

*Reaction of 1 : 2 : 3 : 6-Tetrahydrobenzaldehyde with Alkali.**

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The reaction of 1 : 2 : 3 : 6-tetrahydrobenzaldehyde with alkali has been studied. With increasing temperature these reactants provide (a) a trimer, (b) a glycol and the tetrahydrobenzoic acid, (c) the tetrahydrobenzyl alcohol and Δ^3 -tetrahydrobenzoic acid, and (d) pimelic acid and a mixture of hydrocarbons. Good yields of the alcohol and acid are obtained by the Tischtschenko reaction.

WERBER, JANSEN, AND GRESHAM (*J. Amer. Chem. Soc.*, 1952, **74**, 532) found that, although 1 : 2 : 3 : 6-tetrahydrobenzoic acid and alkali gave pimelic acid in high yield (78%), the corresponding aldehyde, with alkali at 350°, gave a low yield of pimelic acid (42%) together with much hydrocarbon (mainly toluene). Our results with the aldehyde agree with those of the American workers provided that high temperatures and concentrated alkali are employed : 48—50% yields of pimelic acid were obtained by use of a 50% excess of 40% aqueous sodium hydroxide at 300—350°. Reduction in the quantity or the concentration of alkali lowered the yield, but variation in time of heating (3—6 hr.) produced little effect. Potassium hydroxide could successfully replace sodium hydroxide, but not calcium hydroxide, sodium carbonate, or trisodium phosphate with which the only products isolated were 1 : 2 : 3 : 6-tetrahydro-benzyl alcohol and -benzoic acid and high-boiling gums. The aldehyde may be replaced by its solid trimer (produced by the action of acid; Chayanov, *J. Gen. Chem. U.S.S.R.*, 1938, **8**, 460) : the acid products from this reaction

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The highest yields of tetrahydro-benzyl alcohol and -benzoic acid were obtained by hydrolysis of the ester obtained from the aldehyde by the Tischtschenko reaction; the anhydrous aldehyde gave 90—95% of tetrahydrobenzyl tetrahydrobenzoate without use of a solvent. Traces of acid (even $\frac{1}{2}$ % formed by autoxidation) in the aldehyde were found to inhibit this condensation, as also did higher temperatures.

The reaction of concentrated alkali at 300—350° with compounds related to the aldehyde was briefly studied (cf. Table 1). The neutral products from the tetrahydro-

TABLE 1.

Starting material	Pimelic acid (%)	Starting material	Pimelic acid (%)
Aldehyde diethyl acetal	3—4	Trimer (II)	48
Aldehyde-ammonia complex	10—15	1 : 2 : 3 : 6-Tetrahydrobenzyl alcohol ...	7
Aldoxime	ca. 90	1 : 2 : 3 : 6-Tetrahydrobenzoic acid	85—90
Glycol (III)	ca. 25		

benzyl alcohol were hydrocarbons, as in the reaction of the aldehyde and alkali at 300—350°, and it is evident that these were derived from the alcoholic portion in the above reaction sequence; dehydration followed by hydrogenation-dehydrogenation and polymerisation must be involved in this degradation.

EXPERIMENTAL

The 1 : 2 : 3 : 6-tetrahydrobenzaldehyde, produced by reaction of butadiene and acraldehyde, was refractionated before use and had b. p. 53°/11 mm., n_D^{20} 1.4724.

Reactions of 1 : 2 : 3 : 6-Tetrahydrobenzaldehyde and Alkali.—(a) *One-stage reaction at 250—350°.* The results of selected experiments are given in Table 2. The reactions were carried out in a rocking autoclave (450 c.c.; stainless steel), and the pimelic acid was removed from the acidified product by continuous extraction with ether. The combined neutral extracts from several experiments were distilled. Fractions boiling from 96°/1 atm. to 200°/0.6 mm. were collected, few having sharp b. p.s: ca. 25% boiled in the range 96°/1 atm. to 76°/26 mm. and contained (by infra-red analysis) toluene (60—70%), 1-methylcyclohexene (15—20%), and conjugated dienes. The higher-boiling fractions were also mainly hydrocarbons (partly aromatic), and there was much undistillable residue.

