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3,5-DINITROBENZOATES AND THEIR 1-NAPHTHYLAMINE ADDITION COMPOUNDS. I. PREPARATION FROM ALCOHOLS AND ESTERS[1]

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DERIVATIVES FROM ALCOHOLS

The use of 1-naphthylamine addition compounds of alkyl 3,5-dinitrobenzoates as derivatives of alcohols was first proposed by Reichstein (1). Sutter (2) was able to distinguish the seventeen isomeric hexanols by means of the melting points of the dinitrobenzoates and their adducts. Further addition compounds have since been described (3–10). When the 3,5-dinitrobenzoate is an oil or is difficult to crystallize, the amine adduct can often be obtained with ease (9, 10). Dinitrobenzoates can be purified by formation of the addition compound and subsequent decomposition with dilute acid.

Table I lists new 3,5-dinitrobenzoates and addition compounds.

DERIVATIVES FROM ESTERS

Renfrow and Chaney (11) developed a method for the direct identification of the alcohol component of esters without prior saponification. The ester is heated with 3,5-dinitrobenzoic acid in the presence of sulfuric acid and the resulting 3,5-dinitrobenzoate is isolated. The method yielded satisfactory derivatives for simple esters but failed for esters of tertiary alcohols, benzyl esters, esters of molecular weight above 250, unsaturated esters, phenolic esters, and some others. By modifying the method we have been able to characterize esters in the first four groups. Phenolic esters did not yield derivatives under the modified conditions.

Tertiary esters failed to give the desired product in the original procedure undoubtedly because under acid conditions at refluxing temperatures an olefin is liberated which escapes. Altschul (12) has studied the equilibrium between tertiary butyl esters, the corresponding acid, and isobutylene, in the presence of sulfuric acid, using dioxane as solvent, at 25 and 35°. Since equilibrium conditions were attained readily, a reaction between these esters and 3,5-dinitrobenzoic acid in dioxane near room temperature was carried out. Good yields of *tert*-butyl-3,5-dinitrobenzoate resulted after ½–3 days standing. Under these conditions ethyl esters gave no yield, suggesting a predominant carbonium ion mechanism for the tertiary esters.

Benzyl esters, like benzyl alcohol, polymerize to a gummy mass when in contact with concentrated sulfuric acid. By adding a small amount of dioxane to the reaction mixture prior to addition of the sulfuric acid, benzyl acetate and

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TABLE I

3,5-DINITROBENZOATES AND THEIR 1-NAPHTHYLAMINE ADDUCTS FROM ALCOHOLS AND PHENOL

ROH	3,5-dinitrobenzoate, M.P., °C[b]	Amine Adduct, M.P., °C[b]	Formula[a]	Analyses					
				Calc'd			Found		
				C	H	N	C	H	N
2-Butanol		109–110	$C_{21}H_{21}N_3O_6$	61.3	5.15		61.3	5.09	
2-Pentanol		88	$C_{22}H_{23}N_3O_6$	62.1	5.45		62.5	5.39	
3-Pentanol		99	$C_{22}H_{23}N_3O_6$	62.1	5.45		62.1	5.58	
3-Methyl-2-butanol		97–98	$C_{22}H_{23}N_3O_6$	62.1	5.45		62.0	5.39	
1-Hexanol		63–64[c]	$C_{23}H_{25}N_3O_6$	62.9	5.73		63.3	5.70	
2-Heptanol		73	$C_{24}H_{27}N_3O_6$	63.6	6.00		63.7	5.97	
4-Heptanol		66–67	$C_{24}H_{27}N_3O_6$	63.6	6.00		63.3	6.14	
1-Nonanol		49–51[d]	$C_{26}H_{31}N_3O_6$	64.9	6.49		65.0	6.42	
1-Octadecanol	77		$C_{25}H_{40}N_2O_6$	64.6	8.68	6.0	64.7	8.71	5.9
1-Octadecanol		68	$C_{35}H_{49}N_3O_6$	69.2	8.13		68.5	8.14	
dl-Phenylmethylcarbinol		106–107.5	$C_{25}H_{21}N_3O_6$	65.4	4.61	9.1	64.6	4.69	9.1
Dimethylbenzylcarbinol	101–103		$C_{17}H_{16}N_2O_6$	59.3	4.68		59.2	4.69	
Dimethylbenzylcarbinol		152–153	$C_{27}H_{25}N_3O_6$	66.5	5.17		66.4	5.35	
Cinnamyl alcohol		104	$C_{26}H_{21}N_3O_6$	66.2	4.49		65.8	4.56	
Diphenylcarbinol		102	$C_{30}H_{23}N_3O_6$	69.1	4.45	8.1	68.9	4.62	8.1
2-Chloroethanol	95		$C_9H_7ClN_2O_6$	39.4	2.57		39.5	2.54	
2-Chloroethanol		123–124	$C_{19}H_{16}ClN_3O_6$	54.6	3.86		55.1	3.75	
2-Bromoethanol	85–86		$C_9H_7BrN_2O_6$	33.9	2.21		34.1	2.07	
2-Bromoethanol		126–127	$C_{19}H_{16}BrN_3O_6$	49.4	3.49		49.5	3.42	
2,3-Dibromopropanol	85–86		$C_{10}H_8Br_2N_2O_6$			38.8[f]			39.4[f]
2,3-Dibromopropanol		126,130[e]	$C_{20}H_{17}Br_2N_3O_6$	43.3	3.09	7.6	43.8	3.00	7.6
Phenol		148	$C_{23}H_{17}N_3O_6$	64.0	3.97		64.1	3.93	

