The Addition of Di-*t*-butyl Glutarate to Ketones to Yield Hydroxy Diesters by Means of Lithium Amide. Influence of Metallic Cation. Conversion to Unsaturated Acids

W. H. PUTERBAUGH

Department of Chemistry, Thiel College, Greenville, Pennsylvania

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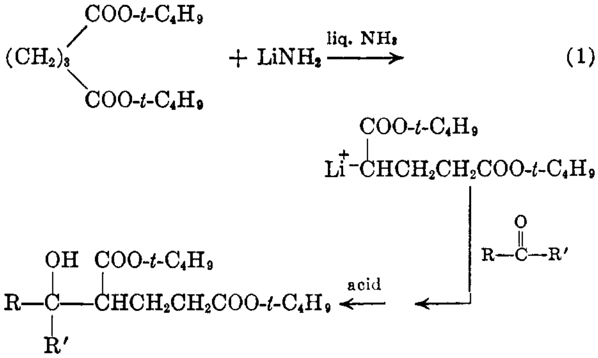
The aldol addition of a diester to a ketone, which represents the first step in the Stobbe condensation, has now been extended to glutaric esters by employing lithium amide and di-*t*-butyl glutarate. Excellent yields of hydroxy diesters have been obtained using a wide variety of ketones. Success of the reaction is dependent upon the cation employed, as only low yields of products result when potassium or sodium bases are used. Experiments demonstrated the relatively greater stability of the lithium salts of the hydroxy diesters as compared to the sodium salts, which undergo both cleavage and lactonization. The hydroxy diesters are converted by refluxing in xylene with acid catalyst in high yields to unsaturated mono acids of four more carbons than the original ketone, if the latter contains at least one aromatic ring, or to unsaturated derivatives of glutaric acid if the original ketone was aliphatic. The method failed when attempts were made to substitute diethyl glutarate for the di-*t*-butyl ester, or to extend it to include di-*t*-butyl adipate.

Attempts to extend the Stobbe condensation to esters of glutaric acid have not previously been generally successful. It has been suggested that this may possibly be due to lower ease of formation of a six-membered lactone ring in comparison with that of the five-membered ring, which has been shown to be an integral part of the Stobbe mechanism when succinic esters are used, thus allowing competing reactions, such as ester self-condensation, to take place.[1] Even when the hindered di-*t*-butyl glutarate was employed to minimize self-condensation, and a ketone having no α-hydrogen, such as benzophenone, was used to prevent acid–base exchange, only a 10% yield of half-ester was obtained when potassium *t*-butoxide was employed as the condensing agent.[2]

However, in view of the fact that lithium salts of β-hydroxy esters have been shown to be relatively stable, whereas sodium salts of such esters undergo relatively facile cleavage and reversal to ester enolate and ketone,[3] it was felt possible that by employing the lithium enolate of glutaric esters the lactonization process followed by elimination to give an olefinic acid salt, which ordinarily occurs in the Stobbe,[1] may not be required to provide the irreversible step needed when the sodium or potassium cation is used. This expectation was further supported by the fact that lithium enolates of *t*-butyl[4] and ethyl[5] acetates may be added to ketones to give aldol products in good yield, but the method fails when the sodium enolates of these esters are employed.

This expectation has been realized, and it has now been found that excellent yields of hydroxy diesters can be obtained by treating the lithium enolate of di-*t*-butyl glutarate (prepared from lithium amide) with a wide variety of ketones. The general method is illustrated in equation 1.


(1)

The scope of the method has been illustrated by the preparation of hydroxy diesters I–XI, and the results are summarized in Table I.

In the general procedure employed, one molecular equivalent of di-*t*-butyl glutarate was added rapidly to 1.25 moles of lithium amide in liquid ammonia, followed after a few minutes by one mole of the ketone. After stirring one hour in liquid ammonia–ether solution, the mixture was decomposed with ammonium chloride and the ammonia evaporated. In certain cases, as noted in the table, longer reaction periods were employed to improve yields. The effect of the mole ratio of amide/ester on yield was investigated with cyclohexanone by varying this ratio from one to 1.25 to 2. This gave yields of 75, 84, and 76%, respectively.

As can be seen in the table, all of the ketones investigated gave high yields, although *m*-nitroacetophenone (VI) may be an exception (see below). Most of the hydroxy diesters were obtained as residue products after distilling recovered starting materials. Only esters X and XI were low boiling enough to permit distillation *in vacuo* without undergoing thermal decomposition by hydrolysis of the *t*-butyl ester groups. Esters I–V solidified slowly on standing, the first four apparently as mixtures of diastereomers, and one of them (II) was separated into the two forms. Thus, the yields

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[1] W. S. Johnson and G. H. Daub, "Organic Reactions," Vol. VI, John Wiley & Sons, Inc., New York, N. Y., 1951, p. 1.

