ganic bases. Strong alkalies and certain adsorbents also caused alteration of the carotenoid pigments. Esters of the xanthophylls were isomerized more slowly than the free xanthophylls.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

Condensation Reactions. II. Alkylidene Cyanoacetic and Malonic Esters

BY ARTHUR C. COPE, CORRIS M. HOFMANN, CORNELIA WYCKOFF AND ESTHER HARDENBERGH

A method for condensing aliphatic ketones with cyanoacetic ester was reported recently,[1] in which the reactants were heated in the presence of acetamide and acetic acid, the water formed in the condensation being removed continuously by slow distillation of the acetic acid. The method is not convenient for condensing ethyl cyanoacetate with low boiling ketones, which are removed during the distillation and must be used in large excess, or for inert ketones, which condense too slowly. In the previous paper it was pointed out that salts catalyze the condensation, and that the water formed could be removed by distillation with an inert solvent such as benzene. Variations of this general method have now been investigated, and experimental conditions developed under which a number of ketones have been condensed with ethyl cyanoacetate (see Table I).

Condensations.—In the preferred procedure, a mixture of the ketone, ethyl cyanoacetate, ammonium acetate, acetic acid and benzene is refluxed in a flask which is attached to a constant water separator (Fig. 1). Ammonium acetate and acetic acid are used in larger amounts for aromatic and hindered aliphatic ketones (Experimental Part, procedure B) than for reactive ketones (procedure A). Under these conditions, methyl ketones which are not branched at the α-carbon atom, as well as diethyl, dipropyl and diamyl ketones gave 75 to 87% yields of alkylidene esters. Aromatic ketones, such as acetophenone, propiophenone, caprophenone and benzophenone condensed to the extent of 60 to 80%. Sufficient branching of the carbon chain retards or inhibits the condensation. The yield of alkylidene cyanoacetic ester obtained from diisobutyl ketone was 40%, while no condensation occurred with pinacolone or camphor. Anthrone also failed to condense with ethyl cyanoacetate under these conditions.

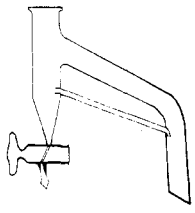


Fig. 1.—Constant water separator (one-third actual size), see ref. 11.

Piperidine acetate and acetic acid also have been used to condense a number of ketones with ethyl cyanoacetate. The condensations are slower than with ammonium acetate, and the procedure offers no advantage. Ammonium acetate is not a suitable catalyst for the condensation of aldehydes with ethyl malonate, however, while piperidine acetate and acetic acid are useful in certain cases. For example, isobutyraldehyde and isovaleraldehyde were condensed with ethyl malonate very readily by this method in 88 to 92% yield (procedure C). Similar conditions have been employed with other aldehydes (Table I), but the occurrence of side reactions beginning with the aldol condensation of the aldehydes diminished the yields of alkylidene esters to 25 to 59%. Propionaldehyde and butyraldehyde condensed with ethyl malonate most satisfactorily in the presence of acetic anhydride (procedure D).

Several of the alkylidene esters have been used as intermediates in the preparation of substituted vinyl alkylmalonic and cyanoacetic esters.[2]

Reductions.—Monoalkylmalonic and cyanoacetic esters have been prepared from a number of the alkylidene esters by hydrogenation in 90 to 97% yield. Palladinized charcoal was used as the catalyst in reducing the alkylidene cyanoacetic esters; platinum also may be used.[3] These catalysts as well as nickel[4] and copper chromite[5] are suitable for use in hydrogenating alkylidene malonic esters.

Ring Closure.—When benzyl methyl ketone was condensed with ethyl cyanoacetate in the presence of piperidine acetate in acetic acid solution, a small amount of a solid by-product was

(1) Cope, THIS JOURNAL, **59**, 2327 (1937).