The combined acid products were converted into ethyl esters, fractionation of which esters gave the following fractions: (1) b. p. 74°/9.5 mm., (2) b. p. 88—90°/10 mm., (3) b. p. 135—137°/10 mm., (4) b. p. 86°/0.5 mm., (5) b. p. 125°/0.5 mm., and (6) b. p. 135—138°/0.5 mm.

TABLE 2.

Reactants		Temp.	Time (hr.)	Yield of pimelic acid	
Aldehyde (g.)	NaOH (c.c.)			Wt. (g.)	%
45	123 (40%)	300°	6	31.5	48.2
59	108 (40%)	300	6	34.5	40.3
53.5	114 (47.8% KOH)	300	6	28.8	37.0
60	164 (15%)	250	24	3.4	3.9
45	123 (40%)	300	3	28.6	43.7
45	164 (30%)	300	6	21.6	33.0
50	75 g. NaCO ₃ } 115 c.c. water }	300	6	0	—
110	120 g. solid NaOH	300	6	8.5	5.3
80	80.8 g. Ca(OH) ₂ } 100 c.c. water }	295	6	0	—
34.5	155 g. Na ₃ PO ₄ } 48.6 c.c. water }	295	6	0	—
45 *	123 (40%)	300	6	30.5	46.6

* Solid trimer.

Fraction 1 consisted mainly of ethyl hexahydrobenzoate, hydrolysis yielding slightly impure hexahydrobenzoic acid, m. p. ca. 30° [*p*-bromophenacyl ester, m. p. 90—91.5° (Found: C, 55.4; H, 5.45; Br, 24.2. C₁₅H₁₇O₃Br requires C, 55.4; H, 5.2; Br, 24.6%); amide, m. p. 184—185° (Found: C, 66.3; H, 10.1; N, 11.1. Calc. for C₇H₁₃ON: C, 66.1; H, 10.2; N, 11.0%); anilide, m. p. 145—146° (Found: C, 76.8; H, 8.2; N, 7.0. Calc. for C₁₃H₁₇ON: C, 76.8; H, 8.4; N, 6.9%)]].

Fraction 2 consisted mainly of ethyl 2 : 3 : 4 : 5-tetrahydrobenzoate, hydrolysis yielding a

product, b. p. 134°/14 mm. (Found: equiv., 127. Calc. for $C_7H_{10}O_3$: equiv., 126). A small quantity of benzoic acid was removed from a cooled light petroleum solution, and the filtrate, after evaporation, provided the following derivatives of 2 : 3 : 4 : 5-tetrahydrobenzoic acid: *p*-bromophenacyl ester, m. p. 102—103° (Found: C, 55.8; H, 4.8; Br, 24.9. $C_{15}H_{15}O_3Br$ requires C, 55.7; H, 4.6; Br, 24.8%); amide, m. p. 121—123° (Found: C, 67.6; H, 8.3; N, 10.7. Calc. for $C_7H_{11}ON$: C, 67.2; H, 8.8; N, 11.2%); anilide, m. p. 105—107° (Found: C, 76.3; H, 7.25; N, 7.9. Calc. for $C_{13}H_{15}ON$: C, 77.6; H, 7.5; N, 7.0%). Treatment with bromine in chloroform, followed by evaporation, gave 1 : 2-dibromocyclohexane-1-carboxylic acid, m. p. 144—146° (Found: C, 29.6; H, 3.6; Br, 55.9%; equiv., 280. Calc. for $C_7H_{10}O_2Br_2$: C, 29.4; H, 3.5; Br, 55.9%; equiv., 286). The reported m. p.s are 124° and 129—130.5° (amide), 110—111° (anilide), and 147° (dibromo-compound).

Fractions 3 and 4 were practically identical and the physical constants (n_D^{20} 1.4332—1.4360; d_4^{20} 0.991, 0.996) agree with those of diethyl pimelate (b. p. 92—93°/0.7 mm., n_D^{20} 1.4306, d_4^{20} 0.994).