[2] W. S. Johnson, A. L. McCloskey, and D. A. Dunnigan, *J. Am. Chem. Soc.*, **72**, 514 (1950).

[3] C. R. Hauser and W. H. Puterbaugh, *ibid.*, **75**, 4756 (1953).

[4] C. R. Hauser and W. H. Puterbaugh, *ibid.*, **75**, 1068 (1953).

[5] C. R. Hauser and J. K. Lindsay, *ibid.*, **77**, 1050 (1955); W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, **25**, 1693 (1960).

TABLE I

HYDROXY DIESTERS FROM KETONES AND DI-*t*-BUTYL GLUTARATE BY MEANS OF LITHIUM AMIDE[a]

Ketone	Hydroxy diester *t*-butyl 4-carbo-*t*-butoxy-5-hydroxy-	Yield,[b] %	M.p.[c] or b.p. (mm.), °C.	Carbon		Hydrogen	
				Calcd.	Found	Calcd.	Found
Acetophenone	5-Phenylhexanoate (I)	86	88–90 (pentane)	69.20	68.98	8.85	8.81
Butyrophenone	5-Phenyloctanoate (II)	92	111–112.5 (hexane)[d]	70.37	70.46	9.25	9.05
			112–113.5 (pentane)[d]	70.37	70.17	9.25	9.21
p-Methoxyacetophenone	5-(*p*-Methoxyphenyl)-hexonate (III)	77	93.5–95.5 (hexane–benzene)	66.98	66.82	8.69	8.61
p-Chloropropiophenone	5-(*p*-Chlorophenyl)-heptanoate (IV)[e]	82	107–108.5 (hexane)	63.99	64.11	8.05	8.06
Benzophenone[f]	5,5-Diphenylpentanoate (V)	83	101–101.5 (ethanol)	73.21	73.14	8.03	8.03
m-Nitroacetophenone	5-(*m*-Nitrophenyl)-pentanoate (VI)	73[g]	...[h]				
1-Tetralone[f]	Di-*t*-butyl α-(1-hydroxy-1,2,3,4-tetrahydro-1-naphthyl)glutarate (VII)	81	...[h]				
Cyclohexanone	Di-*t*-butyl α-(1-hydroxy-1-cyclohexyl)glutarate (VIII)	84	...[h]				
Cyclopentanone	Di-*t*-butyl α-(1-hydroxy-1-cyclopentyl)glutarate (IX)	81	...[h]				
3-Pentanone	5-Ethylheptanoate (X)	82	135–139 (1 mm.)	65.42	65.41	10.37	10.33
Acetone	5-Methylhexanoate (XI)	65	132–135 (2 mm.)	63.54	63.39	10.00	10.06

[a] All reaction times one hour except as noted. [b] Of the residue product remaining after recovery of starting ester and ketone. [c] After recrystallization from the solvent indicated in parentheses. [d] The m.m.p. of these apparent diastereoisomers was 106.5–111.5°. [e] *Anal.* Calcd. for $C_{22}H_{33}O_5Cl$: Cl, 8.59. Found: Cl, 8.69. [f] Reaction run two hours in liquid ammonia, the ammonia replaced by ether, and the ether solution refluxed two hours. [g] This residue product likely contaminated with tarry material, as this ester gave only a 50% yield of acidic products on hydrolysis. [h] Viscous oils which could not be distilled without decomposition, nor induced to crystallize.

as represented by the residue product are probably somewhat higher than the actual yield of hydroxy diester, but not greatly so, since with the exceptions of esters VI and XI, all crude products as obtained were hydrolyzed in high yield into unsaturated acids (see below). No allowance was made for recovery of starting materials in calculations of yield.

Attempted Extension to Diethyl Glutarate and Di-*t*-butyl Adipate.—A number of attempts were made to employ the more available diethyl glutarate in place of the *t*-butyl ester. It was felt that this might be possible, since it was shown that ethyl acetate could be used in place of *t*-butyl acetate in aldol condensations with ketones by lithium amide either by employing two moles of lithium amide per mole of ester,[5] or even with only one mole of lithium amide provided the ketone is added immediately to the ester enolate.[6] However, all attempts to treat diethyl glutarate with acetophenone under a variety of conditions similar to the above were unsuccessful. Mole ratios of lithium amide/ester were varied from 2, 3, 3.2, and 4/1, times between addition of ester and ketone from immediate to 4, 5, 6, and 20 minutes, and reaction times from five minutes to one hour, with no variation yielding more than a 7% yield of hydroxy diester (see Experimental for several examples). In most cases the bulk of the acetophenone, but very little, if any, of the diethyl glutarate was recovered. These results suggest rapid self-condensation of the diethyl glutarate to yield water-soluble products.

