[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Alkylation of Tertiary Esters of Dialkylacetic Acids by Means of Alkali Amides. Synthesis of Trialkylacetic Acids[1]

BY CHARLES R. HAUSER AND WILLIAM J. CHAMBERS

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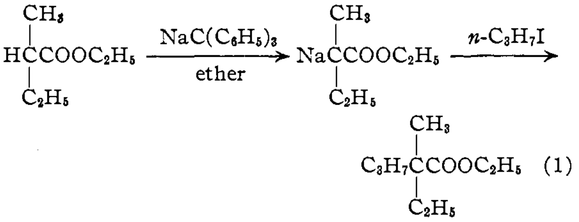
A general method has been developed for the synthesis of trialkylacetic acids involving the alkylation of esters of dialkylacetic acids by means of sodium amide or potassium amide, and the hydrolysis of the resulting alkylated esters. The success of this method depends on hindering the usual attack of the amide ion at the carbonyl carbon of the dialkylacetic acid ester so as to permit the preferential ionization of its α-hydrogen as required for the alkylation. This was accomplished by employing esters having a relatively large tertiary alkoxy group. The present method of synthesis of trialkylacetic acids is considered superior to other known methods for these compounds. Also, a procedure was developed for the preparation of tertiary esters from tertiary alcohols and acid chlorides by means of sodium amide or potassium.

It has been shown previously in this Laboratory[2] that the alkylation of ethyl isobutyrate and ethyl methylethylacetate may be effected in satisfactory yield by means of sodium triphenylmethide in ether. Thus, the propylation of the latter ester was realized in 61% yield (equation 1).



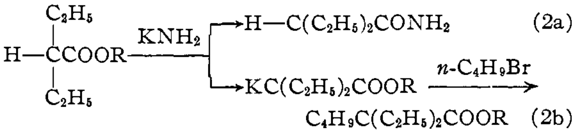
$$\underset{C_2H_5}{\overset{CH_3}{HCCOOC_2H_5}} \xrightarrow[\text{ether}]{NaC(C_6H_5)_3} \underset{C_2H_5}{\overset{CH_3}{NaCCOOC_2H_5}} \xrightarrow{n\text{-}C_3H_7I} \underset{C_2H_5}{\overset{CH_3}{C_3H_7CCOOC_2H_5}} \quad (1)$$

Although such alkylated esters are rather difficult to hydrolyze, Polgar and Robinson[3] have successfully employed this method for the synthesis of certain high molecular weight trialkylacetic acids. For example, methyl decylduodecylacetate was ethylated with ethyl iodide by means of sodium triphenylmethide, and the resulting alkylated ester saponified with propanolic potassium hydroxide to form ethyldecylduodecylacetic acid.[4] Attempts to prepare such acids by two other methods failed.[3,5]

Apparently no other reagent has been satisfactory for the alkylation of ethyl or methyl esters of dialkylacetic acids.[6] Most reagents that are sufficiently strong bases to effect the required ionization (metalation) of the α-hydrogen of such esters[7] react instead with the carbonyl carbon of the ester. Thus, sodium amide, which is widely employed for analogous alkylations of ketones and nitriles, has been observed to react mainly with the carbonyl carbon of ethyl isobutyrate to form isobutyramide.[8]

In the present investigation it was found that, although not suitable with ethyl isobutyrate, sodium and potassium amides are quite satisfactory for the alkylation of certain tertiary esters of dialkylacetic acids. Moreover, the resulting alkylated tertiary esters are readily convertible to the corresponding trialkylacetic acids.

A preliminary study was made of amide formation *vs.* alkylation on treating several esters of diethylacetic acid with potassium amide, followed after 30 minutes by *n*-butyl bromide. The two courses of reaction may be represented by equations 2a and 2b, respectively. The results are summarized in Table I.



$$\underset{C_2H_5}{\overset{C_2H_5}{H—CCOOR}} \xrightarrow{KNH_2} \begin{cases} H—C(C_2H_5)_2CONH_2 & (2a) \\ KC(C_2H_5)_2COOR \xrightarrow{n\text{-}C_4H_9Br} C_4H_9C(C_2H_5)_2COOR & (2b) \end{cases}$$

It can be seen from Table I that each of the diethylacetic acid esters studied produced both the amide and the alkylated ester, and that the yields of amide decreased while those of alkylated ester increased as the alkyl group in the alkoxy portion was varied in the order: ethyl, *t*-butyl, *t*-amyl and triethylcarbinyl [R = $C(C_2H_5)_3$]. This order was anticipated on the basis of a previous observation that increasing the size or complexity of the alkoxy portion of certain esters favors attack of the amide ion at the α-hydrogen over that at the carbonyl carbon.[8]

TABLE I

AMIDE FORMATION *vs.* ALKYLATION WITH $HC(C_2H_5)_2COOR$, KNH_2 AND n-C_4H_9Br

R of alkoxy group	Amide, yield, %	Alkylated ester, yield, %	Unalkylated ester, recovd., %
Ethyl	51	17	22
t-Butyl[a]	22	35	20
t-Amyl	14	41	13
Triethylcarbinyl	1	55	20

[a] Essentially the same result was obtained with sodium amide. Lithium amide gave 12% of the amide and 9% of the alkylated ester, 50% of the unalkylated ester being recovered.