[a] Formulas for addition compounds are those for a 1:1 molecular ratio of dinitrobenzoate to naphthylamine. [b] All melting points taken on an Arthur H. Thomas Co. Kofler micro hot stage. [c] Melting point for hexanol addition compound given as 104° by Reichstein (1). Comparison with other melting points of straight chain alcohol derivatives (methyl 122°, ethyl 121°, propyl 104°, butyl 93°, amyl 85°, heptyl 58°, octyl 49°, nonyl 51°, decyl 50°) suggested this was an error. [d] Tended to form gel with ethanol and with petroleum ether. Latter yielded soft crystals on standing. Excess solvent removed with a vacuum pump. [e] Two crystalline modifications. Lower-melting modification orange-red, higher-melting dark red. [f] Analysis for bromine.

benzyl succinate were successfully characterized as the naphthylamine adduct of benzyl-3,5-dinitrobenzoate.

High molecular weight esters were reacted in the presence of dioxane and where the 3,5-dinitrobenzoate was difficult to crystallize, the addition compound was made.

Unsaturated esters probably react at the double bond, thus preventing forma-

tion of the simple dinitrobenzoate. On brominating the unsaturated ester, derivatives of ethanol were obtained in the case of ethyl cinnamate and of 2,3-dibrompropanol in the case of allyl acetate.

The results suggest that the Renfrow-Chaney method for identifying esters can be made more widely applicable by the use of dioxane as solvent and increasing the concentration of acid catalyst. Suggested quantities are: 2 ml. of ester, 2 g. of 3,5-dinitrobenzoic acid, 1–2 ml. of dioxane (5–10 ml. if the smaller quantity leads to polymerization or charring) and 0.5 ml. of concentrated sulfuric acid. Refluxing for one-half to one hour is sufficient in most instances. If a very small yield is obtained, a second run should be carried out for a longer period. Where prior tests indicate unsaturation, the ester is first brominated. Where olefin is liberated on heating the reaction mixture, a second mixture containing 3 ml. of dioxane and 0.1 ml. of sulfuric acid is allowed to stand for 24 hours. In all cases the 1-naphthylamine addition compound is prepared for further characterization or where the dinitrobenzoate is difficult to obtain in a pure state.

Table II shows the effect of water concentration on the yield of ethyl 3,5-dinitrobenzoate obtained from ethyl acetate. It appears that a small amount of water catalyzes the acid-ester exchange reaction indicating that concentrated sulfuric acid is a more suitable catalyst than is 100% sulfuric acid.

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The use of 1-naphthylamine has recently been questioned because industrial workers exposed to it have shown a tendency to develop bladder tumors (13). However, studies on dogs have detected no tumors on exposure to the pure amine, whereas its isomer, 2-naphthylamine is strongly carcinogenic to dogs and humans (14). A recent study (15) suggests that commercial 1-naphthylamine is appreciably contaminated with its 2-isomer.

TABLE II

EFFECT OF WATER ON YIELD OF ETHYL 3,5-DINITROBENZOATE FROM 2.50 g. OF 3,5-DINITROBENZOIC ACID, 2.30 ml. OF ETHYL ACETATE, 1.00 ml. OF DIOXANE, AND 0.50 ml. OF 100% SULFURIC ACID

Water, ml.	Refluxing Time, mins.			
	30	60	120	330
	Yield of Ester, in grams			
0	0.15	0.35	0.73	—
0.01	.24	—	—	—
.04	.59	1.27	1.36	—
.10	.89	1.31	1.37	1.43
		1.31		1.46
.50	1.11	1.30	—	—
	1.18			
1.00	.58	—	0.88	0.97

EXPERIMENTAL

3,5-Dinitrobenzoates from alcohols and phenol. These were prepared by standard methods (6, 16).