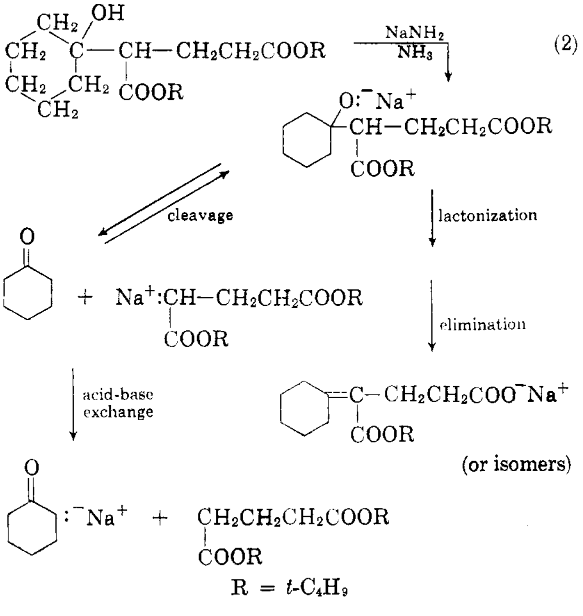
Similarly, attempts to extend the reaction using di-*t*-butyl adipate have not been successful. Despite the use of the protective *t*-butyl groups, this ester underwent Dieckmann cyclization in preference to aldol addition to the acetophenone, even though the conditions were designed to minimize the self-condensation. It is felt, however, that the method could be extended to higher diesters which are not prone to Dieckmann cyclization and this is to be investigated.

Influence of the Metallic Cation.—The nature of the cation accompanying the glutarate enolate is of prime importance to the success of the reaction. It has already been reported that only a 10% yield of half-ester was obtained from the potassium enolate of di-*t*-butyl glutarate and benzophenone,[2] whereas we have obtained an 83% yield of hydroxy diester (V) with the lithium enolate and this ketone. Further, in comparable runs with cyclohexanone, lithium amide gave 84% yield of hydroxy diester (VIII) and 10% recovery of di-*t*-butyl glutarate, while sodium amide gave a 9% yield of hydroxy diester, a 19% yield of Stobbe product (half-ester), and 53% recovery of starting ester.

It was suggested above that the success with lithium, but not with potassium or sodium, may be due to the relatively greater stability of the lithium salt of the hydroxy diester. To investigate this postulate, di-*t*-butyl glutarate was treated with cy-

(6) W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, **25**, 1693 (1960).

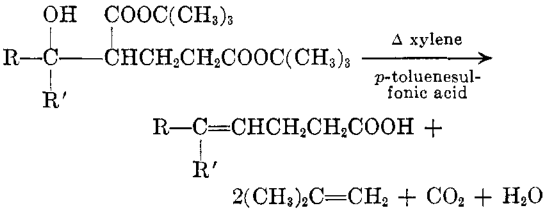
clohexanone by means of lithium amide under comparable conditions, except that in one case the general conditions of one-hour reaction in liquid ammonia was employed, while in the other, after one hour in liquid ammonia, the ammonia was replaced by ether and the solution refluxed an additional twenty-two hours. The results in the first case are given in the paragraph above, while with the longer heating there was obtained a 63% yield of hydroxy diester, a 3% yield of Stobbe product, and 29% recovery of starting ester. These results indicate that while some cleavage of the lithium salt of the hydroxy diester apparently occurred, it is nevertheless reasonably stable and surprisingly resistant to lactonization. To demonstrate the relative stability of the sodium salt, the hydroxy diester product from cyclohexanone (VIII) was converted into its sodium salt by treating with a 10% excess of sodium amide in liquid ammonia, the ammonia was replaced by ether, and the solution refluxed for 3.5 hours. There was obtained only a 15% recovery of hydroxy diester, a 36% yield of di-*t*-butyl glutarate resulting from cleavage, and a 46% yield of mainly half-ester resulting from lactonization. These reactions are illustrated in equation 2.



These results do demonstrate the less stable nature of the sodium salt. However, the fact that nearly half of the hydroxy ester salt was converted to half-ester (presumably a nonreversible process) suggests that acid–base exchange between ester enolate and ketone to form the more weakly basic ketone anion and generate free ester must be partly responsible, along with the tendency of the sodium salts of the hydroxy diester to undergo reverse cleavage, for the failure of sodium amide to effect the addition of ester enolate to the ketone in good yield. This is in accord with previous observations on the role of the cation in the aldol addition of acetate ester enolates to ketones.[3]

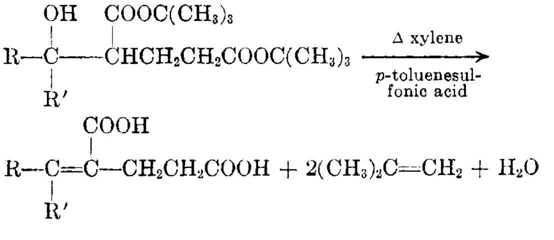
Hydrolyses of Hydroxy Diesters of Unsaturated Acids.—Various methods for effecting the hydrolysis of the hydroxy diesters were investigated. These included refluxing with 6 *M* hydrochloric acid in dioxane, 6 *M* hydrochloric acid in acetic acid, 7 *M* sulfuric acid in acetic acid, and with catalytic amounts of *p*-toluenesulfonic acid in benzene, toluene, and xylene. While all of the methods were applicable, the latter was most convenient, using a three-hour reflux period. High yields of unsaturated acids were obtained in nearly all cases directly from the crude residue products as obtained from the preceding reactions.

