[Contribution from the Chemistry Department of Boston University]

Decarboxylative Condensation. α-Alkylcinnamic Acids from Aromatic Aldehydes and Alkylmalonic Acids[1]

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The decarboxylative condensation occurring when a pyridine solution of aromatic aldehyde, alkylmalonic acid and piperidine is warmed on the steam-bath produces α-alkylcinnamic acids. The presence of electron-withdrawing groups on the benzaldehyde *m*- and *p*-positions favors the reactions. The trend in yield is downward as the alkyl group of the alkylmalonic acid becomes larger.

Exploratory experiments performed earlier in these laboratories showed that benzaldehyde and methylmalonic acid react in pyridine solvent containing piperidine to give α-methylcinnamic acid[2a,b] (I, Ar = C_6H_5, R = CH_3). We undertook to develop and to exploit this extension of the Doebner condensation. The results, as described in the present paper, indicate the process to be

$$\text{ArCHO} + \text{RCH(COOH)}_2 \longrightarrow \underset{\text{I}}{\text{ArCH=C(R)COOH}}$$

a generally effective and convenient method for the preparation of α-alkylcinnamic acids I.

Yield *vs.* Reaction Conditions.—At the outset it was considered desirable to find and to use one set of directions for all the aldehyde–alkylmalonic acid combinations. To help in defining an acceptable set of reaction conditions, the dependence of yield on reaction parameters was examined. As far as reaction temperature is concerned, it was found that the initial experiments, which were carried out at the boiling point of pyridine, could be improved by lowering the temperature to 100°. To illustrate, a boiling pyridine solution of 0.03 mole of benzaldehyde, 0.035 mole of ethylmalonic acid and 0.035 mole of piperidine furnished α-ethylcinnamic acid after 2.5 hours in 18% yield. The same mixture on the steam-bath for one day gave the same product in more than double the yield. In both runs the yield of carbon dioxide was close to the theoretical 0.035 mole. In another set of experiments benzaldehyde, methylmalonic acid and piperidine (1:1:1) in boiling pyridine solution for 1.5 hours gave α-methylcinnamic acid in 68% yield; when the same reactants in pyridine were heated on the steam-bath for 14 hours, the yield of α-methylcinnamic acid went up to 80%. In the direction of lower temperatures, a pyridine solution of 3-nitrobenzaldehyde, methylmalonic acid and piperidine (equimolar amounts) at 50° for 10 days gave carbon dioxide in 92% yield and α-methyl-3-nitrocinnamic acid in 69% yield. The same mixture on the steam-bath for 6 hours gave carbon dioxide and α-methyl-3-nitrocinnamic acid in 100 and 62% yields, respectively. Because of the convenience of heating with steam as well as the shorter reaction time, it was decided to standardize at a 100° reaction temperature.

The effect of piperidine concentration was followed by using pyridine solutions containing benzaldehyde and ethylmalonic acid in equimolar amounts together with piperidine in various proportions. The temperature was held at 100° for at least one day, after which time the temperature in some of the experiments was raised to the boiling point. In the absence of piperidine, no α-ethylcinnamic acid was obtained, and 98% of the benzaldehyde could be recovered. As the proportion of piperidine was increased the yield of α-ethylcinnamic acid also was increased. When an equimolar amount of piperidine was used, the yield was a maximum, both greater and lesser proportions giving poorer results. On the basis of these experiments, the molar ratio of alkylmalonic acid to piperidine was set at 1:1. It is noteworthy that when the benzaldehyde, ethylmalonic acid and piperidine were in the molar ratio of 1:1:2 no unreacted benzaldehyde was recovered although the yield of α-ethylcinnamic acid was only 18%. Presumably the benzaldehyde was transformed to benzaldipiperidine,[3] which was discarded in the isolation procedure.

Experiments bearing on the ratio of alkylmalonic acid to aldehyde showed that benzaldehyde, ethylmalonic acid and piperidine in molar ratios of 1:1:1, 1:2:2 and 1:4:4, when warmed in pyridine solutions at 100° for one day, gave carbon dioxide in 95–97% yield and α-ethylcinnamic acid in 40, 47 and 60% yields, respectively. Although somewhat better results were obtained with a 1:4 molar ratio of benzaldehyde to ethylmalonic acid, it was considered that the usefulness of the process could be amply demonstrated with the malonic acids at the more economical ratio of 1:2.