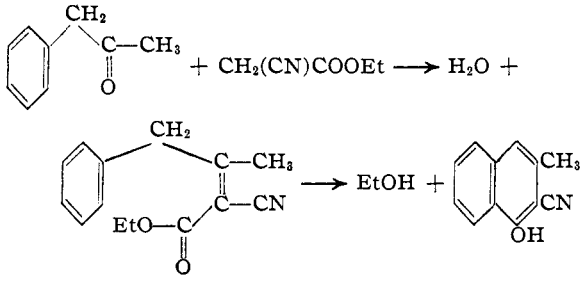
(2) Cope, Hartung, Hancock and Crossley, *ibid.*, **62**, 314 (1940), and preceding papers.

(3) U. S. Patent 2,176,018.

(4) Wojcik and Adkins, THIS JOURNAL, **56**, 2424 (1934).

(5) Connor, Folkers and Adkins, *ibid.*, **54**, 1140 (1932).

formed, m. p. after recrystallization 200–201°. It was subsequently found that this solid could be prepared easily by heating the normal condensation product, ethyl (1-methyl-2-phenyl-ethylidene)-cyanoacetate (I) to 200–220° in the presence of acetamide.

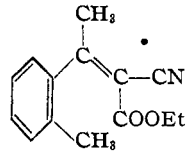


I II

The solid was proved to be 2-cyano-3-methyl-1-naphthol (II) by a series of reactions described in the Experimental Part.

After this work was completed, Marion and McRae[6] reported that a solid, m. p. 202°, was formed when the ester (I) was heated to 250° in glycerol solution. These authors correctly assigned structure (II) to their product by analogy with a similar ring closure of ethyl α-cyano-α-styrylacetate to 2-cyano-1-naphthol, which they had observed previously.[7]

Since (I) yielded (II) readily on heating with acetamide, it was of interest to determine whether related esters could be converted into naphthol or tetralone derivatives in the same way. No ring closure occurred with the other esters which were studied. Ethyl γ-phenylbutyrate was not affected by heating with acetamide, while γ-phenylbutyric acid was converted to the amide. Ethyl 4-phenyl-2-butenoate[8] was recovered after heating with acetamide. Ethyl (1-*o*-tolylethylidene)-cyanoacetate (III), which could give a β-



III

naphthol derivative if alcohol were eliminated from the ester and methyl groups, was also recovered unchanged after heating with acetamide.

(6) Marion and McRae, *Can. J. Research*, **18B**, 265 (1940).
(7) McRae and Marion, *ibid.*, **15B**, 480 (1937).
(8) Linstead and Williams, *J. Chem. Soc.*, 2742 (1926).

Experimental[9]

Condensation Methods.—The following methods were used in preparing the compounds listed in Table I. The preferred procedures are indicated by *italic* letters in the yield column of Table I.

A. Reactive Aliphatic Ketones with Ethyl Cyanoacetate.—Ethyl cyanoacetate[10] (56.5 g., 0.5 mole), the ketone (0.55 to 0.6 mole), ammonium acetate (3.85 g., 0.05 mole), glacial acetic acid (6.0 g., 0.1 mole) and 50 cc. of benzene were placed in a 500-cc. flask attached to a modified Dean and Stark constant water separator[11] (Fig. 1), which in turn was attached to a reflux condenser. The flask was heated in an oil-bath at 130 to 160°, and the water which distilled out of the mixture with the refluxing benzene was drawn off at intervals. The mixtures were usually refluxed for one hour after the formation of water ceased.[12] Longer heating did not increase the yield. The total reaction time was usually two to six hours.

Two methods were used to purify the alkylidene cyanoacetic esters. The esters prepared from ketones with six or more carbon atoms are most easily purified by distillation. The reaction mixtures were cooled and washed with three 100-cc. portions of water. The washings were extracted with two small portions of benzene, and the benzene solutions were combined and distilled in vacuum through a Widmer column. This method may be used to purify all of the alkylidene esters, but the esters derived from ketones with four or five carbon atoms must be distilled carefully to ensure complete separation from small amounts of ethyl cyanoacetate.