The hydrolyses took two courses depending on the structure of the hydroxy diester. If one or more of the groups in the ester was aromatic, the hydrolysis was accompanied by dehydration *and* decarboxylation of the acid group beta to the hydroxy group in the original ester to yield unsaturated mono acids. When both groups were aromatic, as with the product from benzophenone, the hydrolysis and decarboxylation was particularly facile, an 87% yield of the unsaturated mono acid (5,5-diphenyl-4-pentenoic) resulting after only one-hour reflux in toluene. This course is illustrated by equation 3.



$$R\text{—}\overset{\displaystyle OH}{\underset{\displaystyle R'}{C}}\text{—}\overset{\displaystyle COOC(CH_3)_3}{C}HCH_2CH_2COOC(CH_3)_3 \xrightarrow[p\text{-toluenesulfonic acid}]{\Delta\ \text{xylene}} R\text{—}\underset{\displaystyle R'}{C}{=}CHCH_2CH_2COOH + 2(CH_3)_2C{=}CH_2 + CO_2 + H_2O \qquad (3)$$

When neither group was aromatic, the hydrolysis was accompanied by dehydration, but not decarboxylation, to yield unsaturated derivatives of glutaric acid (equation 4).



$$R\text{—}\overset{\displaystyle OH}{\underset{\displaystyle R'}{C}}\text{—}\overset{\displaystyle COOC(CH_3)_3}{C}HCH_2CH_2COOC(CH_3)_3 \xrightarrow[p\text{-toluenesulfonic acid}]{\Delta\ \text{xylene}} R\text{—}\underset{\displaystyle R'}{C}{=}\overset{\displaystyle COOH}{C}\text{—}CH_2CH_2COOH + 2(CH_3)_2C{=}CH_2 + H_2O \qquad (4)$$

The results from these hydrolyses are summarized in Table II.

As can be seen from the table, yields were excellent for all the hydroxy diesters except those from *m*-nitroacetophenone (VI) and acetone (XI). In the former case this is probably due to impure hydroxy diester, since a considerable amount of insoluble tarry residue remained in the flask after hydrolysis. This could not be the case with the latter product, however, since this was one of the few hydroxy diesters which could be distilled, and redistilled material was used for the hydrolysis. The product was a mixture of solid with a small amount of liquid, and probably some decarboxyla-

TABLE II

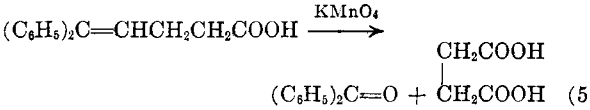
HYDROLYSIS OF HYDROXY DIESTERS TO UNSATURATED ACIDS[a]

Hydroxy[b] diester	Acid	Yield,[c] %	Neut. equiv.[c]	M.p.,[d] °C.	Neut.[d] equiv.	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
I	5-Phenyl-4-hexenoic	87	183 (190)	. . .[e]					
II	5-Phenyl-4-octenoic	92	193 (218)	. . .[e]					
III	5-(*p*-Methoxyphenyl)-4-hexenoic	87	236 (220)	85.0–86.0	222	70.88	71.01	7.32	7.42
IV	5-(*p*-Chlorophenyl)-4-heptenoic	95	208 (239)	. . .[e]					
V[f]	5,5-Diphenyl-4-pentenoic	87	260 (252)	78.0–78.5[g]	252	80.92	80.67	6.39	6.24
VI	5-(*m*-Nitrophenyl)-4-hexenoic[h]	50[i]	222 (235)	97.0–100.5	231	61.27	61.16	5.57	5.43
VII[j]	γ-(3,4-Dihydro-1-naphthyl)-butyric	71	220 (216)	86.0–87.5[k]	217				
VIII	α-(1-Cyclohexenyl)glutaric	89	128 (106)	109.5–110	107	62.25	62.34	7.60	7.66
IX	α-Cyclopentylideneglutaric (or isomers)	93	115 (99)	. . .[e]					
X	α-(3-Pentylidene)glutaric	86	115 (100)	93–101.5	100	59.98	60.02	8.06	8.20
XI	α-Isopropylideneglutaric	39	111 (86)	161–163.5[l]	88	55.80	55.96	7.03	6.91