The fact that an appreciable yield (17%) of the alkylated ester was obtained with ethyl diethylace-

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[1] Supported by the National Science Foundation.

[2] B. E. Hudson and C. R. Hauser, THIS JOURNAL, **62**, 2457 (1940).

[3] N. Polgar and R. Robinson, *J. Chem. Soc.*, 615 (1943).

[4] Methyldecylduodecylacetic acid obtained through an analogous methylation could not be separated readily from the acid corresponding to the unalkylated ester (see ref. 3) but this difficulty could presumably have been avoided by last introducing into the molecule one of the larger alkyl groups.

[5] A. J. Birch and R. Robinson, *J. Chem. Soc.*, 488 (1942).

[6] A combination of potassium hydroxide and diethylacetal has recently been reported to effect the alkylation of ethyl isobutyrate with benzyl chloride but the yield was only 23%; C. H. Weizmann, E. Bergmann and M. Sulzbacher, *J. Org. Chem.*, **15**, 918 (1950).

[7] The success with sodium triphenylmethide may be ascribed to its relatively bulky nature which favors the preferential metalation of the α-hydrogen of the ester. However, not all bulky reagents that preferentially metalate the α-hydrogen of ethyl isobutyrate and related esters are suitable for their alkylation. Thus, diisopropylaminomagnesium bromide converts such esters to intermediate metallo esters that condense so rapidly with unchanged ester that their alkylation does not seem feasible; see F. C. Frostick and C. R. Hauser, THIS JOURNAL, **71**, 1350 (1949). The corresponding sodio or potassio reagent should be more suitable for the alkylation.

[8] C. R. Hauser, R. Levine and R. F. Kibler, THIS JOURNAL, **68**, 26 (1946).

TABLE II

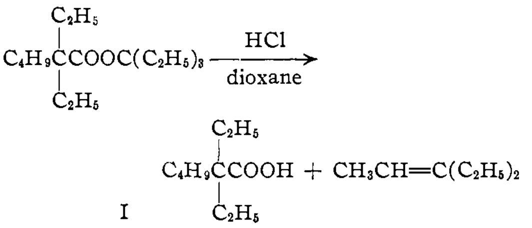
TRIETHYLCARBINYL ESTERS, $RR'CHCOOC(C_2H_5)_3$

R[a]	R'[a]	B.p. °C.	B.p. Mm.	$n^{25}D$	Yield, %	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3	CH_3	68–70	9.1	1.4199	75[b]	$C_{11}H_{22}O_2$	70.92	71.42	11.90	12.54
CH_3	C_2H_5	88–89	9.4	1.4256	..[b]	$C_{12}H_{24}O_4$	71.95	72.01	12.08	12.08
C_2H_5	C_2H_5	102–103	10	1.4311	80[c]	$C_{13}H_{26}O_2$	72.84	72.62	12.23	12.08
C_2H_5	n-C_4H_9	111–112	4.8	1.4350	81[d]	$C_{15}H_{30}O_2$	74.32	74.40	12.48	12.39

[a] R and R' were originally part of the acid chloride; see equation 4. [b] Potassium was employed as reagent. [c] Sodium amide was employed as reagent; the yield with potassium was 74%. [d] Obtained with either sodium amide or potassium.

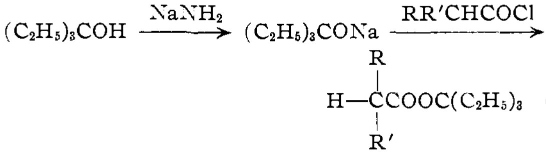
tate is interesting since none of the corresponding alkylated ester was isolated on similarly treating ethyl isobutyrate with potassium amide and butyl bromide.[9] Evidently ethyl diethylacetate either has a more reactive α-hydrogen or a less reactive carbonyl carbon than ethyl isobutyrate.[10]