Fractions 5 and 6 appeared to be esters of high molecular weight.

Although ethyl 1 : 2 : 3 : 6-tetrahydrobenzoate was not isolated the acid was subsequently found in the products of many experiments.

(b) *Reaction at <65°*. (i) The aldehyde (180 g.) was added gradually, with cooling and stirring, to 40% sodium hydroxide solution (492 c.c.); the highest temperature reached was 60°. The product was diluted and ether-extracted; the extract on distillation provided some unchanged aldehyde (29.4 g., containing a little 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol), a main fraction (125.4 g.; n_D^{20} 1.5311, b. p. 208—214°/0.7 mm.), and residue (14.5 g.). The properties of the main distillate, the trimer (II), are given in Table 3. The compound gave no evidence of the presence of a carbonyl group with hydroxylamine hydrochloride or 2 : 4-dinitrophenylhydrazine hydrochloride. The aqueous alkali solution from the aldehyde-alkali reaction was acidified and continuously extracted with ether; it yielded an oily acid (1 g.; equiv., 148).

(ii) The aldehyde (50 g.) and 4% aqueous sodium hydroxide (250 c.c.), stirred for 5 hr. at room temperature, gave aldehyde (40.5 g.), high-boiling material (1.0 g.), and acid (1.1 g.).

(iii) (cf. Celanese Corp., *loc. cit.*). The aldehyde (300 g.), when stirred with a saturated solution of sodium hydroxide in 95% ethanol at <65°, provided low-boiling products (16.5 g.), trimer, b. p. 195—210°/1.5 mm. (248 g.), and residue (13 g.).

TABLE 3.

	Found	Calc. for:	
		aldol	trimer
<i>M</i> (cryoscopic)	326, 346	220	330
Unsaturation equiv. (hydrogenation)	107.3	110	110
OH (%) (Smith & Bryant)	4.6, 4.67	7.73	5.15
Active H (Zerewitinov)	0.34	0.45	0.303

(iv) The aldehyde (200 g.), ether (200 g.), and di-*n*-butylamine (few drops) were cooled, with stirring, to -20°, and aqueous 10% potassium hydroxide was added dropwise at -15° to -20°. A white solid (100 g.) was formed and removed by filtration: it had m. p. ca. 80° [Found: H_2O , 12 (Smith and Bryant), 14% (Dean and Stark); CO equiv., 131. $C_7H_{10}O_3H_2O$ requires H_2O , 14.1%; CO equiv., 128], and provided the 2 : 4-dinitrophenylhydrazone of 1 : 2 : 3 : 6-tetrahydrobenzaldehyde. The filtrate yielded the aldehyde (78 g.). A cooled mixture of aldehyde and water gave a similar hydrate, m. p. 83—84°.

(c) *Reaction at 65° to ca. 120°*. The results are given in Table 4.

In a typical experiment aldehyde (220 g.) and sodium hydroxide (40%; 100 c.c.) were heated under reflux for $\frac{1}{2}$ hr. and the neutral and acid products distilled.

The neutral product gave, on distillation, fractions: (1) (7.7 g.) b. p. 70—80°/2 mm.; (2) (120.8 g.) b. p. 170—175°/2 mm.; residue (2.6 g.). Fraction 1 on redistillation had b. p. 80—85°/18 mm., n_D^{20} 1.4866, and provided a phenylurethane, m. p. 56—57° (from benzene-light petroleum) (Found: C, 73.1; H, 7.3; N, 5.8. Calc. for $C_{14}H_{17}O_2N$: C, 72.7; H, 7.4; N, 6.1%) (m. p. undepressed on admixture with the phenylurethane of 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol obtained by Ponndorf reduction of the aldehyde). The α -naphthylurethane had m. p. 103° (Found: C, 76.5; H, 6.85; N, 5.2. Calc. for $C_{18}H_{19}O_2N$: C, 76.9; H, 6.8; N, 5.0%), and the *p*-nitrobenzoate, m. p. 60—62° (Found: N, 5.4. Calc. for $C_{14}H_{15}O_4N$: N, 5.4%). Fraction 2 was dissolved in benzene and light petroleum was gradually added. A white solid (83.7 g.) crystallised and the filtrate, after evaporation, provided further crystals on storage. The solid glycol (III) had m. p. 98—100° [Found: C, 75.6; H, 10.05;