[a] Reactions effected by three-hour reflux in xylene. [b] See Table I. Hydrolyses performed on residue products as obtained. [c] On the product as obtained without purification. Theoretical neutralization equivalent for the acid named is in parentheses. [d] After recrystallization from hexane–benzene. [e] Oil. [f] Used recrystallized hydroxy diester. Refluxed one hour in toluene. [g] Recrystallization from hexane gave the acid as a complex with one-half molecule of solvent, m.p. 78.5–80.0°. *Anal.* Calcd. for $C_{17}H_{16}O_2 \cdot {}^1/_2C_6H_{14}$: C, 81.32; H, 7.85; neut. equiv., 295. Found: C, 81.36; H, 7.94; neut. equiv., 295. Drying in a vacuum oven overnight at 68° gave the solvent free product whose analysis is reported in the table. [h] *Anal.* Calcd. for $C_{12}H_{13}O_4N$: N, 5.95. Found: N, 5.98. [i] 31% of original starting weight of diester left as insoluble tarry residue in flask after hydrolysis. [j] Refluxed six hours in xylene. The usual three-hour reflux gave 92% yield of product with neut. equiv., 200. [k] Reported m.p. 85–86°, ref. 7. [l] Purified by warming with hexane, filtering, and retaining the product which did not dissolve in hexane.

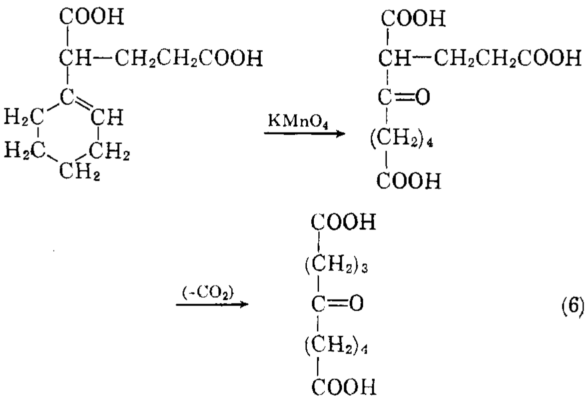
tion had occurred. Probably the conditions of hydrolysis could be varied, particularly with respect to reaction time, to increase the yield. With the exception of the product from 1-tetralone (VII), all of the acids are apparently new compounds, and the seven which were solids were characterized by recrystallization to give neutralization equivalents and analyses in accord with theory. The remaining four, which were oils, were not further studied, but the neutralization equivalent values of these were close enough to theory to indicate they consisted mainly of the acid product indicated.

The structures of one product resulting from each course of hydrolysis were proved by oxidation with potassium permanganate. The 5,5-diphenyl-4-pentenoic acid resulting from hydrolysis of ester V yielded benzophenone and succinic acid (equation 5).



$$(C_6H_5)_2C{=}CHCH_2CH_2COOH \xrightarrow{KMnO_4} (C_6H_5)_2C{=}O + \begin{array}{l}CH_2COOH\\ |\\ CH_2COOH\end{array} \qquad (5)$$

The α-(1-cyclohexenyl)glutaric acid resulting from hydrolysis of ester VIII gave, on permanganate oxidation and acidification with accompanying decarboxylation, 5-oxodecanedioc acid (equation 6).



Thus, the combination of aldol type addition of di-*t*-butyl glutarate to ketones, followed by acidic hydrolysis, offers a convenient method of increasing the length of aromatic ketones by four carbon atoms with a carboxy terminus, or, with aliphatic ketones, offers a route to new derivatives of glutaric acid. As the only comparative example, 1-tetralone was converted by our method in two steps to γ-(3,4-dihydro-1-naphthyl)butyric acid in over-all yield of 58%, whereas this acid was previously prepared in over-all yield of 50% from 1-tetralone by the successive steps of Reformatsky reaction with methyl γ-bromocrotonate, reduction with Raney nickel, dehydration with potassium bisulfate, and saponification with potassium hydroxide.[7]

Experimental[8]

Di-*t*-butyl Glutarate.—Glutaryl chloride was prepared by stirring 2.7 moles of glutaric acid[9] with 800 ml. of thionyl chloride at room temperature for 15 hr., followed by heating at 76° for 1.5 hr. The excess thionyl chloride was removed and the mixture distilled to yield 354 g. (77%), b.p. 105–108° (16 mm.). This was converted by treating with *t*-butyl alcohol and dimethylaniline[10] to di-*t*-butyl glutarate in 78% yield, b.p. 96–97° (3 mm.).

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(7) W. E. Bachmann and N. L. Wendler, *J. Am. Chem. Soc.*, **68**, 2580 (1946).

(8) Analyses by Galbraith Laboratories, Knoxville, Tenn. Melting points are corrected.

(9) The author is indebted to the E. I. du Pont de Nemours and Co. for a generous sample of glutaric anhydride.

(10) C. R. Hauser, B. E. Hudson, B. Abramovitch, and J. C. Shivers, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p. 142.

