1320. *The Preparation of Tetrahydrofurfuryl Esters of Certain Mono- and Di-basic Carboxylic Acids*

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A number of tetrahydrofurfuryl esters of mono- and di-carboxylic acids bearing a variety of functional groups have been prepared. In most instances the yield of ester is high and only in the case of di(tetrahydrofurfuryl) oxalate was a poor conversion obtained, owing to the competing decarboxylation process.

Twenty-seven esters derived from tetrahydrofurfuryl alcohol have been prepared and characterised, and their physical data recorded. Many of them were obtainable by direct esterification, but others could only be prepared by indirect methods. The esters listed in the Table were prepared by refluxing toluene solutions of the appropriate acids with tetrahydrofurfuryl alcohol in the presence of a catalytic amount of toluene-*p*-sulphonic acid. The water produced during the reaction was removed continuously by azeotropic distillation. In the case of cyanoacetic and oxalic acid, benzene was used as the solvent in order to minimise decarboxylation, and, although a good conversion into the cyanoacetate resulted, the oxalate was obtained in only 30% yield.

In addition to the tabulated compounds, the half-esters of certain dibasic acids were also prepared, generally by the partial hydrolysis of the corresponding diester. In this manner tetrahydrofurfuryl hydrogen sebacate and tetrahydrofurfuryl hydrogen terephthalate were obtained in good yield. With the latter compound, it was interesting that when the partial hydrolysis was carried out in ethanol the product was ethyl hydrogen terephthalate, showing that ester interchange was also a facile reaction.

Attempts to prepare the ester of *p*-aminobenzoic acid by direct esterification failed.

No.	Acid	Reaction period (hr.)	B. p./mm.	n_D^{23}	Yield (%)
		Monoesters			
1	Monochloroacetic	36	106/2	1·4630	80
2	Trichloroacetic	23	80/0·05	1·4820	85
3	Cyanoacetic *	72	119/0·3	1·4614	80
4	*p*-Nitrobenzoic	48	163/0·2; m. p. 48°	—	80
5	Benzoic	72	89/0·1	1·5240	65
6	Dichloracetic	17	68/0·2	1·4733	76
7	*p*-Nitrophenylacetic †	24	186/0·2	1·5416	77
8	Salicyclic	265	106/0·05	1·5372	84
9	Furoic	48	96/0·25	1·5040	90
10	γ-Phenylbutyric ‡	24	146/0·2	1·5090	78
11	β-Chloropropionic	30	88/0·2	1·4640	74
12	*p*-Toluic	72	110/0·1	1·5232	72
13	β-Phenylpropionic	120	161/0·2	1·5260	70
14	*p*-Chlorobenzoic	120	183/0·4	1·5361	82
15	*o*-Chlorobenzoic	168	134/0·6	1·5353	90

	Found (%)					Calc. (%)			
No.	C	H	Cl	N	Formula	C	H	Cl	N
1	47·0	6·0	20·2	—	$C_7H_{11}ClO_3$	47·1	6·2	19·9	—
2	33·6	3·6	42·6	—	$C_7H_9Cl_3O_3$	33·9	3·6	43·0	—
3	56·6	6·7	—	8·2	$C_8H_{11}NO_3$	56·8	6·5	—	8·3
4	57·0	5·1	—	5·3	$C_{12}H_{13}NO_5$	57·4	5·2	—	5·5
5	69·5	6·8	—	—	$C_{12}H_{14}O_3$	69·8	6·8	—	—
						Required (%)			
6	39·9	5·0	33·2	—	$C_7H_{10}Cl_2O_3$	39·4	4·7	33·3	—
7	58·4	5·5	—	5·3	$C_{13}H_{15}NO_5$	58·8	5·7	—	5·3
8	64·9	6·2	—	—	$C_{12}H_{14}O_4$	64·9	6·3	—	—
9	60·8	6·1	—	—	$C_{10}H_{12}O_4$	61·2	6·1	—	—
10	73·0	8·1	—	—	$C_{15}H_{20}O_3$	72·6	8·1	—	—
11	49·8	6·7	18·5	—	$C_8H_{13}ClO_3$	49·9	6·8	18·4	—
12	71·3	7·4	—	—	$C_{13}H_{16}O_3$	70·9	7·3	—	—
13	68·4	6·8	—	—	$C_{15}H_{18}O_4$	68·7	6·9	—	—
14	59·6	5·4	14·6	—	$C_{12}H_{13}ClO_3$	59·9	5·4	14·8	—
15	59·6	5·4	14·6	—	$C_{12}H_{13}ClO_3$	59·9	5·4	14·8	—

No.	Acid	Reaction period (hr.)	B. p./mm.	n_D^{23}	Yield (%)
		Diesters			
16	Maleic	45	152/0·5	1·4850	71
17	Sebacic	18	210/0·2	1·4692	88
18	Oxalic *	72	188/0·2	1·4726	30

	Found (%)					Required (%)			
No.	C	H	Cl	N	Formula	C	H	Cl	N
16	58·6	7·1	—	—	$C_{14}H_{20}O_6$	59·1	7·0	—	—
17	64·9	9·2	—	—	$C_{20}H_{34}O_6$	64·9	9·2	—	—
18	56·0	7·0	—	—	$C_{12}H_{18}O_6$	55·8	7·0	—	—

* Benzene solvent. † *Org. Synth.*, Coll. Vol. I, pp. 396, 406. ‡ *Org. Synth.*, Coll. Vol. II, p. 499.