The difficulty in these cases can be avoided as follows. The benzene solution containing the condensation product was washed with three 25-cc. portions of 10% sodium chloride solution, after which the benzene was removed in vacuum. The ester was then shaken for two to ten hours with a solution of 65 g. of sodium bisulfite in 260 cc. of water. The aqueous solution, containing the soluble sodium bisulfite addition compound of the ester,[13] was diluted with an equal volume of water and extracted four times with 25-cc. portions of benzene to remove ethyl cyanoacetate. The bisulfite solution was then cooled in ice and a cold solution of 28 g. of sodium hydroxide in 110 cc. of water was added with stirring. The ester layer was separated at once, and the aqueous layer extracted with benzene. The combined solutions were washed with very dilute hydrochloric acid and the product was distilled as before.[14]

B. Aromatic (and Hindered Aliphatic) Ketones with Ethyl Cyanoacetate.—Under the best experimental condi-

(9) All melting and boiling points are uncorrected.
(10) Obtained from the Benzol Products Co., Newark, N. J.
(11) Dean and Stark, *Ind. Eng. Chem.*, **12**, 486 (1920)
(12) Part of the ammonium acetate is dehydrated to acetamide during the condensation. The water layer (10 to 12 cc.) contains acetamide and acetic acid.
(13) Lapworth and McRae, *J. Chem. Soc.*, **121**, 2745 (1922); Cope and Hancock, THIS JOURNAL, **60**, 2904 (1938).
(14) We are indebted to Dr. James M. Sprague and Frederick W. Landau for details of the purification of ethyl (1-methylbutylidene)-cyanoacetate through its sodium bisulfite addition product. This method was used for the purification of the following alkylidene cyanoacetates: ethyl (1-methylpropylidene)-, ethyl (1-methylbutylidene)-, isopropyl (1-methylbutylidene)-, ethyl (1-ethylpropylidene)-, ethyl (1-methylhexylidene)- and ethyl (1,3-dimethylbutylidene).

