[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. IV. (Primary 1-Alkenyl) Alkyl Malonic Esters

BY ARTHUR C. COPE, WALTER H. HARTUNG,[1,2] EVELYN M. HANCOCK AND FRANK S. CROSSLEY[2]

Previous articles in this series have described practical methods of preparing disubstituted malonic and cyanoacetic esters in which one substituent is a "secondary 1-alkenyl" group, RCH=C(R′)—.[3] These esters were produced by alkylating alkylidene esters, obtained by condensing ketones with malonic and cyanoacetic esters.

In order to introduce "primary 1-alkenyl" groups, RCH=CH—, or RR′C=CH—, into malonic ester by a similar process, it would be necessary to start with the condensation products of aldehydes with ethyl malonate.

$$\underset{\text{I}}{\mathrm{RCH_2CH{=}C(COOEt)_2}} \xrightarrow[\text{or NaNH}_2]{\text{NaOR, Na,}} \underset{\text{II}}{\underline{[\mathrm{RCH{=}CH{-}C(COOEt)_2}]^-\mathrm{Na}^+}}$$

$$\text{II} + \mathrm{R'X} \longrightarrow \underset{\text{III}}{\mathrm{RCH{=}CHC(R')(COOEt)_2}} + \mathrm{NaX}$$

Ethyl (1-butenyl)-methylmalonate has been prepared in this manner by Kon, Linstead and Maclennan.[4] The utility of the reaction as a general synthetic method remained open to question, however, both because of the ease with which substituted vinyl alkylmalonic esters undergo alcoholysis,[3a,b] and the instability of "primary alkylidene" malonic esters. These alkylidene esters (I), in the presence of alkaline reagents, readily undergo a reversal of the condensation reaction by means of which they are prepared, giving the aldehyde and malonic ester, or products derived from them.

Actually, the synthesis of *vinyl* alkylmalonic esters according to the above equation (R = H) proved to be very unsuccessful, almost all of the ethylidene malonic ester being transformed into a high boiling polymer. With alkylidene malonic esters prepared from propionaldehyde, butyraldehyde, and other higher aldehydes, however, the synthesis is successful if conditions are chosen which minimize alcoholysis and polymerization.

The alkylidene esters are preferably added to sodium alkoxide–alcohol solutions at low temperatures, in the preparation of the sodium derivatives, and then alkylated rapidly by adding the alkylating agent in one portion and immediately heating to the boiling point. Under these conditions, a large part of the enolate is alkylated, and the proportion of high boiling polymer is greatly reduced.

The success of these alkylations in alcohol solution is surprising, for similar alkylations of secondary alkylidene malonic esters in alcohol gave poor yields.[3a,b] This difference in behavior on alkylation is probably due to the fact that the branched groups present in enolates derived from secondary alkylidene esters (*i. e.*, $[\mathrm{RCH{=}C(R')C(COOEt)_2}]^-\mathrm{Na}^+$) hinder the introduction of alkyl groups.[5] Consequently, when such enolates are treated with alkyl halides in alcohol solution, a large part of the reaction which occurs involves the sodium alkoxide with which the enolate is in equilibrium and the alkyl halide. This side reaction converts most of the enolate back into the original alkylidene ester. The primary 1-alkenyl groups present in the enolates (II) derived from primary alkylidene malonic esters, however, present no steric hindrance opposing the introduction of an alkyl group, and the alkylation of these enolates proceeds normally.

The data recorded in Table I show that in this series the yield of alkylated esters (III) depends in part upon the size of the alkylidene group in the ester employed. The yields become higher as the size of the alkylidene group increases, reaching a maximum of 86 to 93% with the isopentylidene ester. The alkylations occur more rapidly with the higher members of the series; as a result the products are in contact with the sodium enolates (and the sodium alkoxides with which they are in equilibrium) for a shorter time, and there is less opportunity for their destruction by alcoholysis.

The use of sodamide in liquid ammonia or in inert solvents is inadvisable for preparing the

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[1] Present address: University of Maryland, School of Pharmacy, Baltimore, Maryland.

[2] Technical Division, Sharp and Dohme, Inc.

[3] (a) Cope and Hancock, THIS JOURNAL, **60**, 2644 (1938); (b) **60**, 2901 (1938); (c) **60**, 2903 (1938).