OH (Smith and Bryant) 13.8%; *M* (Rast), 221; unsaturation equiv. (McIlhiney), 110.5. $C_{14}H_{13}O_3$ requires C, 75.7; H, 9.9; OH, 15.3%; *M*, 222; unsaturation equiv., 111]. It gave no reaction with 2 : 4-dinitrophenylhydrazine hydrochloride, and no carbonyl content (hydroxylamine hydrochloride). The non-crystalline part of this fraction had active hydrogen content (Zerewitinov), 0.84% (calc. for glycol, 0.90%), and infra-red examination indicated no essential difference from the crystalline material.

TABLE 4.

Compound used	Wt. (g.)	Aq. NaOH (c.c.)	Temp.	Reaction time (hr.)	Products (g.):			
					aldehyde and alcohol	trimer	glycol	acid
Aldehyde ...	102	492 (40%)	B. p.	3	3.2	—	61.0	32.8
" ...	102	492 (40%)	"	$\frac{1}{2}$	3.7	—	57.7	33.7
" ...	220	100 (40%)	"	$\frac{1}{2}$	7.7	—	120.8	76.0
" ...	50	250 (4%)	"	2	32.0	← 5.7 →	—	5.2
" ...	50	240 (10%)	"	3	15.5	← 18.6 →	—	9.0
" ...	50	200 (25%)	"	3	4.1	—	24.9	17.3
" ...	110	37 g. Ca(OH) ₂ 100 g. water	"	3	48.8	37.4	—	3.4
" ...	127.5 in MeOH (165 c.c.)	135 g. KOH 82.5 c.c. water	70°	2	17.8 *	—	54.4	52.0
" ...	127.5 in MeOH (165 c.c.)	96.5 g. NaOH 82.5 c.c. water	70	2	18.5 *	—	52.3	51.5
" ...	45.5 in MeOH (20 g.)	21.1 g. Na 125.2 g. MeOH	70	2	5.9 *	—	18.5	16.1
" ...	46.0 in MeOH (20 g.)	19.8 g. Na 155 g. MeOH	18	2	5.0 *	—	18.1	10.5
Trimer (II)	50	200 (4%)	B. p.	3	—	45.9	—	2.1
"	50	200 (10%)	"	3	—	47.6	—	2.7
"	117	100 (40%)	"	1	—	—	76.1	34.2
Solid trimer	30	40 (40%)	"	3	—	—	—	No reaction

* Mainly alcohol.

The acid product gave material (76.0 g.), b. p. 125—130°/15 mm., and a residue (2.1 g.). The distillate of 1 : 2 : 3 : 6-tetrahydrobenzoic acid provided a *p*-bromophenacyl ester, m. p. 83—84° (Found: C, 55.3; H, 4.9; Br, 24.6. $C_{15}H_{15}O_3Br$ requires C, 55.7; H, 4.6; Br, 24.8%), and a dibromo-compound, m. p. 82—84° (Found: C, 29.6; H, 3.5; Br, 55.5. Calc. for $C_7H_{10}O_2Br_2$: C, 29.4; H, 3.5; Br, 55.9%).

(d) *Reaction at 200—240°*. These experiments, carried out in a stainless steel rocking autoclave, are reported in Table 5.

TABLE 5.

Reactant	Wt. (g.)	Aq. NaOH (c.c.)	Temp.	Time (hr.)	Neutral products (%)			Acid products (%)	
					$C_6H_5 \cdot CH_2 \cdot OH$	Higher alcohols	Residue	$C_6H_5 \cdot CO_2H$	Residue
Aldehyde	90.0	240 (40%)	220°	6	56.3	10.0	24.0	94.7	5.3
"	45.0	123 (40%)	220	3	54.4	8.05	22.5	90.0	10.0
"	50.0	{ Na ₂ CO ₃ (75 g.), water (115 c.c.) }	190—230	6	48.2	5.3	21.2	85.0	15.0
"	59.0	40 (30%)	220—230	6½	65.5	6.2	21.4	86.7	7.6
Liquid glycol	78.5	235.5 (40%)	210—240	6	57.0	17.7	25.3	66.0	20.6
Solid glycol	47.6	143 (40%)	210—230	6	75.4	16.8	5.5	68.4 *	12.8

* 2 : 3 : 4 : 5-Tetrahydro-acid (*p*-bromophenacyl ester).