The compound was readily obtainable, however, by the catalytic hydrogenation of tetrahydrofurfuryl *p*-nitrobenzoate. By a similar hydrogenation the ester of furoic acid was converted into tetrahydrofurfuryl tetrahydrofuroate in 87% yield.

Di(tetrahydrofurfuryl) terephthalate was converted into a mixture of the mono- and di-hydrazides by reaction with anhydrous hydrazine. Further reaction of the mono-hydrazide with nitrous acid afforded the corresponding azide, which decomposed readily to form tetrahydrofurfuryl *p*-isocyanatobenzoate, characterised as the ethylurethane.

EXPERIMENTAL

Direct Esterification Reactions.—These compounds were prepared by refluxing a mixture of the carboxylic acid and tetrahydrofurfuryl alcohol (100% mol. excess) in toluene in the presence of toluene-*p*-sulphonic acid (1—2%). The water produced in the reaction was azeotropically distilled and removed continuously with a Dean and Stark trap until the calculated amount had been formed. The product was then isolated by fractional distillation.

Tetrahydrofurfuryl p-*Aminobenzoate*.—Tetrahydrofurfuryl *p*-nitrobenzoate (10 g.) in ethanol (50 ml.) was hydrogenated at atmospheric pressure using a 5% palladised charcoal catalyst (0·2 g.). When the calculated quantity of hydrogen had been absorbed, the catalyst was filtered off, the filtrate evaporated, and the residue recrystallised from benzene, to yield the *product* (7·8 g., 100%), m. p. 98—99°, in colourless needles (Found: C, 65·3; H, 6·7; N, 6·0. $C_{12}H_{15}NO_5$ requires C, 65·1; H, 6·8; N, 6·3%).

Tetrahydrofurfuryl Tetrahydrofuroate.—Tetrahydrofurfuryl furoate (33·0 g.) in light petroleum (b. p. 60—80°) (200 ml.) was hydrogenated for 6 hr. at 90—100°/80 atm. in the presence of Raney nickel (2 g.). The autoclave was then cooled to room temperature and the hydrogenation continued for 48 hr. At the end of this time the products showed no evidence of unsaturation (infrared spectrum). After filtration and removal of the solvent, distillation afforded the *product* (36·0 g., 87%), b. p. 80°/0·1 mm., n_D^{23} 1·4670 (Found: C, 60·1; H, 8·2. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0%).

Di(tetrahydrofurfuryyl) Sebacate.—Dimethyl sebacate was heated to reflux with an excess of tetrahydrofurfuryl alcohol containing toluene-*p*-sulphonic acid (2%). Methanol was taken off slowly through a short fractionating column, and after the theoretical amount had been removed the pot residue was fractionally distilled under reduced pressure. A quantitative yield of the diester was obtained, identical with the product formed by the direct esterification of sebacic acid.

Tetrahydrofurfuryl Hydrogen Sebacate.—Sebacic acid (50 g.), di(tetrahydrofurfuryl) sebacate (50 g.), dibutyl ether (10 ml.), and concentrated hydrochloric acid (8 ml.) were heated together on a steam-bath. Then, after the addition of tetrahydrofurfuryl alcohol (26 g.), the mixture was heated for a further 3 hr. Distillation under reduced pressure afforded unchanged diester and a fraction boiling at 220°/0·15 mm. which solidified in the condenser. This fraction was dissolved in hot benzene, and, upon cooling, the unchanged sebacic acid which crystallised was filtered off and the filtrate evaporated to afford crystals of the *product* (20 g.), m. p. 45—46° (Found: C, 63·0; H, 9·3. $C_{15}H_{26}O_5$ requires C, 62·9; H, 9·1%).

Tetrahydrofurfuryl (β-*Cyano*-β-*ethoxycarbonyl*) *Propionate*.—The sodium salt of ethyl cyanoacetate was prepared by the slow addition of the ester (76·6 g.) to a solution of sodium (16 g.) in absolute ethanol (250 ml.). Dry distilled dimethylformamide was then added in sufficient quantity to dissolve the salt, and the ethanol subsequently removed *in vacuo*.