The three alkylated tertiary esters were not only obtained in considerably better yields than the alkylated ethyl ester (Table I) but they also were found to be convertible to diethylbutylacetic acid (I) much more readily than the ethyl ester. Thus, whereas the alkylated ethyl ester failed to undergo appreciable hydrolysis on long heating with 20% potassium hydroxide or sulfuric acid, the three alkylated tertiary esters were readily converted to I in yields of 92–99% on refluxing two hours with hydrochloric acid in dioxane. This alkyl-oxygen fission,[11] which produces as by-product the olefin corresponding to the alkoxy portion of the ester,[12] may be illustrated with the triethylcarbinyl ester (equation 3).[13]



$$C_4H_9C(C_2H_5)_2COOC(C_2H_5)_3 \xrightarrow[\text{dioxane}]{HCl} \underset{I}{C_4H_9C(C_2H_5)_2COOH} + CH_3CH{=}C(C_2H_5)_2 \quad (3)$$

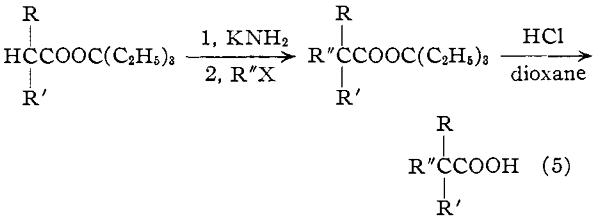
On the basis of these preliminary experiments (see Table I) the triethylcarbinyl type of ester was chosen for further study. Four of them were prepared in yields of 75–80% from triethylcarbinol and the acid chlorides of commercially available dialkylacetic acids[14] by means of sodium amide or potassium (Table II). The reaction may be illustrated with sodium amide which is the preferred reagent (equation 4).



$$(C_2H_5)_3COH \xrightarrow{NaNH_2} (C_2H_5)_3CONa \xrightarrow{RR'CHCOCl} H{-}C(R)(R')COOC(C_2H_5)_3 \quad (4)$$

Incidentally this procedure, using sodium amide or potassium, was found to be superior to adaptations of the procedures described in "Organic Syntheses" for *t*-butyl acetate in which the reaction of the alcohol and acid chloride is effected by means of dimethylaniline[15] or magnesium.[16] The present procedure was the preferred one also for the preparation of *t*-amyl diethylacetate (see Experimental).

The alkylation of the triethylcarbinyl esters was effected generally by means of potassium amide in liquid ammonia (and a little ether) allowing 45 minutes[17] for the ionization (metalation) of the α-hydrogen of the ester, and one hour for the reaction of the intermediate potassio ester with the alkyl halide. The resulting alkylated esters were converted to the corresponding trialkylacetic acids as mentioned above, the over-all reaction being represented by general equation 5.



$$HC(R)(R')COOC(C_2H_5)_3 \xrightarrow[2,\ R''X]{1,\ KNH_2} R''C(R)(R')COOC(C_2H_5)_3 \xrightarrow[\text{dioxane}]{HCl} R''C(R)(R')COOH \quad (5)$$

In Table III are summarized the data for the alkylated esters, and in Table IV, those for the trialkylacetic acids. The alkyl groups R, R' and R'' in these tables correspond to those represented in equation 5. The yields for the trialkylacetic acids given in Table IV are over-all yields obtained from the dialkylacetic acid esters when their crude alkylation products were treated directly with hydrochloric acid without first isolating the alkylated esters. Generally, better over-all yields of the acids were

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[9] As reported previously for sodium amide (ref. 8), potassium amide produced mainly isobutyramide (50%); also a little (5%) isobutyric acid was obtained, and some (15%) of the unchanged ethyl isobutyrate was recovered.

[10] Since ethyl diethylacetate has a less reactive α-hydrogen toward sodium triphenylmethide than ethyl isobutyrate (see D. G. Hill, B. Stewart, S. W. Kantor, W. A. Judge and C. R. Hauser, THIS JOURNAL, **76**, 5129 (1954)), the former ester apparently has a much less reactive carbonyl carbon than the isobutyrate. This would be in line with Newman's rule of six (M. S. Newman, *ibid.*, **72**, 4783 (1950)) on the basis of which the two α-ethyl groups of ethyl diethylacetate would be expected to offer more hindrance to the attack of a base at the carbonyl carbon atom than the two α-methyl groups of ethyl isobutyrate.

[11] See C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 779.

[12] The relative ease of such an acid-catalyzed hydrolysis of the *t*-butyl ester group has been taken advantage of in the synthesis of β-keto esters from acylated ethyl *t*-butyl malonates; D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1288 (1944).

[13] The by-product appeared to consist of olefin, presumably 3-ethyl-2-pentene, along with some alkyl halide and alcohol.