The fourth of these experiments gave, in addition to the products soluble in water or ether, an insoluble brown solid (7.8 g.) which on recrystallisation from benzene-light petroleum afforded a light brown powder not molten at 285° and giving an ash on ignition. The main products were neutral materials, (1) (19.0 g.) b. p. 82—90°/11 mm., (2) (2.0 g.) b. p. 90—130°/11 mm., (3) (1.8 g.) b. p. >130°/11 mm., and a residue (6.2 g.). Fraction 1 was 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol (phenylurethane). Fraction 3 contained an alcohol (probably the Guerbet product from tetrahydrobenzyl alcohol) [Found: active H (Zerewitinov), 0.47%; unsaturation equiv., 111.9. $C_{14}H_{22}O$ requires active H, 0.48%; unsaturation equiv., 103], which provided a *phenylurethane*, m. p. 140—142° (Found: C, 77.9; H, 8.0; N, 4.4. $C_{21}H_{27}O_2N$ requires C, 77.5; H, 8.3; N, 4.3%). The residue was mainly hydrocarbons (infra-red examination).

Reaction of Alkali with Related Compounds.—The reactions of the trimer and glycol at temperatures up to 240° are given in Tables 4 and 5. The conversion at *ca.* 300° into pimelic acid is mentioned in Table 1. The experiments described below are the reactions, at 300°, of the glycol and alcohol with alkali.

Solid glycol. The glycol (100 g.) and 15.5% aqueous sodium hydroxide (271 c.c.) were heated in the autoclave for 6 hr. at 300°. The neutral product on distillation gave fractions: (1) (6.7 g.) b. p. 30—106°/1 atm., n_D^{20} 1.4745; (2) (0.9 g.) b. p. 70—100°/16 mm., n_D^{20} 1.4713; (3) (8.3 g.) b. p. 100—125°/16 mm., n_D^{20} 1.5139; (4) (3.5 g.), b. p. 140—160°/1 mm.; (5) (5.7 g.) b. p. 160—185°/1 mm.; (6) (3.5 g.) b. p. 185—260°/1 mm.; and a residue (7.5 g.). Fraction 1 showed slight carbonyl and hydroxyl content, and its infra-red spectrum showed it to contain toluene (70%), a *trans*-CH:CH system (5%), some OH, and the remainder mainly 1-methylcyclohexene. Fraction 2 had an active hydrogen content of 0.78% and carbonyl equiv. 1010, and although hexahydrobenzyl and 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol appeared to be absent infra-red examination suggested the presence of the 2 : 3 : 4 : 5-tetrahydro-alcohol. Fractions 3 and 6 were mainly monosubstituted aromatic hydrocarbons with some unsaturated contaminants. Fractions 4 and 5 crystallised and were largely unchanged glycol. The acid product gave some crystalline pimelic acid (12.7 g.) and the remainder on distillation provided hexahydrobenzoic, 1 : 2 : 3 : 6-tetrahydrobenzoic, pimelic, and higher-boiling acids.

Liquid glycol. The glycol (69.1 g.) and 40% aqueous sodium hydroxide (187 c.c.) were heated at 300° for 6 hr. The neutral products provided mainly hydrocarbons and a fraction (1.8 g.), b. p. 80—100°/16 mm., containing hexahydrobenzyl alcohol (70—75%), 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol (20—25%), and 2 : 3 : 4 : 5-tetrahydrobenzyl alcohol (*ca.* 5%) (infra-red). This fraction afforded the phenylurethane, m. p. and mixed m. p. 74—75°, of hexahydrobenzyl alcohol. The acid products, when distilled, gave a hexahydrobenzoic acid fraction (6.3 g.), which crystallised, and a pimelic acid fraction (12.5 g.).