TABLE I

ALKYLIDENE CYANOACETIC AND MALONIC ESTERS

Ethyl alkylidene cyanoacetate (or malonate)	Ketone or aldehyde[a] used in prepn.	Yield, %[b]	B. p., °C.	Mm.	$n^{25}D$	d^{25}_{25}	M_D Calcd.[y]	M_D Found	Exaltation[c]	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
1-Methylpropylidene cyanoacetate[d]	Methyl ethyl ketone	65–85 (*A*,C)	116–118	11	1.4650	1.0001	44.78	46.33	1.55	$C_9H_{13}O_2N$		
1-Methylbutylidene cyanoacetate[e]	Methyl propyl ketone	77–85 (*A*,B,C)	138–139	19	1.4650	0.9835	49.40	51.06	1.66	$C_{10}H_{15}O_2N$	7.73	7.81
1-Methylbutylidene cyanoacetate[f]	Methyl propyl ketone	80–85 (*A*,C)	143–146	25	1.4590	.9583	54.02	55.82	1.80	$C_{11}H_{17}O_2N$	7.17	7.10
1-Ethylpropylidene cyanoacetate[g,e]	Diethyl ketone	55–65 (A,C) 75 (*B*)	116–118	9	1.4653	.9855	49.40	50.99	1.59	$C_{10}H_{15}O_2N$	7.73	7.82
1-Methylpentylidene cyanoacetate	Methyl butyl ketone[g]	85 (C)	149–150	19	1.4652	.9709	54.02	55.74	1.72	$C_{11}H_{17}O_2N$	7.17	7.29
1,3-Dimethylbutylidene cyanoacetate[h]	Methyl isobutyl ketone	75 (*A*)	130–133	12	1.4658	.9684	54.02	55.98	1.96	$C_{11}H_{17}O_2N$	7.17	7.14
1-Propylbutylidene cyanoacetate[e,h]	Dipropyl ketone	52 (A) 80 (*B*)	136–137	11	1.4660	.9584	58.64	60.66	2.02	$C_{12}H_{19}O_2N$	6.69	6.69
Cyclohexylidene cyanoacetate[i]	Cyclohexanone	83 (*A*)	150–151	9	1.4950					$C_{11}H_{15}O_2N$		
1-Methylhexylidene cyanoacetate[h]	Methyl amyl ketone	80 (*A*)	143–145	11	1.4662	.9597	58.64	60.59	1.95	$C_{12}H_{19}O_2N$	6.69	6.66
1-Methylheptylidene cyanoacetate	Methyl hexyl ketone	80 (*A*,B)	124–125	2	1.4656	.9503	63.26	65.22	1.96	$C_{13}H_{21}O_2N$	6.27	6.11
1-Isobutyl-3-methyl butylidene cyanoacetate	Diisobutyl ketone	<5 (A) 40 (*B*)	116–118	3	1.4656	.9435	67.88	69.82	1.94	$C_{14}H_{23}O_2N$	5.90	5.86
1-Amylhexylidene cyanoacetate	Diamyl ketone[j]	48 (A) 87 (*B*)	138–139	1	1.4662	.9292	77.12	79.35	2.23	$C_{16}H_{27}O_2N$	5.28	5.16
1-Phenylethylidene cyanoacetate[d]	Acetophenone	60 (A) 69 (*B*)	136–137	2	1.5468	1.0925	59.65	62.60	2.95	$C_{13}H_{13}O_2N$	6.51	6.40
1-*o*-Tolylethylidene cyanoacetate	Methyl *o*-tolyl ketone[k]	47 (*B*)	141–143	3	1.5326	1.0678	64.27	66.74	2.47	$C_{14}H_{15}O_2N$	6.11	6.07
1-Phenylpropylidene cyanoacetate[e]	Propiophenone	73 (*B*)	136–138	2	1.5360	1.0674	64.27	67.13	2.86	$C_{14}H_{15}O_2N$	6.11	6.23
1-Phenylbutylidene cyanoacetate	Butyrophenone[m]	78 (*B*)	135–136	1	1.5318	1.0493	68.89	71.99	3.10	$C_{15}H_{17}O_2N$	5.76	5.93
1-Phenylhexylidene cyanoacetate	Caprophenone[m]	75 (*B*)	146–148	1	1.5231	1.0201	78.13	81.45	3.32	$C_{17}H_{21}O_2N$	5.16	5.21
1-Methyl-3-phenylpropylidene cyanoacetate	4-Phenylbutan-2-one[n]	64 (*B*)	167–168	3	1.5273	1.0594	68.89	70.80	1.91	$C_{16}H_{17}O_2N$	5.76	5.77
1-Methyl-2-phenylethylidene cyanoacetate[l,o]	Benzyl methyl ketone	76 (*B*)	139–140	1	1.5338	1.0761	64.27	66.35	2.08	$C_{14}H_{15}O_2N$	6.11	6.15
1-Phenylbenzylidene cyanoacetate[p,z]	Benzophenone	66 (*B*)	195–200 (m. p. 95–96°)	3						$C_{18}H_{15}O_2N$	5.05	5.03
Propylidene malonate[q]	Propionaldehyde	25 (C) 46 (*D*)	119–120	15	1.4402					$C_9H_{16}O_4$		
Butylidene malonate[r]	Butyraldehyde	59 (C) 60–70 (*D*)	122–124	10	1.4425					$C_{10}H_{18}O_4$		
Isobutylidene malonate[s]	Isobutyraldehyde	90–92 (*C*)	135–137	27	1.4398					$C_{10}H_{18}O_4$		
n-Pentylidene malonate	*n*-Valeraldehyde	44 (C)	146–147	23	1.4414	0.9829	60.47	61.53	1.06	$C_{12}H_{20}O_4$		
Isopentylidene malonate[u]	Isovaleraldehyde	88–90 (*C*)	149–150	26	1.4420	.9816	60.47	61.69	1.22	$C_{12}H_{20}O_4$		
n-Hexylidene malonate	*n*-Hexanal	40–46 (C)	162–164	27	1.4464	.9770	65.09	66.35	1.26	$C_{13}H_{22}O_4$	[v]	
2-Ethylbutylidenemalonate	2-Ethylbutanal	43–45 (C)	146–148	21	1.4450	.9749	65.09	66.31	1.22	$C_{13}H_{22}O_4$	[w]	