[4] Kon, Linstead and Maclennan, *J. Chem. Soc.*, 2452 (1932).

[5] Monoalkyl malonic esters containing saturated secondary alkyl groups, such as isopropyl and secondary butyl, are difficult to alkylate: *cf.* Fischer and Dilthey, *Ann.*, **335**, 337 (1904); Shonle, Keltch and Swanson, THIS JOURNAL, **52**, 2440 (1930).

TABLE I

PRIMARY 1-ALKENYL ALKYL MALONIC ESTERS

Primary 1-alkenyl group	Alkylating agent	Hours refluxed[a]	Yield, %	Boiling point, °C. (uncor.)	Mm.	$n^{25}D$	d^{25}_{25}	Molecular refraction		Formula	Carbon,[b] %		Hydrogen,[b] %	
								Calcd.	Found		Calcd.	Found	Calcd.	Found
Propenyl	PrI	4	51	138–140	20	1.4371	0.9774	65.09	65.11	$C_{13}H_{22}O_4$	64.42	64.43	9.16	9.33
$CH_3CH=$	*i*-PrI	4.5	35[c]	135–135.5	19	1.4404	.9842	65.09	65.09	$C_{13}H_{22}O_4$	64.42	64.20	9.16	9.20
CH—	BuI	5.5	50	148–151	20	1.4390	.9687	69.71	69.77	$C_{14}H_{24}O_4$	65.58	65.38	9.42	9.51
1-Butenyl	EtI	5	75	134–135	18	1.4367	.9745	65.09	65.31	$C_{13}H_{22}O_4$	64.42	64.27	9.16	9.25
CH_3CH_2-	PrBr	5	55	142–145	19	1.4375	.9637	69.71	69.92	$C_{14}H_{24}O_4$	65.58	65.35	9.42	9.48
CH=CH—	*i*-PrBr	6	67[d]	141–143	19	1.4400	.9710	69.71	69.73	$C_{14}H_{24}O_4$	65.58	65.62	9.42	9.41
	Allyl Br	1	79	144–145	17	1.4470	.9776	69.24	69.67	$C_{14}H_{22}O_4$	66.10	66.01	8.73	8.87
	BuBr	5	59	152–156	19	1.4390	.9561	74.33	74.55	$C_{15}H_{25}O_4$	66.62	66.75	9.70	9.78
	s-BuBr	7	21	159–160	28	1.4425	.9689	74.33	74.08	$C_{15}H_{26}O_4$	66.62	66.36	9.70	9.74
Isobutenyl	EtI	0.5	40[e]	140–141	24	1.4395	.9837	65.09	65.01	$C_{13}H_{22}O_4$	64.42	64.24	9.16	9.25
$(CH_3)_2C=CH$—														
1-Pentenyl	EtBr	3.5	60	154–157	27	1.4374	.9656	69.71	69.77	$C_{14}H_{24}O_4$	65.58	65.41	9.42	9.56
$CH_3CH_2CH_2$-	PrBr	3	65	161–163	26	1.4381	.9551	74.33	74.49	$C_{15}H_{26}O_4$	66.62	66.42	9.70	9.94
CH=CH—	*i*-PrI	3.5	70	160–163	28	1.4410	.9627	74.33	74.34	$C_{15}H_{26}O_4$	66.62	66.48	9.70	9.69
1-Isopentenyl	MeI	0.1	93	119–122	9	1.4348	.9647	65.09	65.68	$C_{13}H_{22}O_4$	64.42	64.17	9.16	9.16
$(CH_3)_2CH$-	EtI	0.3	88	141–142	19	1.4350	.9568	69.71	70.07	$C_{14}H_{24}O_4$	65.58	65.43	9.42	9.42
CH=CH—	PrBr	1	86	154–156	26	1.4349	.9487	74.33	74.52	$C_{15}H_{26}O_4$	66.62	66.27	9.70	9.68
	i-PrBr	0.5	86	152–153.5	26	1.4372	.9545	74.33	74.41	$C_{15}H_{26}O_4$	66.62	66.75	9.70	9.63
1-Hexenyl	MeI	0.8	82	164–166	27	1.4407	.9647	69.71	70.29	$C_{14}H_{24}O_4$	65.58	65.63	9.42	9.69
$CH_3CH_2CH_2$-	EtBr	3	58	168–169.5	28	1.4410	.9612	74.33	74.45	$C_{15}H_{26}O_4$	66.62	66.37	9.70	9.61
$CH_2CH=CH$—														