To the above solution at 0° was slowly added tetrahydrofurfuryl monochloroacetate (123·6 g.), with rapid stirring. After standing for 15 hr. the mixture was concentrated under reduced pressure, and the residue washed thoroughly with water and extracted with ether. Distillation of the dried ($MgSO_4$) extracts through a short fractionating column afforded the *product* (20 g.), b. p. 150°/0·1 mm., n_D^{23} 1·4602 (Found: C, 56·4; H, 6·6; N, 5·5. $C_{12}H_{17}NO_5$ requires C, 56·5; H, 6·6; N, 5·5%).

Di(tetrahydrofurfuryl) Terephthalate.—Dimethyl terephthalate (250 g.) and tetrahydrofurfuryl alcohol (300 ml.) containing a trace of sodium hydride (*ca.* 1 g.) were heated until methanol began to distil at a steady rate. After the calculated amount of methanol had been removed the mixture was cooled and dissolved in ether. After removal of excess tetrahydrofuryl alcohol by repeating washing with water, the ether solution was dried ($MgSO_4$). Removal of the solvent left a low-melting solid which was recrystallised from light petroleum (b. p. 60—80°), to afford the *product* (88%), m. p. 53—54° (Found: C, 64·8; H, 6·6. $C_{18}H_{22}O_6$ requires C, 64·7; H, 6·6%).

Half-hydrolysis of Di(tetrahydrofurfuryl) Terephthalate.—(*a*) A solution of potassium hydroxide (2·0 g.) in a mixture of water (3 ml.) and ethanol (15 ml.) was added slowly with stirring to the above ester (10 g.) in ethanol at 10—15°. After 45 min. the mixture was evaporated to dryness and the residue dissolved in water. Unchanged diester was removed by ether extraction, and the aqueous layer was acidified with hydrochloric acid. The resulting precipitate was recrystallised from aqueous ethanol, to afford *ethyl hydrogen terephthalate* (4·5 g.), m. p. and mixed m. p. 170—172° (Found: C, 62·4; H, 5·2. Calc. for $C_{10}H_{10}O_4$: C, 62·2; H, 5·2%).

((*b*) Di(tetrahydrofurfuryl) terephthalate (20 g.) was dissolved in tetrahydrofurfuryl alcohol (30 ml.) and cooled with stirring to 10°, during the slow addition of a solution of potassium hydroxide (4·0 g.) in water (6 ml.) and tetrahydrofurfuryl alcohol (20 ml.).

After being stirred for 1 hr. at room temperature and 1 hr. at 80° the cloudy reaction mixture was poured into cold water (300 ml.). After removal of unchanged diester by ether extraction, acidification (HCl) of the aqueous layer afforded a colourless precipitate. This was dried *in vacuo*, extracted with boiling ether (200 ml.) for 1 hr., and the insoluble terephthalic acid removed by filtration. Evaporation of the ether extracts then afford *tetrahydrofurfuryl hydrogen terephthalate* (9·5 g.) which crystallised from ethanol in small needles, m. p. 122—124° (Found: C, 62·7; H, 7·5. $C_{14}H_{14}O_5$ requires C, 62·4; H, 5·6%).

Tetrahydrofurfuryl Terephthalate Monohydrazide.—Di(tetrahydrofurfuryl) terephthalate (33·5 g.) dissolved in absolute ethanol (40 ml.) was refluxed overnight with anhydrous hydrazine (3·5 ml.). The precipitated dihydrazide (4·1 g.), m. p. >300°, was filtered off and the filtrate evaporated to dryness. After shaking the residual gum with ether for 20 min., the resulting solid was removed and recrystallised from propan-2-ol, to afford the *product* (18·0 g.), m. p. 109—110° (Found: C, 59·0; H, 6·1. $C_{13}H_{16}N_2O_4$ requires C, 59·1; H, 6·1%). It was very soluble in alcohol, water, and dilute acids, but insoluble in ether and benzene.

Tetrahydrofurfuryl p-*Isocyanatobenzoate.*—To a stirred solution of tetrahydrofurfuryl phthalate monohydrazide (5·0 g.) in hydrochloric acid (20 ml.; 2N) at 0—5° was added sodium nitrite (1·4 g.) in water (3·0 ml.). After stirring for 15 min. the heavy oily azide was extracted with ether and dried ($MgSO_4$). After removal of the ether under reduced pressure, toluene (20 ml.) was added and the mixture heated on a steam-bath until no more nitrogen was evolved (*ca.* 2 hr.). Fractional distillation then afforded the *isocyanate* (3·5 g.), b. p. 138°/0·2 mm., n_D^{23} 1·5492 (Found: C, 63·4; H, 5·3; N, 5·6. $C_{13}H_{13}NO_4$ requires C, 63·2; H, 5·3; N, 5·7%); *ethyl urethane*, needles from ethanol, m. p. 104—105° (Found: C, 61·6; H, 6·6; N, 4·6. $C_{15}H_{19}NO_5$ requires C, 61·4; H, 6·5; N, 4·8%).

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