[a] Redistilled commercial products unless otherwise indicated. [b] Capital letters refer to condensation methods designated by these letters in the Experimental Part. *Italicized* letters indicate the preferred methods. [c] See Table III, ref. 1. [d] Described by Scheiber and Meisel, *Ber.*, **48**, 238 (1915). [e] Physical properties of these esters have been reported by Cowan and Vogel, *J. Chem. Soc.*, 1528 (1940), since this work was completed. [f] Isopropyl ester, prepared from isopropyl cyanoacetate. [g] Prepared from ethyl propylacetoacetate. [h] We are indebted to Miss Elizabeth M. Osman for data on these esters. [i] Harding, Haworth and Perkin, *J. Chem. Soc.*, **93**, 1943 (1908); also ref. 1. [j] Prepared by the method of Briese and McElvain, THIS JOURNAL, **55**, 1697 (1933). [k] Prepared in 76% yield by adding *o*-tolunitrile to two equivalents of methylmagnesium iodide, refluxing the ether solution one-half hour, distilling the ether and heating the residue on a steam-bath for one hour. [l] Described by Hugh and Kon, *J. Chem. Soc.*, 775 (1930). [m] From the Friedel–Crafts reaction. [n] From the hydrogenation of benzal acetone with palladinized charcoal catalyst. [o] Washed with dilute sodium hydroxide before distillation to remove any traces of the substituted naphthol (II). [p] Characterized by the hydrogenation of a 3-g. sample in acetone solution in the presence of palladinized charcoal, which gave 1.8 g. of ethyl benzhydrylcyanoacetate, m. p. and mixed m. p. with a sample prepared as by Kohler and Reimer, *Am. Chem. J.*, **33**, 339 (1905) 75–76°. [q] Kötz, *J. prakt. Chem.*, [2] **75**, 477 (1907). [r] See ref. 16. [s] Schryver, *J. Chem. Soc.*, **63**, 1344 (1893). [t] Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.12; H, 8.85. [u] Ruhemann and Cunnington, *J. Chem. Soc.*, **73**, 1011 (1898). [v] Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.59; H, 9.02. [w] Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.75; H, 9.25. [z] This product was purified by distillation and crystallization, or, more simply, by removing ethyl cyanoacetate and benzophenone by distillation in vacuum and crystallizing the residue from alcohol after treatment with decolorizing charcoal. [y] The value 3.12 was used for the atomic refraction of nitrogen, rather than 3.05 which was used in ref. 1; see Eisenlohr, *Z. physik. Chem.*, **79**, 142 (1912). [z] Birch and Kon, *J. Chem. Soc.*, **123**, 2448 (1923).

tions, ethyl cyanoacetate (28.3 g., 0.25 mole), the ketone (0.25 mole), ammonium acetate (3.85 g., 0.05 mole), acetic acid (12 g., 0.2 mole) and 50 cc. of benzene were placed in a flask attached to a constant water separator and refluxed for four to twelve hours (one hour or more after water stopped collecting in the separator). The mixture was cooled, washed with water and the product distilled as described in procedure A.

Simple aliphatic ketones could not be condensed with ethyl malonate by procedure A or B.