[14] We are indebted to Carbide and Carbon Chemicals Co. for generous samples of two of these acids, diethyl- and ethylbutylacetic acids.

[15] C. R. Hauser, B. E. Hudson, B. Abramovitch and J. C. Shivers, "Organic Syntheses," Col. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 142. This method produced only a 17% yield of triethylcarbinyl diethylacetate.

[16] A. Spassow, *ibid.*, p. 144. This method gave a negligible yield of triethylcarbinyl diethylacetate.

[17] The 55% yield of the triethylcarbinyl ester of butyldiethylacetic acid obtained in the preliminary study (Table I) in which a 30-minute metalation was allowed, was increased to 65% by increasing the metalation time to 45 or 60 minutes.

TABLE III

ALKYLATED TRIETHYLCARBINYL ESTERS, $RR'R''CCOOC(C_2H_5)_3$

R[a]	R'[a]	R''[b]	B.p. °C.	B.p. Mm.	$n^{25}D$	Yield, %	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
C_2H_5	C_2H_5	n-C_4H_9	141–144	10	1.4455	65	$C_{17}H_{34}O_2$	75.50	75.61	12.67	12.78
C_2H_5	C_2H_5	$C_6H_5CH_2$	123–124	0.25	1.4982	59	$C_{20}H_{32}O_2$	78.89	78.91	10.59	10.81
C_2H_5	C_2H_5	n-C_6H_{17}	131–132	.40	1.4506	64	$C_{21}H_{42}O_2$	77.23	76.83	12.96	12.84
C_2H_5	n-C_4H_9	$C_6H_5CH_2$	130–132	.25	1.4918	75	$C_{22}H_{36}O_2$	79.46	79.81	10.92	10.97

[a] R and R' were originally part of the dialkylacetic ester; see equation 5. [b] R'' was originally part of the alkyl halide; see equation 5.

TABLE IV

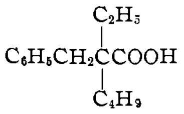
TRIALKYLACETIC ACIDS, $RR'R''CCOOH$

R[a]	R'[a]	R''[b]	B.p., °C.	B.p., Mm.	$n^{25}D$	Yield,[c] %	Neut. equiv. Calcd.	Neut. equiv. Found	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3	CH_3	n-C_8H_{17}	137–140[d]	3.9	1.4389	50	200.3	203.3	$C_{12}H_{24}O_2$	71.95	72.28	12.08	12.58
CH_3	C_2H_5	n-C_3H_7	115–117[e]	14	1.4288	69	144.2	144.9	$C_8H_{16}O_2$	66.63	66.47	11.18	11.31
C_2H_5	C_2H_5	n-C_4H_9	133–134[f]	10	1.4388	79[g]	172.3	173.5	$C_{10}H_{20}O_2$	69.72	69.89	11.71	11.72
C_2H_5	C_2H_5	$C_6H_5CH_2$	121–122[h]	0.25	1.5125	84	206.3	207.7	$C_{13}H_{18}O_2$	75.69	75.56	8.80	8.73
C_2H_5	C_2H_5	n-C_8H_{17}	131–133	.65	1.4480	81	228.4	229.0	$C_{14}H_{28}O_2$	73.63	73.66	12.36	12.27
C_2H_5	n-C_4H_9	$C_6H_5CH_2$	139–140	.45	1.5050	78[i]	234.3	233.0	$C_{15}H_{22}O_2$	76.88	76.79	9.46	9.71
C_2H_5	n-C_4H_9	n-C_8H_{17}	138–139[j]	.40	1.4500	74	246.3	247.0	$C_{16}H_{23}O_2$	74.94	74.89	12.58	12.72

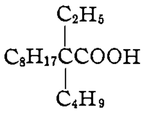
[a] R and R' were originally part of the dialkylacetic ester. [b] R'' was originally part of the alkyl halide. [c] Over-all yields from the dialkylacetic esters. [d] Reported b.p. 153–158° at 19 mm.; ref. 21. [e] Reported b.p. 115.5–116.5° at 14 mm., $n^{25}D$ 1.4300; ref. 24. [f] Reported b.p. 135° at 25 mm.; ref. 21. [g] An 81% yield was obtained employing sodium amide instead of potassium amide. [h] Reported b.p. 197–199° at 17 mm.; A. Haller and E. Bauer, *Ann. chim.*, 16, 340 (1921). [i] A 75% yield was obtained employing sodium amide instead of potassium amide. [j] Reported b.p. 175–195° at 16 mm.; ref. 21.

obtained in this manner than when the alkylated esters were isolated and then hydrolyzed.