1 : 2 : 3 : 6-Tetrahydrobenzyl alcohol. The alcohol (38.9 g.) and 40% aqueous sodium hydroxide (110 c.c.) were heated at 300° for 6 hr. The neutral products contained no carbonyl compounds and distillation yielded fractions: (1) (5.2 g.) b. p. 100—150°/1 atm.; (2) (2.8 g.) b. p. 90—110°/19 mm.; (3) (2.6 g.) b. p. 110—150°/19 mm.; (4) (3.6 g.) b. p. 150—240°/19 mm.; and a residue (2.4 g.). Fraction 1 contained (infra-red) 35—40% of toluene and some 1-methylcyclohexene; fraction 2 contained hexahydro- (85%) and 1 : 2 : 3 : 6-tetrahydro-benzyl alcohol (15%), and provided the phenylurethane of the former; fraction 3 contained *ca.* 10% of the 1 : 2 : 3 : 6-tetrahydro-alcohol and hydrocarbons; fraction 4 contained mainly hydrocarbons but also 5—10% of glycol. The acid products contained approx. equal parts of hexahydrobenzoic (with a little tetrahydrobenzoic) and pimelic acid.

Tischtschenko Reaction of the Aldehyde.—Freshly distilled 1 : 2 : 3 : 6-tetrahydrobenzaldehyde was added gradually, with stirring or shaking, to the catalyst (*e.g.*, aluminium isopropoxide, 1.5—2.5% calc. on aldehyde) dissolved in a little preformed ester; the temperature of the exothermic reaction was kept below 50°. After the addition was complete stirring was continued until the temperature began to fall without external cooling; then the product was distilled. 1 : 2 : 3 : 6-Tetrahydrobenzyl 1 : 2 : 3 : 6-tetrahydrobenzoate, b. p. 152—153°/7 mm., n_D^{20} 1.4963, was usually formed in 90—95% yield. The aluminium isopropoxide could be replaced by aluminium ethoxide or magnesium ethoxide, but larger quantities of these were usually required.

The effect of acid and of temperature on this reaction is shown in Tables 6—8. The aldehyde was estimated by hydroxylamine hydrochloride.

TABLE 6. *Unchanged aldehyde (%)*. [Redistilled aldehyde (500 g.) added to the catalyst (aluminium isopropoxide, 12.5 g.) in preformed ester (60 g.) during *ca.* 30 min.]

Time (min.) after addn. of aldehyde	0	10	20	40	100
Reaction at: 70°	4.4	—	3.2	1.6	—
90°	17.4	12.4	8.3	—	5.4
110°	42.1	—	41.0	39.3	38.7

TABLE 7. *Unchanged aldehyde (%)*. [Aldehyde (500 g.), containing 0.5% of tetrahydrobenzoic acid, treated as in Table 6. The addition took 20—40 min.]

Time (min.) after addn. of aldehyde	0	10	20	40	70	120
Reaction at: 50°	30.5	10.7	4.9	4.6	2.4	1.0
60°	22.0	14.0	10.4	8.6	4.5	—
70°	63.2	38.2	37.0	—	37.0	35.8

TABLE 8.

Aldehyde (50 g.), containing the appropriate amount of added 1 : 2 : 3 : 6-tetrahydrobenzoic acid, added to the catalyst (aluminium isopropoxide, 1.25 g.) dissolved in preformed ester (3 g.).

Acid (% w/w) present in the aldehyde	0	0.78	1.58	3.10	4.77
Unchanged aldehyde (%) after 2 hr. at 40°	0	43.0	57.6	78.6	77.6

In one experiment, the ester (330 g.) was heated with 40% aqueous sodium hydroxide (300 c.c.) for 1 hr. with stirring; the neutral product, on distillation, gave 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol (137 g.) and a residue (3.5 g.), whilst the acid product consisted of 1 : 2 : 3 : 6-tetrahydrobenzoic acid (183.3 g.) and a residue (6.0 g.).

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