C. Isobutyraldehyde and Isovaleraldehyde with Ethyl Malonate.—Ethyl malonate (80 g., 0.5 mole), freshly distilled isobutyraldehyde (39.6 g., 0.55 mole), piperidine (1.7 g., 0.02 mole), acetic acid (6 g., 0.1 mole) and 50 cc. of benzene were refluxed under a constant water separator for three hours, after which the product was washed and distilled as in procedure A.[15]

This procedure was equally satisfactory for isovaleraldehyde, but not completely satisfactory for condensing other aldehydes listed in Table I with ethyl malonate, although it was used for that purpose. In each of the other cases, the aldol condensation of the aldehyde with itself was a competing reaction, and both low and high boiling by-products were formed. This procedure should be satisfactory for condensing ethyl malonate with aldehydes which do not undergo the aldol reaction readily. Reactive ketones also condensed with ethyl cyanoacetate satisfactorily under these conditions.

D. Butyraldehyde and Propionaldehyde with Ethyl Malonate.—Conditions similar to those employed by Boxer and Linstead[16] were used, except that the reaction mixtures were refluxed rather than heated in pressure bottles. Ethyl malonate (1 kg., 6.25 moles), freshly distilled butyraldehyde (900 g., 12.5 moles) and acetic anhydride (1 kg., 9.8 moles) were refluxed (bath temperature 130°) for twenty-four hours. The reaction mixture was then distilled through a Vigreux column until the b. p. reached 130°, after which the residue was fractionated through a Fenske type column in vacuum. Propionaldehyde was condensed in the same way.

Reductions.—The esters were dissolved in one to two volumes of alcohol and shaken with hydrogen at one to two atmospheres pressure in the presence of 1–2 g. of palladinized charcoal catalyst[17] per mole. The reductions were usually exothermic and rapid if the esters were pure. If no reduction occurred, the ester was redistilled, or the alcohol solution was heated with decolorizing charcoal, filtered, and hydrogenated as before. After the reduction had become very slow and the theoretical quantity of hydrogen had been absorbed (two to ten hours for 0.2 to 1.0 mole), the solution was filtered and distilled in vacuum. In some cases the reduced ester was washed with dilute hydrochloric acid to remove any bases formed through addition of hydrogen to the nitrile group. In this manner were prepared: ethyl *s*-butylcyanoacetate (90% yield), ethyl (1-methylbutyl)-cyanoacetate (90–97%), ethyl cyclohexylcyanoacetate (92%) and ethyl (1-methyl-2-phenylethyl)-cyanoacetate (94%). The last of these esters has not been described previously. Its properties were: b. p. 140–142° (2 mm.); $n^{25}D$ 1.4979; d^{25}_{25} 1.0446; M_D calcd., 64.74; found, 65.03.

Anal. Calcd. for $C_{14}H_{17}O_2N$: N, 6.06. Found: N, 6.00.

Several alkylidene malonic esters were hydrogenated in the same way, or in the presence of nickel[4] or copper chromite[5] catalysts at pressures of one hundred to two hundred atmospheres and temperatures sufficiently high to cause rapid hydrogenation. The following esters were prepared: ethyl ethylmalonate (90% yield, palladium catalyst); ethyl propylmalonate (90%, palladium); ethyl isopropylmalonate (96%, nickel); ethyl butylmalonate (93–96%, palladium); ethyl isoamylmalonate (96–97%, palladium, nickel, copper chromite).

2-Cyano-3-methyl-1-naphthol (II).—The substituted naphthol (II) may be prepared directly from benzyl methyl ketone and ethyl cyanoacetate, or the ester (I) may be isolated and then cyclized. The latter procedure offers no advantage, and gives about the same over-all yield.