[a] In each case, the reaction of the alkyl halide with the sodium enolate was exothermic at the boiling point, and most of the material had reacted in the first few minutes of refluxing. [b] We are indebted to Miss Corris Hofmann for semimicro combustions. [c] Yield of the mixed ethyl and isopropyl esters obtained by alkylation in isopropyl alcohol was 82%, calculated as the ethyl ester. [d] Yield of the mixed ethyl and isopropyl esters obtained by alkylation in isopropyl alcohol was 83%. [e] The sodium enolate prepared from isobutylidene malonic ester was quite insoluble in alcohol. An impurity was removed from this ester by shaking with concd. aqueous ammonia.

sodium enolates (II) in this series. Apparently, partial decomposition occurs during the reaction with sodamide, and subsequent alkylation gives rather impure products in poor yield. The poor results obtained with sodamide in this series are in contrast with those obtained with secondary alkylidene malonic esters, which are alkylated in the highest yield by the sodamide procedure.[3a,b] Powdered sodium in inert solvents reacts readily with the primary alkylidene esters to give sodium enolates but, as in the series previously described, a part of the ester is reduced in the process, and alkylation gives a product containing the corresponding saturated ester as an impurity.

Experimental Part

The primary alkylidene malonic esters were prepared by condensing aldehydes with ethyl malonate, either in the presence of acetic anhydride,[6] or by a method using amine salts which will be described in a future communication.

Alkylation Procedures. A.—A description of the synthesis of ethyl (1-isopentenyl)-ethylmalonate will illustrate a procedure which gave good results in all of the alkylations. A solution of 8.05 g. of sodium (0.35 mole) in 300 cc. of absolute alcohol contained in a 500-cc. three-necked flask was cooled to −5°. Ethyl isopentylidene malonate, 79.8 g. (0.35 mole), was added dropwise with stirring during ten minutes. The solution was stirred for twenty minutes at −5 to −10°, after which 65.5 g. (0.42 mole) of ethyl iodide was added in one portion and the solution rapidly heated to boiling. The vigorous reaction which took place at the boiling point made it necessary to cool the flask momentarily in an ice-bath. The mixture was practically neutral to litmus after five minutes, and it was refluxed for only twenty minutes. The contents of the flask were cooled and diluted with 800 cc. of water. The ester layer was separated, and the water layer extracted four times with benzene. The combined ester and benzene extracts were washed twice with water, after which the benzene was removed in vacuum and the residue distilled through a Widmer column. The ester so prepared is one of nineteen substituted vinyl alkylmalonic esters described in Table I.

In the first preparations, the esters were shaken with concd. aqueous ammonia before the final distillation, in order to remove any alkylidene ester which might remain in the product. The portion of the alkylidene ester which is not alkylated is usually converted to a high boiling polymer during the reaction, however, and trial showed that the treatment with ammonia is superfluous, as there was no loss in weight on shaking with ammonia and no change in physical constants of the products, except in one case (*cf.* Table I). The alkylations carried out with the less active alkyl halides do not become completely neutral. In such cases, small aliquot portions were removed and titrated with standard acid from time to time. The refluxing was continued until the per cent. neutralization was constant.

In two cases in which relatively low yields of alkylated esters were obtained by the above procedure, alkylations

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(6) *Cf.* Schryver, *J. Chem. Soc.*, **63**, 1344 (1893); Kötz, *J. prakt. Chem.*, [2] **75**, 477 (1907); Boxer and Linstead, *J. Chem. Soc.*, 749 (1931).

also were carried out in isopropyl alcohol solution, under conditions recently used for the alkylation of alkylidene cyanoacetic esters.[3c] In both cases the yields were higher in isopropyl than in ethyl alcohol (see footnotes to Table I). This is evidence that alcoholysis is an important factor influencing the yields in this synthesis.