Hydroxy Diesters from Ketones and Di-*t*-butyl Glutarate by Lithium Amide. General Procedure.—To a stirred suspension of lithium amide[4] prepared from 1.37 g. (0.197 g.-atom) of lithium wire in 300 ml. of liquid ammonia in a flame-dried, nitrogen-purged flask, was added over 2–3 min. a solution of 36.6 g. (0.15 mole) of di-*t*-butyl glutarate in 50 ml. of ether. The black, nearly clear, solution was stirred 2 min., and 0.15 mole of the ketone dissolved in 50 ml. of ether was added over 2 min. After stirring for 1 hr. the mixture was decomposed by slowly adding 10.7 g. (0.2 mole) of ammonium chloride from an Erlenmeyer flask connected to the reaction flask by Gooch tubing. Two hundred milliliters of stock ether was added, a hot water bath applied, and the ammonia driven off to ether reflux, which was continued for 3 min. A cold water bath was applied, and 100 ml. of water added, slowly at first. The ether layer was separated and washed with 1.5 *M* hydrochloric acid. The combined aqueous layers were made strongly acidic and extracted with ether. The combined ether extracts were then washed with 5% sodium carbonate solution, saturated sodium chloride solution, and dried over sodium sulfate. The sodium carbonate extracts were acidified to test for the presence of acidic products but only traces were found. The solvent was removed from the dried solution and the residue distilled *in vacuo* to recover starting ketone and ester. To remove starting materials as completely as possible, the last stages of distillation were conducted at about 1 mm. and a pot temperature of 185° (well above the b.p. of di-*t*-butyl glutarate, which was generally the highest boiling of the starting materials). Above this temperature, however, decomposition of the ester product began as evidenced by loss of vacuum in the system. Yield was calculated on the residue weight remaining. As indicated in Table I, esters X and XI could be distilled, the others were very viscous oils, five of which solidified on standing, while the remaining four remained oils on standing for one year.

Hydrolyses of Hydroxy Diesters to Unsaturated Acids (Table II).—In a 250-ml. flask connected to a Freidrichs condenser and from this to a wet test meter, was placed a solution of 0.05 mole of crude hydroxy diester in 75 ml. of xylene. One gram of *p*-toluenesulfonic acid was added and the mixture heated to reflux. A vigorous gas evolution began at reflux and was essentially complete after the first half hour. Refluxing was continued for a total of 3 hr., the mixture was cooled, 75 ml. of ether added, and the solution washed with 15 ml. of water to remove catalyst. The solution was then extracted with three portions of 10% sodium carbonate solution. These were extracted with ether and then made strongly acid with concentrated hydrochloric acid. The precipitated oil was taken up in ether, washed with water and saturated sodium chloride solution, and dried over sodium sulfate. The solvent was removed and the residue heated in a hot water bath in a rotating evaporator under water pump vacuum. Neutralization equivalents and yields were determined on the residue, and if it solidified it was recrystallized to give analytical samples.

Attempted Reactions Using Diethyl Glutarate.—To 0.63 mole of lithium amide in 600 ml. of liquid ammonia was added over 4 min., 0.15 mole of diethyl glutarate in 50 ml. of ether. The gray mixture was stirred 2 min., and 0.30 mole of acetophenone in 50 ml. of ether added over 2 min. The mixture was stirred 1 hr. and then completed essentially as described for the *t*-butyl esters. No acid fraction was found. Distillation of the neutral residue gave recovery of all of the excess acetophenone plus 80% of the stoichiometrically required amount, b.p. 62–70° (5 mm.), 7% recovery of diethyl glutarate, b.p. 90–98° (3 mm.), and 4.1 g. (less than 9% even if all were hydroxy diester) of oily residue which was not further characterized.

To 0.49 mole of lithium amide in 400 ml. of liquid ammonia was added immediately 0.145 mole of diethyl glutarate in ether. The dark gray solution was stirred 1 min., and 0.145 mole of acetophenone added at once. The mixture was stirred only 5 min., then decomposed and worked up by the general procedure. There was obtained 69% recovery of acetophenone, no diethyl glutarate, and 9.0 g. of residue. The latter was fractionated to give 3.0 g. of material, b.p. 155–160° (1.5 mm.), whose infrared spectrum indicated it was a hydroxy diester. However, as this represents only a 7% yield it was not further characterized.

Attempted Reactions Using Di-*t*-butyl Adipate.—To 0.315 mole of lithium amide in 350 ml. of liquid ammonia was added over 1 min., 0.15 mole of di-*t*-butyl adipate[11] in ether. The gray solution was stirred 2 min., and 0.15 mole of acetophenone in ether was added at once. The mixture was stirred 1 hr. and worked up as in the general procedure. There was obtained 95% of recovered acetophenone, 13.5 g. of material, b.p. 80–82° (2 mm.) whose infrared spectra indicated it was a β-keto ester (probably the Dieckmann product, *t*-butyl 2-oxycyclopentanecarboxylate, 49% yield), and 7.0 g. of brown oily residue.

