[CONTRIBUTION FROM THE FULMER CHEMICAL LABORATORY, THE STATE COLLEGE OF WASHINGTON]

Synthesis of β-Alkyl-α-bromoacrylic Ethyl Esters[1]

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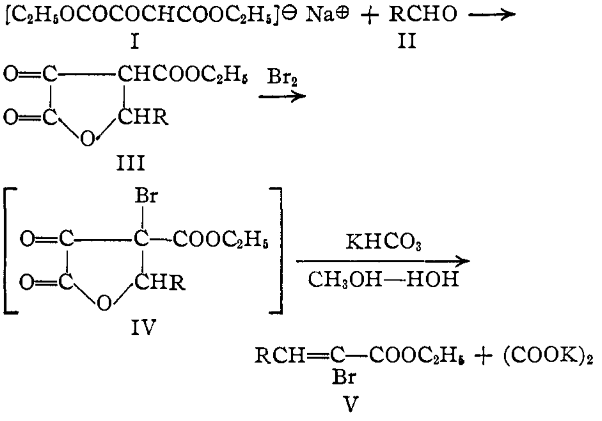
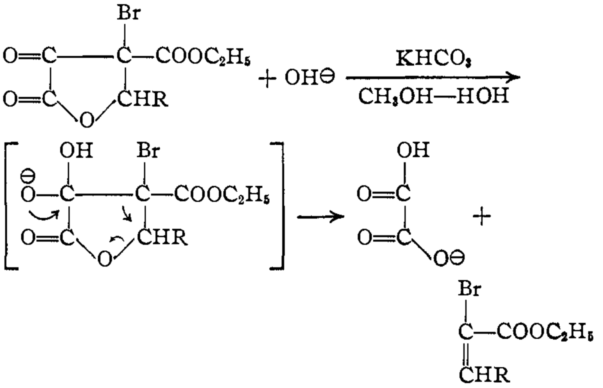
The synthesis of a number of β-alkyl-α-bromoacrylic ethyl esters is described and information pertinent to their characterization is presented. The reactions indicated generally have resulted in satisfactory yields of the desired esters.

In connection with other work under consideration it was of importance for us to ascertain the availability of β-alkyl-α-bromoacrylic ethyl esters. The few such esters that have previously been reported have usually been prepared by conventional methods, such as reaction of the silver salt of the corresponding acid with ethyl iodide,[3] esterification of the acid with ethanol in the presence of concentrated sulfuric acid,[3] or by treatment of the acid with diazomethane (to give the corresponding methyl ester).[4] Nield,[5] however, has reported a scheme of synthesis which would seem to have most attractive possibilities for general application to the synthesis of β-alkyl-α-bromoacrylic ethyl esters. Although this work was devoted primarily to synthesis of α-bromo-α,β-unsaturated ketones, two examples were cited where esters were the products (V, R = H and $(CH_3)_2CH$-).



It was decided to investigate this scheme of synthesis more thoroughly so as to determine its value as a general method of preparing esters of the type V. The condensation of aldehydes (II) with sodium diethyl oxalacetate (I) proceeded readily in all cases in yields of 55–75%. Although this condensation has been known for some time,[6] it is of interest to point out that in principle it closely resembles the Stobbe condensation which has been the subject of recent investigation.[7]

The α-keto-β-carbethoxy-γ-alkylbutyrolactones (III) were brominated in 80% aqueous methanol. The resulting α-keto-β-bromo-β-carbethoxy-γ-alkylbutyrolactones (IV), most probably formed as intermediates, were not isolated, but they were converted directly to the desired esters by addition of potassium bicarbonate to the reaction mixture. This interesting reaction probably proceeds by way of alkaline cleavage of the carbon–carbon bond followed by elimination of a hydrogen oxalate ion to give the β-alkyl-α-bromoacrylic ethyl ester.