Benzyl methyl ketone (13.4 g.), ethyl cyanoacetate (11.3 g.), ammonium acetate (1.5 g.), acetic acid (4.8 g.) and 50 cc. of benzene were refluxed under a constant water separator for three hours. The reaction mixture was placed in a Claisen flask, and the benzene removed in vacuum. Acetamide (35 g.) was added to the residue, which was then heated in a bath at 220° for one hour in an atmosphere of nitrogen. A small amount of alcohol distilled out of the mixture during this period. The residue was cooled, treated with 100 cc. of water and filtered. The crude solid (17.3 g.) was purified by sublimation or distillation and crystallization from alcohol and water; yield 8.6 g. (47%). A preparation of (II) from 5 g. of (I), which was heated with 10 g. of acetamide for one hour at 220°, gave 1.6 g. of the solid, m. p. 200–201°. Small amounts of (II) were formed when (I) was heated to 200–220° in the presence of ammonium acetate or piperidine acetate, but no appreciable amount was formed when (I) was heated alone at 200° for four hours.

Structure of II.—Analysis of (II) gave the following results: *Anal.* Calcd. for $C_{12}H_9ON$: C, 78.67; H, 4.95; N, 7.65; mol. wt. and neutral equivalent, 183.2. Found: C, 78.47; H, 5.06; N, 7.74; mol. wt., 187 (f. p. in dioxane); neutral equivalent, 184.8.

When (II) was coupled with diazotized aniline in alkaline solution, a brick-red azo compound was precipitated. Oxidation of 1 g. of (II) with boiling potassium permanganate gave 0.2 g. of phthalic acid, identified by its m. p. and conversion to phthalic anhydride on heating. Three g. of (II), 3 g. of sodium chloride, 15 g. of zinc chloride and 3 g. of zinc dust were heated to 300° during ten minutes and kept at that temperature for five minutes.[18] The mixture was cooled, treated with dilute hydrochloric acid and filtered. The solid was purified by sublimation and recrystallization from hexane. The product was 3-methyl-1-naphthol,[19] m. p. 89–89.5° (0.9 to 1.4 g.). A small sample of the 3-methyl-1-naphthol was oxidized to 2-methyl-1,4-

(15) The same yield of ethyl isobutylidenemalonate was obtained in six hours from a reaction mixture in which the acetic acid was omitted.

(16) Boxer and Linstead, *J. Chem. Soc.*, 749 (1931).

(17) Hartung, THIS JOURNAL, **60**, 3372 (1928).

(18) These conditions are similar to those used by Clar, *Ber.*, **72**, 1645 (1939), for deoxygenating polynuclear compounds. Elimination of the phenolic hydroxyl was anticipated, but the results obtained confirm the structure of (II).

(19) Fittig, *Ann.*, **255**, 263 (1889); **314**, 73 (1901); Cason, THIS JOURNAL, **63**, 831 (1941).

napthoquinone (m. p. 102–103.5, mixed m. p. 103–104°) by the method described in "Organic Syntheses"[20] for oxidizing 1-naphthol.

The following results were obtained on heating other esters with acetamide: ethyl γ-phenylbutyrate (9.3 g.), was heated with 20 g. of acetamide for fifteen hours at 220°; 7.6 g. of the ester was recovered. γ-Phenylbutyric acid (6.4 g.), heated with 15 g. of acetamide at 220° for two hours, gave 2.9 g. of γ-phenylbutyramide, m. p. 83–84°. Ethyl 4-phenyl-2-butenoate[8] (5 g.) and 10 g. of acetamide, were heated for one and one-half hours at 220°; 3.8 g. of the ester was recovered. Ethyl (1-*o*-tolylethylidene)-cyanoacetate III (Table I) (10 g.) and acetamide (20 g.), were heated at 220° for one and one-half hours; 6.8 g. of the ester was recovered.