To 0.188 mole of lithium amide in 300 ml. of liquid ammonia was added immediately 0.15 mole of di-*t*-butyl adipate in ether, and as the last of the ester was run in it was immediately followed by 0.15 mole of acetophenone in ether (total time from start of ester addition to completion to ketone addition was 80 sec.). The clear, light brown mixture was stirred 20 min., then decomposed and worked up as usual. There was obtained 70% of recovered acetophenone, 34% of apparent Dieckmann product, 49% of recovered di-*t*-butyl adipate, 102–106° (2 mm.), and 5.5 g. of oily residue.

Use of Sodium Amide with Di-*t*-butyl Glutarate.—This experiment was conducted by the general procedure, using 0.158 mole of sodium amide,[12] 0.12 mole of di-*t*-butyl glutarate, and 0.12 mole of acetophenone. Acidification of the sodium carbonate extracts yielded 6.0 g. (19%) of yellow oil which was apparently the half-ester, *t*-butyl acid α-cyclohexylideneglutarate, or isomers of it. Neut. equiv. calcd. for $C_{15}H_{24}O_4$: 268.3. Found: 268. Distillation of the neutral layer yielded 53% recovery of di-*t*-butyl glutarate, and left 3.9 g. (9% for hydroxy diester) of residue which was not further studied. This compares with a residue yield of 84% under the same conditions using lithium amide.

Stability of Sodium Salt of Hydroxy Diester.—To 0.126 mole of sodium amide in 200 ml. of liquid ammonia was added over 7 min., 38.7 g. (0.113 mole) of hydroxy diester VIII, obtained as residue product from cyclohexanone and di-*t*-butyl glutarate with lithium amide. After stirring 10 min. in liquid ammonia, the ammonia was driven off and replaced by 150 ml. of ether. The resulting yellow-brown mixture was refluxed for 3.5 hr., then cooled, neutralized by adding 80 ml. of 2 *M* hydrochloric acid, and worked up in the usual manner. Acidification of the basic extracts yielded 13.8 g. (46% for half-ester) of orange oil. The infrared spectrum of this product was essentially the same as that of the half-ester obtained in the preceeding experiment, but it gave a neut. equiv. of 233. It seems likely that some of the second ester group may have been partially hydrolyzed. Distillation of the neutral products yielded 2.0 g. of cyclohexanone (18%), b.p. 62–64° (38 mm.), 10.1 g. (36%) of di-*t*-butyl glutarate, b.p. 105–110° (4 mm.), and 6.1 g. of residue whose infrared spectrum indicated it consisted mainly of recovered hydroxy diester (15%).

Stability of Lithium Salt of Hydroxy Diester.—Cyclohexanone reacted with di-*t*-butyl glutarate and lithium amide by the general procedure, except that after one hour's stirring in liquid ammonia, the ammonia was driven off,

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(11) Prepared similarly to di-*t*-butyl glutarate, b.p. 102–103° (2 mm.).

(12) C. R. Hauser, F. W. Swamer, and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley & Sons, Inc., New York, N. Y., 1954, p. 122

replaced by 250 ml. of ether, and the ether solution refluxed for 22 hr. The reaction mixture was decomposed by the addition of cold, 2 *M* hydrochloric acid and worked up as usual. Acidification of the sodium carbonate extracts yielded an oil which was taken up in ether and the solvent removed to give 1.5 g. (3.7%) of oily acid, neut. equiv., 272 (theory for half-ester, 268.3). Distillation of the neutral fraction yielded 29% recovery of di-*t*-butyl glutarate, and a 63% yield of residual hydroxy diester whose infrared spectrum was identical to that of the similar hydroxy diester obtained from the general procedure in 84% yield.

Proof of Structure of 5,5-Diphenyl-4-pentenoic Acid.[13]—To a solution of 19.7 g. (0.125 mole) of potassium permanganate in 250 ml. of water at 35° was added in three increments over 5 min., a solution of 12.6 g. (0.05 mole) of the acid, m.p. 78–78.5°, obtained by acidic hydrolysis of diester V, dissolved in 100 ml. of water containing 4.0 g. of potassium hydroxide. The permanganate color disappeared as the last was added, and the temperature rose to a maximum of 68°. After stirring for 2 hr. at room temperature, the manganese dioxide was filtered off, stirred with three portions of ether, and each of these were then used to extract the aqueous filtrate. The solvent was removed from the dried ether extracts to yield 5.0 g. of benzophenone, m.p. 46–48°, m.m.p. with an authentic sample, 46–47.5°. The basic aqueous filtrate was evaporated to dryness in a rotating evaporator under water pump vacuum at 140°, the residue was dissolved in 35 ml. of water, acidified with concentrated hydrochloric acid, and cooled. The mother liquor was decanted from the potassium chloride which first precipitated and cooled further to yield a mixture of inorganic and organic precipitate. This was warmed with 50 ml. of absolute ethanol, filtered, and the solvent removed to yield 3.0 g. of succinic acid, m.p. 186–188°, m.m.p. with an authentic sample, 188–189°.