In most cases yields of the β-alkyl-α-bromoacrylic ethyl esters ranged from 60–70% (Table I). In the case of ethyl α-bromocrotonate a sample of analytical purity was not obtained even after fractional distillation. It seems probable, however, that the composition of this substance is substantially ethyl α-bromocrotonate, as it was possible to saponify the material to yield α-bromocrotonic acid. This was in turn characterized by a neutralization equivalent and by conversion to a *p*-bromophenacyl ester and a *p*-bromoanilide.

Experimental[8]

α-Keto-β-carbethoxy-γ-alkylbutyrolactones.—In 350 ml., of absolute ethanol (commercial) was placed 114 g. (92%, 0.5 mole) of sodium diethyl oxalacetate, and to this mixture with vigorous stirring was added 0.655 mole of the appropriate aldehyde in one portion. With aldehydes of lower molecular weight an immediate evolution of heat occurred and the temperature rose to 35–40°. The temperature was then increased gradually by heating over a period of about one hour until a temperature of 45–50° was finally attained. In most cases the reaction was carried out over a period of 20–24 hours. In the case of aldehydes containing six or more carbon atoms the reaction time was 35–40 hours.

At the termination of the reaction period the mixture was cooled in an ice-bath to 25° or below and 250 ml. of water added. The mixture was then acidified to congo red with 150 ml. of 4 *N* hydrochloric acid. The mixture was then further diluted with 1 l. of water in a large separatory funnel and the organic layer removed. The aqueous layer was extracted with several portions of ether which were combined with the organic material previously separated, and the combined extracts washed with saturated salt solution and dried over anhydrous sodium sulfate.

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[1] Presented in part before the Division of Organic Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Ill., September 5, 1950.

[2] A portion of this work was carried out by George D. Wagner as an undergraduate research project.

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[5] C. H. Nield, THIS JOURNAL, **67**, 1145 (1945).

[6] (a) W. Wislicenus, *Ber.*, **26**, 2144 (1893); (b) E. E. Blaise and H. Gault, *Compt. rend.*, **142**, 452 (1902).

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[8] All melting points are corrected. The microanalytical work was performed by the Clark Microanalytical Laboratory, Urbana, Illinois.

TABLE I

β-ALKYL-α-BROMOACRYLIC ETHYL ESTERS

V, R =	Yield, %[a]	B.p., °C.	B.p., Mm.	$n^{25}D$	Formula	Analyses, %[b] Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
CH_3-[c]	70	76–77	13	1.4775	$C_6H_9BrO_2$	37.33	34.61	4.70	4.28
1[d]		78–79	14	1.4764			35.68		4.63
CH_3CH_2-	72	78–81	14	1.4752	$C_7H_{11}BrO_2$	40.60	38.37	5.36	4.99
3–4[e]		83–84	13	1.4760			37.54		4.85
9–11[f]		87–88	13	1.4745			40.13		5.23
$(CH_3)_2CH-$[g]	76	90–92	19	1.4704	$C_8H_{13}BrO_2$	43.45	43.00	5.92	5.94
$CH_3CH_2CH_2-$	72	111–113	22	1.4768	$C_8H_{13}BrO_2$	43.45	43.10	5.92	6.05
$(CH_3)_2CHCH_2-$	65	99–104	16	1.4712	$C_8H_{15}BrO_2$	45.97	45.94	6.43	6.73
$(CH_3CH_2)_2CH-$	62	104–106	16	1.4747	$C_{10}H_{17}BrO_2$	48.20	48.55	6.88	6.63
$CH_3(CH_2)_4-$	66	125–126	15	1.4730	$C_{10}H_{17}BrO_2$	48.20	48.46	6.88	6.93
$CH_3(CH_2)_5-$	49	99–104	1	1.4736	$C_{11}H_{19}BrO_2$	50.20	50.43	7.28	7.31

[a] Product once-distilled. [b] Analytical samples obtained by redistillation of the once-distilled product. [c] This ester had been reported previously by E. Preisweck, *Ber.*, **36**, 1085 (1903), as prepared by another method, b.p. 95–97° (15 mm.). This did not represent a sample of analytical purity, however, as a bromine analysis was 0.69% low. [d] This sample was from the first fraction obtained by the fractional distillation of 138 g. of once-distilled ethyl α-bromocrotonate. Of the several fractions investigated it afforded the analysis closest in agreement with the calculated value. [e] From fractions 3–4 obtained by fractional distillation. [f] From fraction 9–11 obtained by fractional distillation. [g] Reported by Nield (ref. 5), b.p. 30.5–31.5° (0.1 mm.), $n^{25}D$ 1.4688, carbon analysis 0.73% low.

