excess of dilute hydrochloric acid; the crude 2 : 4-dinitrophenyl ether is collected by filtration (if a solid) or ether extraction (if an oil) and freed from any 2 : 4-dinitrophenol by washing it with aqueous sodium hydrogen carbonate. The product may be crystallised from alcohol, aqueous alcohol, or frequently more conveniently from glacial acetic acid as many of the ethers are only sparingly soluble in alcohols and prolonged heating to ensure solution is undesirable because of the dangers of trans-etherification. One crystallisation is usually sufficient to remove the small quantities of dark by-products.

The following typical preparations illustrate variations of the general method:

(a) 2 : 4-*Dinitrophenetole.*—Triethylamine (3 drops) was added to a solution of 1-fluoro-2 : 4-dinitrobenzene (0·5 g.) in excess of 95% ethyl alcohol. The solution darkened, heat was evolved, and the product separated on cooling. 30 Minutes later excess of N-hydrochloric acid solution was added and the solid was collected, washed with 2N-sodium hydrogen carbonate solution, and crystallised from aqueous ethyl alcohol whereupon 2 : 4-dinitrophenetole (0·5 g.) separated in almost colourless glistening plates, m. p. 85° (Found: C, 45·4; H, 3·9; N, 13·5. Calc. for $C_8H_8O_5N_2$: C, 45·3; H, 3·8; N, 13·2%). Blanksma and Van der Weyden (*loc. cit.*) give m. p. 85°.

(b) 2 : 4-*Dinitrophenyl* n-*propyl ether.* To a solution of 1-fluoro-2 : 4-dinitrobenzene (0·5 g.) in *n*-propyl alcohol (0·2 g.), triethylamine (3 drops) was added. 12 Hours later the dark mixture was acidified by the addition of excess of N-hydrochloric acid, the precipitated oil extracted with ether (3 × 20 ml.), the extract washed with 2N-aqueous sodium hydrogen carbonate, dried, and evaporated, and the residue crystallised from aqueous methyl alcohol whereupon 2 : 4-dinitrophenyl *n*-propyl ether (0·4 g.) separated in almost colourless needles, m. p. 29° (Found: C, 47·8; H, 4·5; N, 12·7. Calc. for $C_9H_{10}O_5N_2$: C, 47·8; H, 4·4; N, 12·4%). Blanksma and Van der Weyden (*loc. cit.*) record m. p. 32°; Ogata and Okano (*loc. cit.*) record m. p. 28—30°.

(c) *Cholesteryl* 2 : 4-*dinitrophenyl ether.* A solution of cholesterol (0·3 g.), 1-fluoro-2 : 4-dinitrobenzene (0·2 g.), and triethylamine (0·5 ml.) in benzene (5 ml.) was heated on the steam-bath for 4 hours. The product partly crystallised from the cooled solution, which was decomposed with excess of N-hydrochloric acid solution and extracted with ether (3 × 20 ml.), and the extract washed with 2N-aqueous sodium hydrogen carbonate until the washings were colourless, dried, and evaporated. *Cholesteryl* 2 : 4-*dinitrophenyl ether* (0·3 g.) separated from acetic acid in very pale greenish-yellow, long, slender needles, m. p. 172° (Found: C, 71·9; H, 8·9; N, 5·0. $C_{33}H_{48}O_5N_2$ requires C, 71·7; H, 8·7; N, 5·1%).

tert.-Butyl alcohol and *n*-octyl alcohol furnished 2 : 4-dinitrophenyl ethers which crystallised at 0° but were oils at room temperature. *tert.*-Amyl alcohol, *n*-butyl alcohol, ethylene glycol monoethyl ether, and *cyclo*hexanol gave derivatives which could not be crystallised at 0°. Diacetone alcohol gave a low-melting crystalline solid accompanied by much dark oil.

Caution: 1-Fluoro-2 : 4-dinitrobenzene is a skin irritant and should be handled accordingly.

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UNIVERSITY OF LIVERPOOL. [*Received, May* 11*th*, 1950.]