B.—Ethyl butylidenemalonate reacts with powdered sodium in ether or benzene solution, just as isopropylidene malonic ester does,[3a] giving a soluble sodium derivative. Methylation with dimethyl sulfate gave a 50–60% yield of ethyl (1-butenyl)-methylmalonate, b. p. 130–132° (24 mm.). The ester was purified by shaking with ammonia and refractionation, but quantitative reductions required only 86% of the theoretical quantity of hydrogen, showing the presence of a saturated ester in the product. In preparing a disubstituted barbituric acid derivative from this partially reduced ester, by condensation with urea, in one case a small amount of 5-methyl-5-butylbarbituric acid, m. p. 179–179.5° (uncor.), was isolated,[7] proving the presence of ethyl butylmethylmalonate in the ester prepared by this method.

C.—Ethyl butylidenemalonate was treated with sodamide, in liquid ammonia solution and suspended in both ether and toluene. A sodium derivative was formed in each case, but alkylation in ether or toluene with both diethyl sulfate and allyl bromide gave poor yields (10 to 40%) of impure esters.

Summary

Primary alkylidene malonic esters, $RCH_2CH{=}C(COOEt)_2$, react with sodium ethoxide and sodium isopropoxide to give sodium derivatives of primary 1-alkenylmalonic esters, $[RCH{=}CHC(COOEt)_2]^-Na^+$. These sodium derivatives may be alkylated readily, giving substituted vinyl alkyl malonic esters of the type, $RCH{=}CH{-}C(R')(COOEt)_2$.

BRYN MAWR, PENNSYLVANIA
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[7] Summaire, *Bull. soc. chim.*, **33**, 189 (1923), reports m. p. 181°.

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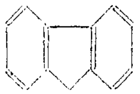
Remarks on the Structure of Fluorene

BY ERNST BERGMANN AND T. BERLIN

W. C. Lothrop has published[1] an interesting paper on the fine structure of fluorene. Some time ago, we experimented on similar lines.[2] Agreeing with the conclusions drawn by Lothrop to the effect that fluorene is not to be represented by exclusively one of the formulas I or II (and possibly IIa), we should like to supplement his evidence by reporting briefly some of our results.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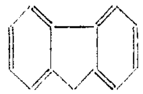
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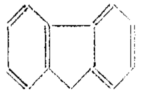
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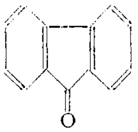
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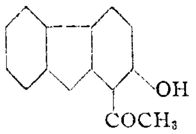
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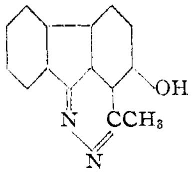
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In addition to the rearrangement of 2-allyloxyfluorene, we have also studied that of 2-acetoxyfluorene. Under the influence of aluminum chloride, an isomer is formed in moderate yield, to which we ascribe the formula III of 1-acetyl-2-hydroxyfluorene on the basis of its unreactivity toward hydroxylamine, III being an *o,o'*-disubstituted acetophenone.[3] This rearranging reaction appears to take place on form I, which, by the way, is also responsible for the formation of the 9-sodium derivative of fluorene.[4] On the other hand, it has been shown before,[5] that the Kolbe reaction with 2-hydroxyfluorene leads to two isomeric 2-hydroxyfluorenecarboxylic acids, most probably the 1- and the 3-compounds. By the same reasoning as above, they would owe their formation to the fine structures I and II, respectively.

Similar observations have been made in the series of fluorenones, the quinone-like properties of which would be accounted for most fittingly by formula (IV).[6] The rearrangement product of 2-acetoxyfluorenone is 1-acetyl-2-hydroxyfluorenone, as it forms with hydrazine hydrate a pyridazine (V), analogous to that we could obtain from 1-benzoylfluorenone. The rearrangement of 2-allyloxyfluorenone, however, gave two isomers,

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[1] Lothrop, THIS JOURNAL, **61**, 2115 (1939).

[2] T. Berlin, Thesis, Jerusalem University, 1939.

[3] See, *e. g.*, Claus and Foecking, *Ber.*, **20**, 3101 (1887); Baum, *ibid.*, **28**, 3207 (1895); V. Meyer and co-workers, *ibid.*, **29**, 830, *seq.* (1896).

[4] Compare Hueckel, *Z. Elektrochem.*, **43**, 779 (1937).

[5] German Patent 350,293; Friedlaender, *Fortschritte der Teerfarben-Industrie*, **13**, 599.

[6] Color! For the spectrum, see Böeseken and co-workers, *Rec. trav. chim.*, **44**, 188 (1925).