TABLE II

α-KETO-β-CARBETHOXY-γ-ALKYLBUTYROLACTONES

III, R =	Yield, %	B.p., °C.	B.p., Mm.	M.p., °C.	$n^{25}D$	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
CH_3-[a]	66	103–104	0.3–0.4		1.4891	$C_8H_{10}O_5$				
CH_3CH_2-[a]	77	110–112	0.4–0.5		1.4867	$C_9H_{12}O_5$				
$CH_3CH_2CH_2-$[b]	55	121–125	0.5–1	33–34	1.4820	$C_{10}H_{14}O_5$	56.07	56.27	6.59	6.36
$(CH_3)_2CH-$[c]	58	128–132	0.2–0.4	55–57		$C_{10}H_{14}O_5$				
$(CH_3)_2CHCH_2-$	58			102–103		$C_{11}H_{16}O_5$	57.88	58.12	7.07	6.79
$(CH_3CH_2)_2CH-$[d]	59	131–134	2	34–36	1.4798	$C_{12}H_{18}O_5$	59.49	59.36	7.49	7.26
$CH_3(CH_2)_4-$	73			42–43		$C_{12}H_{18}O_5$	59.49	59.71	7.49	7.35
$CH_3(CH_2)_5-$	67			40–41		$C_{13}H_{20}O_5$	60.92	61.24	7.87	8.00

[a] Reported by A. Rossi and H. Schinz, *Helv. Chim. Acta*, **31**, 473 (1948) (R = CH_3-, $n^{19}D$ 1.4920; R = CH_3CH_2-, $n^{22}D$ 1.4873). [b] Reported by A. Rossi, *ibid.*, **31**, 1953 (1948), but no analytical data given (R = $CH_3CH_2CH_2-$, $n^{18.5}D$ 1.4832). [c] Reported by Nield (ref. 5). [d] The analytical sample was prepared by recrystallization from petroleum ether, the solution being cooled in a Dry Ice–Cellosolve-bath.

The ether was removed by distillation. Before the butyrolactones were distilled or crystallized, it was found desirable to remove the sizeable quantity of volatile materials present in the mixture. A procedure that was found quite satisfactory involved swirling the mixture in a flask fitted with a Kjeldahl still head, which was attached to a well-protected pump (a 250-ml. fore-trap is recommended as a considerable amount of material is collected). As the contents of the flask were vigorously swirled, the flask was heated by a steam-bath. Several of the γ-butyrolactones (III, R = CH_3-, CH_3CH_2-, $CH_3CH_2CH_2-$, $(CH_3)_2CH-$ and $(CH_3CH_2)_2CH-$, Table II) were then distilled at pressures of less than 1 mm.

In the case of some of the γ-butyrolactones of higher molecular weight (III, R = $CH_3(CH_2)_4-$ and $CH_3(CH_2)_5-$) purification could be effected by crystallization. A small amount of crystalline material for seeding purposes could be obtained by dissolving 5 g. of the residue in petroleum ether (b.p. 30–50°). The solution was chilled in a Dry Ice–Cellosolve mixture. The γ-butyrolactone precipitated as an oil which rapidly changed into a white, crystalline solid. The major part of the residue was then taken up in petroleum ether (3 ml. per g.). The solution was well cooled in an ice-bath to which salt had been added. The seed crystals were added and a copious, crystalline precipitate rapidly developed. After the mixture had been allowed to stand in an ice-bath for about one hour, the precipitate was removed by filtration. The filter cake was washed with 65 ml. of cold solvent and was then air dried. By concentrating the mother liquor and washings to a 50-ml. volume it was possible to collect a second crop of the product.