Proof of Structure of α-(1-Cyclohexenyl)glutaric Acid.—This was carried out using 7.0 g. (0.033 mole) of the acid, m.p. 109.5–110°, obtained by acidic hydrolysis of diester VIII, and 10.5 g. (0.067 mole) of potassium permanganate. The acid was added all at once, and an excess of permanganate was not used, so as to prevent any further oxidation of cyclohexanone if it were formed. An ether extract was not made of the aqueous layers, but instead these were distilled at atmospheric pressure to remove cyclohexanone as an azeotrope. None was found, and the distillation was stopped after removing 25 ml. The residual aqueous solution was then evaporated to dryness as before, taken up in water, and acidified. Gas evolution was noted during the acidification and a precipitate formed at once. This was filtered off at room temperature to yield 3.4 g. of white crystals, m.p. 114.5–115.5°. After one recrystallization from water, they gave m.p. 115–115.2° and neut. equiv., 108.2 (reported[14] m.p. for 5-oxodecanedioic acid, 116°, calcd. neut. equiv., 108.1). The semicarbazone was prepared and gave m.p. 177.5–178.5°, neut. equiv., 136.4 (reported[14] m.p. 179–180°, calcd. neut. equiv., 136.6).

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[13] This and the following oxidation were done by the general procedure as given by J. W. Hill and W. L. McEwen, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p. 53.

[14] W. Huckel, *Ann.*, **441**, 1 (1925).

α-Fluorostyrene: Preparation, Properties, and Polymerization

KEN MATSUDA, JOHN A. SEDLAK, JAMES S. NOLAND, AND GEORGE C. GLECKLER

Stamford Research Laboratories, American Cyanamid Company, Stamford, Connecticut

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α-Fluorostyrene, a new vinyl monomer, was prepared by the pyrolysis of α,α-difluoroethylbenzene. The latter was obtained by the reaction of hydrogen fluoride with phenylacetylene or with α-chlorostyrene. α-Fluorostyrene was polymerized in neutral or basic emulsion systems to a high molecular weight homopolymer. The polymer had the striking property of evolving hydrogen fluoride abruptly and quantitatively when heated to 225–235°, forming poly(phenylacetylene).

Among the five isomers of fluorostyrene the only one not recorded in the literature is α-fluorostyrene.[1] As a result of our interest in the effect of substituents on the properties of vinyl polymers, a study of the preparation and polymerization of α-fluorostyrene was undertaken. A number of routes to α-fluorostyrene were tried but the most satisfactory one was a two-step procedure of which the first step was the synthesis of α,α-difluoroethylbenzene by one of the methods shown in equations 1–4.

$$C_6H_5C{\equiv}CH + 2HF \xrightarrow[0^\circ]{\text{Ether solvent}} C_6H_5CF_2{-}CH_3 \tag{1}$$

$$C_6H_5C{\equiv}CH + 2HF \xrightarrow[150^\circ]{\text{13-14\% HgO on act. carbon}} C_6H_5CF_2{-}CH_3 \tag{2}$$

$$C_6H_5CCl{=}CH_2 + 2HF \xrightarrow[0^\circ]{\text{Ether solvent}} C_6H_5CF_2{-}CH_3 + HCl \tag{3}$$

$$C_6H_5CCl{=}CH_2 + 2HF \xrightarrow{\text{13-14\% HgO on act. carbon}} C_6H_5CF_2{-}CH_3 + HCl \tag{4}$$

The α,α-difluoroethylbenzene, a previously unreported compound, was then pyrolyzed to give the desired α-fluorostyrene plus hydrogen fluoride.

$$C_6H_5CF_2{-}CH_3 \xrightarrow{350-400^\circ} C_6H_5CF{=}CH_2 + HF \tag{5}$$

Reactions of the types represented by equations 1–4 have not previously been applied successfully with phenylacetylene or α-chlorostyrene. Certain

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[1] For *o,m,p*-fluorostyrenes see L. A. Brooks, *J. Am. Chem. Soc.*, **66**, 1295 (1944). Also see M. W. Renoll, *ibid.*, **68**, 1159 (1946), and G. B. Bachman and L. L. Lewis, *ibid.*, **69**, 2022 (1947), for *p*-fluorostyrene. For β-fluorostyrene see F. Swarts, *Bull. soc. chim.*, [4] **25**, 145 (1919); F. Bergmann, A. Kalmus, and E. Breuer, *J. Am. Chem. Soc.* **80** 4540 (1958).