It can be seen from Table IV that most of the yields of the trialkylacetic acids from the dialkyl acetic acid esters were excellent. For example, that of trialkylacetic acid I was approximately 80%. Even when based on diethylacetic acid, the over-all yield of I is good (61%). The method appears to be quite general and applicable to the synthesis of trialkylacetic acids having three different alkyl groups such as acids II and III which were ob-


II

$C_6H_5CH_2C(C_2H_5)(C_4H_9)COOH$


III

$C_8H_{17}C(C_2H_5)(C_4H_9)COOH$

tained in yields of 78 and 74%, respectively (Table IV). Acid III has sixteen carbons, and even higher molecular weight acids could probably be prepared by this method.

As might be expected the higher trialkylacetic acids were viscous liquids which resisted attempts at crystallization, and their sodium salts produced soap-like emulsions with water. The sodium salt of acid III was surprisingly soluble in ether; in fact it appeared to be more soluble in ether than in water.

Although potassium amide was generally employed, sodium amide was shown to produce equally good yields in two typical alkylations. Thus the butylation of the diethylacetic acid ester and the benzylation of the ethylbutylacetic acid ester by means of sodium amide, followed by hydrolysis, gave trialkylacetic acids I and II in yields 81 and 75%, respectively (see notes *g* and *i* of Table IV). Similarly sodium amide gave about the same yield of alkylated ester (and of amide) as potassium amide in the preliminary study with *t*-butyl diethylacetate, but lithium amide was much less effective (see note *a* of Table I). Likewise diisopropylaminolithium was found to be a poor alkylation reagent with this ester.[18]

It should be mentioned that a fairly good yield (46%) of trialkylacetic acid I was realized through the butylation of *t*-amyl diethylacetate, and the hydrolysis of the crude ester. This is slightly more than half the yield (80%) obtained with the triethylcarbinyl ester (Table IV). The similar alkylation and hydrolysis of the corresponding *t*-butyl ester should produce about a 40% yield of I. Since *t*-amyl and *t*-butyl alcohols are somewhat more available than triethylcarbinol, the use of the *t*-amyl or *t*-butyl esters in such alkylations might be expedient in certain cases in spite of the lower yields.

The present alkali amide method of synthesis of trialkylacetic acids is considered preferable to that involving sodium triphenylmethide since the alkali amides are much more convenient to employ than the latter reagent.[19]

The present method is also considered superior to other known methods for the synthesis of trialkylacetic acids, the most widely employed of which is probably that of Haller and Bauer.[20,21] The latter method may be illustrated by the synthesis of diethylbutylacetic acid (I) from butyrophenone, the critical step of which involves the cleavage of the completely alkylated ketone to form the trialkylacetamide and the by-product benzene (equation 6).

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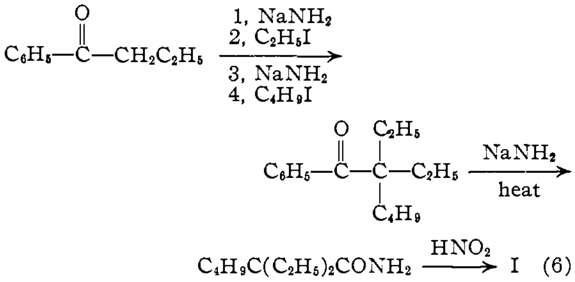
(18) Only a 3% yield of alkylated ester (51% unalkylated ester being recovered) was obtained on refluxing *t*-butyl diethylacetate with diisopropylaminolithium (prepared from butyllithium and diisopropylamine) in ether for three hours, followed by 12 hours of refluxing with *n*-butyl bromide in the same solvent.

(19) Sodium triphenylmethide is rather inconvenient to prepare, and it produces in an alkylation the by-product triphenylmethane which makes the working-up process somewhat troublesome.

(20) For an early review, see A. Haller, *Bull. soc. chim. France*, [4] **31**, 1073 (1922).

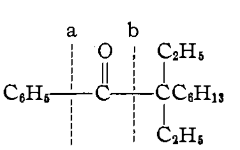
(21) C. L. Carter and S. N. Slater, *J. Chem. Soc.*, 130 (1946).



$$C_6H_5-\overset{\overset{O}{\parallel}}{C}-CH_2C_2H_5 \xrightarrow[3,\ NaNH_2;\ 4,\ C_4H_9I]{1,\ NaNH_2;\ 2,\ C_2H_5I} C_6H_5-\overset{\overset{O}{\parallel}}{C}-\underset{\underset{C_4H_9}{|}}{\overset{\overset{C_2H_5}{|}}{C}}-C_2H_5 \xrightarrow[heat]{NaNH_2}$$

$$C_4H_9C(C_2H_5)_2CONH_2 \xrightarrow{HNO_2} I \quad (6)$$

Whereas the yield of acid I obtained by our method was 80% (61% from diethylacetic acid), that produced by the Haller–Bauer method appears to have been less than 10%.[21] Moreover, the latter method has given even lower yields in the synthesis of certain higher complex homologs. For example, only a very poor yield of diethylhexylacetic acid was obtained from intermediate IV which cleaved mainly at b to form benzamide instead of at a to give the desired trialkylacetamide.[21] Even higher molecular weight acids were obtained in excellent yields by our method (see Table IV).