The γ-isobutylbutyrolactone (III, R = $(CH_3)_2CHCH_2-$), which has a considerably higher melting point (101–102°) than the other butyrolactones prepared, crystallized directly from the reaction mixture upon acidification. Ninety-two grams of the crude material was dissolved in 650 ml. of hot methanol. To this was added 350 ml. of water and the mixture was cooled in an ice-bath; yield 58.9 g. (58%); m.p. 99–100°.

All butyrolactones prepared with pertinent data are presented in Table II.

β-Alkyl-α-bromoacrylic Ethyl Esters.—To 0.2 mole of the γ-alkylbutyrolactone in 240 ml. of methanol and 60 ml. of water was added with stirring 32 g. (0.2 mole) of bromine over a period of 30–45 minutes. During the addition of bromine and subsequent operations, the reaction flask was cooled in an ice-bath so as to maintain the temperature of the reaction mixture at 5–10°.

To the mixture with continued stirring was added 70 g. (0.7 mole) of potassium bicarbonate over a period of about 15 minutes and during this time about 50 ml. of water was added gradually in small portions. The reaction mixture was stirred for one hour and fifteen minutes. During this period an additional 150 ml. of water was added in portions.

The reaction mixture was then filtered with suction to remove some undissolved material. The product, a heavy, yellow oil, separated from the filtrate, and the mixture was extracted with three 200-ml. portions of ether. The combined extracts were washed with 150 ml. of saturated salt solution and dried over anhydrous sodium sulfate. The ether was removed and the residue was distilled through a 15 cm. Vigreux column. In each case a middle fraction was taken for analysis. The experimental results are summarized in Table I.

Fractional Distillation of Esters.—Since the redistilled ethyl α-bromocrotonate (V, R = CH_3-) and ethyl β-ethyl-α-bromoacrylate (V, R = CH_3CH_2-) gave analytical results which were quite unsatisfactory, being over 2% low on carbon, fractional distillation of these two esters was undertaken in an attempt to obtain samples of analytical purity. Ethyl β-ethyl-α-bromoacrylate (170 g.) which had been obtained from several runs was distilled through a 30-cm. column packed with 3-mm. glass helices and provided with a heating jacket. Eleven fractions (15–20 g. each) were collected with refractive indices (25°) ranging from 1.4760 to 1.4745; b.p. 80–92° (13 mm.).

In a similar fashion, 130 g. of ethyl α-bromocrotonate was fractionally distilled, $n^{25}\mathrm{D}$ 1.4772–1.4778 with the exception of the first fraction where the value was 1.4764; b.p. 79–89 (20 mm.). The analytical results are included in Table I.

α-Bromocrotonic Acid.—Ethyl α-bromocrotonate (9.6 g., 0.05 mole) and 100 ml. of 20% potassium hydroxide were heated at 50–55° for 40 minutes. The mixture was cooled and acidified with 45 ml. of 6 *N* hydrochloric acid, the temperature of the mixture being carefully maintained at 10–15°. The mixture was extracted with three 75-ml. portions of ether and the combined extracts dried over anhydrous sodium sulfate. The ether was removed leaving a yellow, crystalline residue; yield 6.1 g. (74%); m.p. 91–98°. One recrystallization from water gave white crystals, m.p. 104–108°.[9] A sample was recrystallized several times for a neutral equivalent determination, m.p. 107.5–108.5°.

Calcd. for $C_4H_5BrO_2$: neut. equiv., 165.0. Found: neut. equiv., 164.4.

p-Bromophenacyl α-Bromocrotonate.—A *p*-bromophenacyl ester could readily be prepared,[10] m.p. 94–97°. A sample for analysis was obtained by two recrystallizations from ethanol, m.p. 96.5–97.5°.