Summary

Experimental conditions are described under which both aliphatic and aromatic ketones, including benzophenone, can be condensed with ethyl cyanoacetate to give ethyl alkylidene cyanoacetates. The condensing agents are ammonium acetate and acetic acid. Piperidine acetate and acetic acid are used under similar conditions to condense certain aldehydes with ethyl malonate. Conditions suitable for the hydrogenation of these esters are described.

The condensation product of benzyl methyl ketone and ethyl cyanoacetate, ethyl (1-methyl-2-phenylethylidene)-cyanoacetate (I), loses alcohol when heated in acetamide solution, producing 2-cyano-3-methyl-1-naphthol (II).

(20) "Organic Syntheses," Coll. Vol. I, 1932, p. 41, and p. 375.

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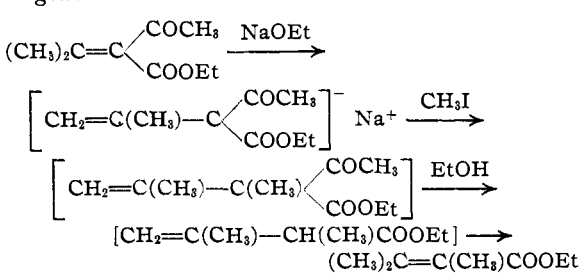
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

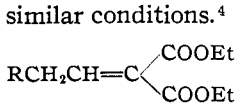
The Introduction of Substituted Vinyl Groups. VIII. Acetoacetic Ester Series[1]

BY ARTHUR C. COPE AND CORRIS M. HOFMANN

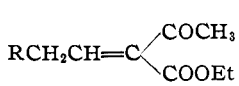
When ethyl isopropylideneacetoacetate is treated with alcoholic sodium ethoxide and methyl iodide, ethyl trimethylacrylate is formed.[2] The sequence of reactions involved is the formation of a sodium enolate from the ester by three-carbon tautomerism, followed by alkylation, cleavage (alcoholysis) of the acetyl group, and migration of the double bond.



Although the alkylation of ethyl isopropylidenemalonate in alcohol solution is accompanied by partial cleavage,[3] primary alkylidene malonic esters (I) can be alkylated successfully under similar conditions.[4]

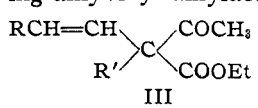


I

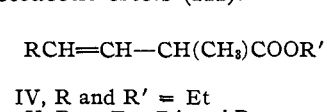


II

It consequently seemed possible that primary alkylidene acetoacetic esters (II) could be alkylated in alcohol solution without cleavage, producing alkyvinyl alkylacetoacetic esters (III).



III



IV, R and R′ = Et
V, R = Et; R′ = *i*-Pr
VI, R = *i*-Pr; R′ = Et
VII, R and R′ = *i*-Pr

A number of primary alkylidene acetoacetic esters (Table I) were prepared by condensing aldehydes with ethyl and isopropyl acetoacetates. Two of them, ethyl butylideneacetoacetate and ethyl isopentylideneacetoacetate, were converted into sodium enolates with alcoholic sodium ethoxide and treated with methyl iodide. The products of the vigorous reactions which occurred were the β,γ-unsaturated monocarboxylic esters, IV and VI (Table II). Cleavage consequently had occurred just as in the ethyl isopropylideneacetoacetate methylation,[2] but the double bond had not migrated to the α,β-position. The double bond probably failed to shift in these cases because the alkylations proceeded very rapidly, removing the sodium enolates (and sodium ethoxide) which would catalyze isomerization of the products.

Methylation of the corresponding isopropyl alkylideneacetoacetates in isopropyl alcohol solu-

(1) From a dissertation presented to the Faculty of the Graduate School of Bryn Mawr College by Corris M. Hofmann in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Jupp, Kon and Lockton, *J. Chem. Soc.*, 1642 (1928).

(3) Cope and Hancock, THIS JOURNAL, **60**, 2644 (1938).

(4) Cope, Hartung, Hancock and Crossley, *ibid.*, **62**, 314 (1940).