IV

Probably the second most widely used method for the synthesis of trialkylacetic acids involves the alkylation and hydrolysis of acetonitrile or a higher homolog.[22,23] Birch and Robinson[5] concluded that this method was of little value for the synthesis of such acids as methyldidecylacetic acid because of the difficulty of hydrolysis of the intermediate alkylated nitrile. However, Sperber and co-workers[23] have obtained over-all yields of 17–56% for certain trialkylacetic acids, the highest yield being realized in the synthesis of tributylacetic acid from acetonitrile or capronitrile (equation 7).

$$C_4H_9CH_2CN \xrightarrow[C_4H_9]{NaNH_2} (C_4H_9)_3CCN \xrightarrow{H_2SO_4}$$

$$(C_4H_9)_3CCONH_2 \xrightarrow[nitrite]{butyl} (C_4H_9)_3CCOOH \quad (7)$$

Apparently the trialkylacetic acids that have been synthesized by this method have had alkyl groups containing seven carbons or less, and only one such acid, methylethylpropylacetic acid, has had three different alkyl groups.[24]

Other methods that have been used to a limited extent include the carbonation of the appropriate Grignard reagents[25] and the rearrangement of α-bromoketones.[26]

Experimental[27]

Triethylcarbinol.—This compound was prepared from ethylmagnesium bromide and diethyl carbonate,[28] or preferably from this Grignard reagent and diethyl ketone by a modification of the method of Lucas.[29] To an ice-cooled, stirred solution of ethylmagnesium bromide, prepared from 109 g. (1.0 mole) of ethyl bromide and 24.3 g. (1.0 g. atom) of magnesium in 400 ml. of anhydrous ether, was added as rapidly as possible 69.8 g. (0.8 mole) of diethyl ketone in 100 ml. of ether. After stirring for 2 hr. and standing overnight, the reaction mixture was cooled and decomposed with 5*N* sulfuric acid. There was isolated 79.6 g. (86%) of triethylcarbinol, b.p. 53–54° (20 mm.), n^{25}D 1.4276 (reported[29] b.p. 72.5–73.5° at 50 mm., n^{25}D 1.4281).

Triethylcarbinyl Esters of Dialkylacetic Acids.[14]—These esters were prepared by means of sodium amide or potassium as described below; the results are summarized in Table II.

(A) **With Sodium Amide.**—To a stirred suspension of 0.52 mole of sodium amide[30] in 500 ml. of liquid ammonia was added 60.4 g. (0.52 mole) of triethylcarbinol in 50 ml. of anhydrous ether. The liquid ammonia was evaporated on the steam-bath while 400 ml. of anhydrous ether was added. The remaining ammonia was removed by refluxing the ethereal solution for 3 hr., sufficient heat being applied during the last 0.5 hr. to distil approximately 100 ml. of ether[31] through the reflux condenser.

To the stirred suspension of the sodium triethylmethoxide was added, during 0.5 hr., 0.5 mole of the acid chloride in 50 ml. of anhydrous ether. After refluxing for 1 hr., the mixture was cooled, and 200 ml. of water was added carefully with stirring. The ethereal layer (to which was added an ether extract of the aqueous layer) was washed with 10% sodium hydroxide, and dried over Drierite. The solvent was removed and the residue fractionally distilled *in vacuo* to give the triethylcarbinyl ester. Some of these esters tended to foam during the first part of the distillation.

(B) **With Potassium.**—To a stirred suspension of 11.7 g. (0.3 g. atom) of potassium in 300 ml. of anhydrous ether was added 34.9 g. (0.3 mole) of triethylcarbinol, and the mixture stirred until essentially all of the metal had reacted (about 16 hr.) leaving a white suspension of potassium triethylmethoxide.[32]

To the stirred suspension of the potassium triethylmethoxide was added 0.29 mole of the acid chloride in an equal volume of anhydrous ether, and the mixture refluxed for 3 hr. After cooling, 100 ml. of water was added carefully. The triethylcarbinyl ester was isolated as described above in the procedure employing sodium amide.