1-Naphthylamine addition compounds. These were prepared by mixing saturated ether solutions of the two components, or an alcoholic solution of the amine with an ether solution of the ester, or by warming the two solid components with a few drops of alcohol. Addition compounds from lower alcohols were recrystallized from ethanol. Higher alcohol and phenyl substituted derivatives tend to decompose in this solvent. They were recrystallized from petroleum ether (b.p. 100–110°), sometimes after a first recrystallization from a 5% solution of 1-naphthylamine in ethanol. The addition compounds are orange-red to dark red, and all except the nonanol derivative crystallized as needles.

Derivatives from esters of tertiary alcohols. To a mixture of 3,5-dinitrobenzoic acid (2 g.), dioxane (3 ml.), and concentrated sulfuric acid (0.1 ml.), was added 2 ml. of *tert*-butyl acetate [prepared by the method of Norris and Rigby (17), b.p. 97.8–97.9°]. After standing for 10 hours *tert*-butyl 3,5-dinitrobenzoate was extracted as described by Renfrow and Chaney (11). Yield, 0.20 g., m.p. 142.5–143.5°; reported (6) m.p. 142°. A second run, standing for 20 hours, gave 0.38 g.

A mixture of 1.80 ml. of *tert*-butyl benzoate [prepared by the method of Bender (18)], 1.20 g. of dinitroacid, 10 ml. of dioxane, and 0.1 ml. of sulfuric acid was warmed at 50° for 78 hours. Yield 0.10 g., m.p. 140–142°.

Benzyl esters. Benzyl acetate (2 ml.), dinitroacid (2 g.), dioxane (10 ml.), and sulfuric acid (0.1 ml.) were refluxed for three hours and the solution was extracted. 1-Naphthylamine (1 g.) was added to the viscous reaction product and the 1-naphthylamine addition compound of benzyl 3,5-dinitrobenzoate was recrystallized from an alcohol-water mixture, m.p. 114–115°; reported (6) m.p. 118°; prepared from benzyl alcohol 115°.

Benzyl succinate (2 g.) was refluxed for one hour with 2 g. of the dinitroacid, 0.5 ml. of sulfuric acid, and 3 ml. of dioxane. Yield of benzyl 3,5-dinitrobenzoate 0.10 g., m.p. 112–113°; reported (6) 113°.

Esters of molecular weight above 250. n-Octadecyl acetate (2 ml.), 2 g. of dinitroacid, 1 ml. of dioxane, and 0.5 ml. of sulfuric acid were refluxed for 90 minutes. The yield of *n*-octadecyl 3,5-dinitrobenzoate was 1.1 g., m.p. 77°; the 1-naphthylamine addition compound had m.p. 68°. Ethyl stearate refluxed for one hour under the same conditions yielded 0.01 g. of ethyl 3,5-dinitrobenzoate-1-naphthylamine, m.p. 121°; reported (6) m.p. 121°. For benzyl succinate see the previous section.

Unsaturated esters. Allyl acetate was brominated dropwise until the bromine color no longer was discharged. The resulting dibromopropyl acetate was treated by the same procedure as for *n*-octadecyl acetate. Naphthylamine was added to the viscous reaction product and the addition compound of 2,3-dibromopropyl 3,5-dinitrobenzoate was obtained, m.p. 126° (orange-red crystals); 130° (dark red crystals). The addition compound was decomposed by shaking its ether solution with dilute hydrochloric acid, then with water, followed by drying over calcium chloride. The ether was evaporated off and the derivative was crystallized from alcohol: 2,3-dibromopropyl 3,5-dinitrobenzoate, m.p. 85–86°; prepared from commercial 2,3-dibromopropanol and from brominated allyl alcohol, m.p. 85–86°.

Ethyl cinnamate was brominated and refluxed for one hour under the same conditions. Yield, 0.01 g. of ethyl 3,5-dinotrobenzoate, m.p. 93–94°; reported (6) m.p. 94°.

Effect of water on yield from ethyl acetate. The 100% sulfuric acid, added to the anhydrous reagents, was prepared by the method of Brand (19). Ethyl 3,5-dinitrobenzoate was extracted from the reaction mixture as before (11).

SUMMARY

3,5-Dinitrobenzoates and their 1-naphthylamine addition compounds of a number of alcohols and of phenol have been prepared.

Methods were developed for obtaining these derivatives without prior saponification from esters of tertiary alcohols, benzyl esters, esters of high molecular weight, and unsaturated esters. A modified general method for identifying the alcohol component of esters has been suggested.

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