Anal. Calcd. for $C_{12}H_{10}Br_2O_3$: C, 39.81; H, 2.78. Found: C, 39.79; H, 2.71.

p-Bromoanilide of α-Bromocrotonic Acid.—α-Bromocrotonyl chloride was prepared[11] by heating 2.4 g. of α-bromocrotonic acid and 2.9 g. of thionyl chloride under reflux for two hours. The 1.8 g. of the acid chloride obtained by distillation was added to 3.5 g. of *p*-bromoaniline dissolved in cold, dry benzene. The mixture was allowed to stand for one hour and the amine hydrochloride was removed by filtration. The benzene was removed *in vacuo* and the residue extracted with anhydrous ether. The ether was removed leaving a white, crystalline residue, yield, 3.8 g.; m.p. 92–93°. The material was twice recrystallized from 70% ethanol to give white needles, m.p. 93.5–94.5°.

Anal. Calcd. for $C_{10}H_9Br_2NO$: C, 37.65; H, 2.84. Found: C, 37.81; H, 2.80.

Acknowledgment.—This investigation was supported in part by a Frederick Gardner Cottrell grant from the Research Corporation.

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[9] α-Bromocrotonic acid melts at 106.5°, and the geometric isomer, α-bromoisocrotonic acid, melts at 92°, A. Michael and L. M. Norton, *Am. Chem. J.*, **2**, 15 (1880).

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The Bromination of Naphthalene[1]

BY FRANK R. MAYO[2a] AND WILLIAM B. HARDY[2b]

The bromination of naphthalene was investigated in several solvents at 20–25°. In carbon tetrachloride in the dark, about 15% addition to the nucleus normally accompanies substitution. Although both reactions are accelerated by ascaridole and retarded by air and isoamyl nitrite, the addition reaction is more susceptible to acceleration and inhibition. Under illumination, more than 80% of the bromine may react by addition. Substitution is accelerated by solvents of higher dielectric constant. Addition is less affected. In benzene and toluene solutions in the absence of light and catalysts, both addition and substitution in naphthalene occur without significant attack on the solvent. In toluene, in the presence of light or ascaridole, side-chain substitution in toluene becomes the predominant reaction, and addition to naphthalene is also accelerated, both at the expense of nuclear substitution in naphthalene. The ratio of side-chain substitution in toluene to addition to naphthalene increases as the bromine concentration decreases. It is concluded that, as in the benzene series, substitution in naphthalene occurs by a polar or molecular mechanism while addition takes place by a free radical mechanism. However, in contrast to benzene derivatives, there is a also a radical mechanism for substitution and a non-radical mechanism for addition, but these have not been fully identified and resolved. Some reactions of 1,2,3,4-tetrabromo-1,2,3,4-tetrahydronaphthalene are described.

The object of this research was to distinguish between addition and substitution reactions in the bromination of naphthalene in terms of polar and free radical mechanisms. Substitutions of chlorine and bromine in benzene are recognized as polar reactions,[3] while the photochemical or peroxide-catalyzed[4] additions to the nucleus proceed through a free radical-chain mechanism. Bromination and chlorination of toluene result in nuclear substitution under conditions favoring a polar mechanism, in side-chain substitution[5] or in both side-chain substitution and nuclear addition[4] by a free radical mechanism. Addition to toluene is favored over side-chain substitution by higher chlorine concentrations,[4] suggesting that the addition reaction is of higher order in chlorine, and the vapor phase photo-addition of chlorine to benzene is considered to involve both a chlorine atom and a chlorine molecule in the rate-determining step.[6] In all these instances, the distinction between the polar mechanism and the free radical mechanism is clear-cut, and the reaction may be directed to give nearly 100% of either type of product. Addition and substitution in the bromination of phenanthrene are similarly distinguished, although a polar mechanism for the addition has also been found.[3,7]

The halogenation of naphthalene has not been studied from the standpoint of competing substitution and addition reactions or of polar and radical

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[1] The work in carbon tetrachloride and "other solvents" is condensed from the Ph.D. Dissertation of William B. Hardy, University of Chicago, December, 1940. The remainder is the work of the senior author as Contribution No. 104 from the General Laboratories of the U. S. Rubber Co. Presented at the XII International Congress of Pure and Applied Chemistry, New York, September, 1951.

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