***t*-Amyl Diethylacetate.**—This ester was prepared essentially as described above for the triethylcarbinyl ester (procedure A) employing 1.0 mole of sodium amide, 88.2 g. (1.0 mole) of *t*-amyl alcohol and 111.0 g. (0.82 mole) of diethylacetyl chloride. The product (121.3 g., 65%) boiled at 70–71° at 10 mm., n^{25}D 1.4146.

Anal. Calcd. for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.87; H, 11.82.

Only a 30% yield of this ester (b.p. 70–72° at 10 mm.) was obtained employing the method described below for *t*-butyl diethylacetate.

***t*-Butyl Diethylacetate.**—To 37.8 g. (0.51 mole) of *t*-butyl alcohol and 40.3 g. (0.51 mole) of pyridine in 300 ml. of anhydrous ether was added slowly 67.3 g. (0.5 mole) of diethylacetyl chloride in 100 ml. of anhydrous ether.[33] After stirring for 1 hr. and standing overnight, the precipitate of

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(22) C. Schuerch and E. H. Huntress, THIS JOURNAL, **70**, 2824 (1948).

(23) N. Sperber, D. Papa and E. Schwenk, *ibid.*, **70**, 3091 (1948).

(24) M. Heintzler, *Ann.*, **569**, 97 (1950).

(25) F. C. Whitmore and D. E. Badertscher, THIS JOURNAL, **55**, 1559 (1933).

(26) J. G. Aston and co-workers, *ibid.*, **62**, 2590 (1940); **64**, 300 (1942).

(27) Melting points and boiling points are uncorrected. Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Distillations were carried out in a 60-cm. Podbielniak-type column.

(28) W. W. Moyer and C. S. Marvel, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 602.

(29) H. J. Lucas, THIS JOURNAL, **51**, 248 (1929).

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

(31) Distillation of some of the ether facilitated the removal of the last traces of ammonia. When none of the ether was distilled ammonia was detected with moist litmus paper at the top of the condenser even after several hours.

(32) Opening of the flask was avoided since exposure to air decomposes the salt (turns brown).

(33) This is a modification of the method described in reference 15 for the preparation of *t*-butyl acetate.

pyridine hydrochloride was removed by filtration. The ethereal filtrate was washed with 10% hydrochloric acid, water and 10% sodium hydroxide, and dried over Drierite. The solvent was removed and the residue distilled to give 43.5 g. (50%) of the ester, b.p. 52–54° at 10 mm., $n^{25}\mathrm{D}$ 1.4052.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.71. Found: C, 69.93; H, 11.61.

Amide Formation *vs.* Alkylation with Various Esters of Diethylacetic Acid.—To a stirred solution of 0.11 mole of potassium amide[34] in 250 ml. of liquid ammonia was added 0.1 mole of the ester in 20 ml. of anhydrous ether and, after 0.5 hr., 15.1 g. (0.11 mole) of butyl bromide in 20 ml. of anhydrous ether was added. After stirring for 15 min., the liquid ammonia was evaporated as an equal volume of anhydrous ether was added, and the resulting suspension was stirred and refluxed for 1 hr. The mixture was cooled, and decomposed carefully with water. The ethereal solution of the reaction products was dried over Drierite, and the solvent distilled. The residue was dissolved in petroleum ether and the solution cooled on Dry Ice for 1 hr. The resulting precipitate of 2-ethylbutyramide (diethylacetamide) was collected on a funnel. The filtrate was evaporated and the residue fractionally distilled to yield the alkylated and unalkylated esters.

The yields of the two products and those of the recovered unalkylated esters are given in Table I. The 2-ethylbutyramide melted at 109.5–111° and, after recrystallization from petroleum ether, at 111–111.5°, reported m.p. 112°.[35] The alkylated ethyl ester, ethyl diethylbutylacetate (b.p. 91–92° at 10 mm., $n^{25}\mathrm{D}$ 1.4265), was unaffected by refluxing 20% potassium hydroxide or 20% sulfuric acid (16 hr.), 98% of the ester being recovered.

Anal. Calcd. for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.97; H, 11.96.

The three alkylated tertiary esters, *t*-butyl diethylbutylacetate (b.p. 99–100° at 10 mm., $n^{25}\mathrm{D}$ 1.4250), *t*-amyl diethylbutylacetate (b.p. 117–118° at 10 mm., $n^{25}\mathrm{D}$ 1.4320) and triethylcarbinyl diethylbutylacetate were hydrolyzed to form diethylbutylacetic acid (I) in yields of 92–96% by means of hydrochloric acid (see below). Data for the triethylcarbinyl ester are given in Table III, and those for acid I, in Table IV.

Alkylation of Triethylcarbinyl Esters.—To a stirred solution of 0.2 mole of potassium amide[34] in 500 ml. of liquid ammonia was added 0.2 mole of the triethylcarbinyl ester in 50 ml. of anhydrous ether. Within 5 min., the resulting mixture became green. After stirring 45 min., 0.2 mole of the alkyl halide in 50 ml. of anhydrous ether was added rapidly, and the stirring continued for 1 hr. Wet ether was then added carefully and the liquid ammonia was allowed to evaporate on the steam-bath as more ether was being added. Water was added with stirring, and the two layers separated. The ether layer (to which was added an ether extract of the aqueous layer) was dried over Drierite. The solvent was removed and the residue distilled *in vacuo* to give the alkylated esters.

The yields and other data are summarized in Table III. The esters were further identified by their conversion to the corresponding trialkylacetic acids as described below.

Hydrolysis of Alkylated Triethylcarbinyl Esters.—The alkylated ester (0.2 mole) was refluxed 2 hr. with a mixture of 30 ml. of 37% hydrochloric acid and 20 ml. of dioxane.[36] The resulting mixture was distilled through a short Vigreux column until the temperature rose to 100°, and the distillate discarded. The residue was cooled and dissolved in ether. The ethereal solution was extracted with three 50-ml. portions of 10% sodium hydroxide and then with 50 ml. of water. The combined aqueous alkaline extracts were made strongly acidic with 5 *N* sulfuric acid and the liberated carboxylic acid extracted with ether. After drying over Drierite, the solvent was removed from the ethereal extract, and the residue distilled *in vacuo* to give the trialkylacetic acid. The yields were 92–99%.

General Method of Synthesis of Trialkylacetic Acids.—Triethylcarbinyl esters of dialkylacetic acids were alkylated with alkyl halides by means of potassium amide or sodium amide on a 0.2-mole scale as described above. After replacing the liquid ammonia by ether and adding water, the mixture was acidified strongly with 5 *N* sulfuric acid. The layers were separated, and the solvent was removed from the ethereal layer. The residue of crude alkylated ester was hydrolyzed to the trialkylacetic acid and isolated[37] as described above.

The yields and other data are summarized in Table IV. The analyses, refractive indices and neutral equivalents given in this table are for redistilled samples. However, the refractive indices of the products on which the yields were based differed from the values given by less than ±0.0007. The neutral equivalents were determined in ethanol using phenolphthalein as indicator.

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[34] R. S. Yost and C. R. Hauser, THIS JOURNAL, **69**, 2325 (1947).

[35] M. M. Tiffeneau and P. Weill, *Compt. rend.*, **204**, 592 (1937).

[36] The hydrogen chloride evolved was caught in a trap. Dilute hydrochloric acid was found unsatisfactory.

[37] The butylethyloctylacetic acid obtained from the alkylation of butylethylacetic ester with octyl bromide and hydrolysis of the crude alkylated product was not removed by the alkali extraction. Therefore, the ethereal solution was washed with dilute hydrochloric acid, dried, and the solvent removed. The crude acid was fractionally distilled.

DURHAM, NORTH CAROLINA

[CONTRIBUTION FROM THE RESEARCH DIVISION, ARMOUR AND COMPANY]

Alcoholysis of Esters with Aluminum Alcoholates[1]

BY EMIL KAISER AND ELLEN P. GUNTHER

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Two procedures are described for the complete exchange of the alkoxyl (or arylalkoxyl) groups between an ester and an aluminum alcoholate without the use of fractional distillation.

The exchange of alkoxyl groups between an ester and an aluminum alcoholate has been reported.[2,3] It was shown by Baker that the equilibrium

$$3\mathrm{R{\cdot}COOR'} + \mathrm{Al(OR'')_3} \rightleftarrows 3\mathrm{R{\cdot}COOR''} + \mathrm{Al(OR')_3} \quad (1)$$

could be forced to the right if the ester R·COOR′ has a higher boiling point than the ester R·COOR″. Thus the ester produced in the alcoholysis could be continuously removed from the reaction mixture and high yields of the desired products could be obtained.

This procedure is not suited for the completion of alkoxyl group interchanges in which the products are higher boiling than the starting materials. Also substances which decompose on distillation cannot be used in this type of alkoxyl exchange. A study was therefore conducted with the object of effecting

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[1] Presented at the 14th International Congress for Pure and Applied Chemistry, Zurich, Switzerland, July, 1955.

[2] R. H. Baker, THIS JOURNAL, **60**, 2673 (1938). See this paper for earlier references.

[3] C. Barkenbus, M. B. Naff and K. E. Rapp, *J. Org. Chem.*, **19**, 1316 (1954).