From these preliminary trials, there emerged a general procedure, *viz.*, of warming a pyridine solution of aldehyde, alkylmalonic acid and piperidine (molar ratio 1:2:2) on the steam-bath at least to such time as most of the carbon dioxide had been evolved. To some extent these reaction conditions were arbitrary. Certainly it would be largely coincidental if the optimum conditions for any particular pair of reactants proved to be the same as our standardized conditions. Nevertheless, these

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[1] Abstracted from the Dissertation submitted by Elliot Berman to the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1956.

[2] (a) Unpublished work. *Cf.* E. H. Rosenberg, Dissertation for the degree of Master of Arts, Boston University, 1953. (b) For related reactions see, *inter alia*, C. M. Stuart, *J. Chem. Soc.*, **43**, 403 (1883), who employed Perkin condensation conditions; W. M. Rodionow and E. A. Postovskaja, This Journal, **51**, 841 (1929), who employed Knoevenagel conditions; V. M. Rodionov and K. P. Preobrazhenskaya, *Zhur. Obshchei Khim.*, **24**, 1971 (1954) [*C. A.*, **49**, 14681 (1955)], who combined the methylimine of benzaldehyde with alkylmalonic acids; and C. Mannich and co-workers, *Ber.*, **53**, 1368 (1920); **55**, 3486, 3504 (1922); **57**, 1116 (1924), who prepared α-alkylacrylic acids by way of Mannich condensations of formaldehyde and alkylmalonic acids.

[3] *Cf.* S. Patai, J. Edlitz-Pfeffermann and Z. Rozner, This Journal, **76**, 3446 (1954).

directions served their purpose, and were applied in all subsequent condensations.

Yield *vs.* Structure.—By means of this procedure, we tried the synthesis of α-alkylcinnamic acids (I) with a variety of benzaldehydes together with methyl-, ethyl-, allyl-, butyl- and undecenylmalonic acids. Tables I, II and III summarize the results. As a rough approximation, the yields of α-methylcinnamic acids from the Doebner reaction with methylmalonic acid (Table I) were as

TABLE I

α-METHYLCINNAMIC ACIDS FROM THE REACTION OF METHYLMALONIC ACID AND BENZALDEHYDES

Benzaldehyde	Reacn. time, hr.	Yield, %	M.p., °C.	M.p. analytical sample, °C.	M.p., °C., reported	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
Unsubstituted	27	96	79 – 80	80 – 81	80 – 81[a]	$C_{10}H_{10}O_2$	74.1	6.2	74.1	6.3
2-Methyl	23	60	98 – 99	99 – 99.5		$C_{11}H_{12}O_2$	75.0	6.9	75.1	7.0
3-Methyl	24	86	56 – 57	56.5– 57.5		$C_{11}H_{12}O_2$	75.0	6.9	75.1	7.0
4-Methyl	42	68	162 –165	168 –169	169 –170[b]	$C_{11}H_{12}O_2$	75.0	6.9	74.7	6.9
4-Isopropyl	24	77	89 – 90		90 – 91[c]					
2,4,6-Trimethyl	21	0[d]								
2-Methoxy	31	85	103 –104[e]		104 –106[c,f]					
3-Methoxy	42	89	90.5– 91.5	91.5– 92	91 – 92[f]	$C_{11}H_{12}O_3$	68.7	6.3	68.7	6.3
4-Methoxy	26	78	154.5–155.5		154 –157[c,f]					
2,3-Dimethoxy	10	99	122 –125	125 –126[g]		$C_{12}H_{14}O_4$	64.9	6.4	65.3	6.6
3,4-Dimethoxy	14	91	140.5–141.5	142 –142.5	140 –141, 144[h,i]	$C_{12}H_{14}O_4$	64.9	6.4	64.9	6.4
3,4-Methylenedioxy	31	79	199 –199.5		200[i]					
3-Methoxy-4-hydroxy	33	34	165 –166	165.5–166.5	167 –168[j]	$C_{11}H_{12}O_4$	63.4	5.8	63.4	5.9
2-Hydroxy	13	65[k]	134 –134.5		138[l]					
3-Hydroxy	20	59	138.5–139	138 –138.5[m]		$C_{10}H_{10}O_3$	67.4	5.7	67.5	5.7
4-Hydroxy	24	69[n]	205 –206	205 –206		$C_{10}H_{10}O_3$	67.4	5.7	67.6	5.7
4-Dimethylamino	38	70[o]	203 –204	204 –204.5		$C_{12}H_{15}O_2N$	70.2	7.4	70.4	7.5
2-Chloro	14	86	108 –110	109.5–110.5[g]		$C_{10}H_9O_2Cl$	61.1	4.6	61.0	4.6
3-Chloro	36	99	106 –107		106[p]					
4-Chloro	24	96	166 –167	166 –167		$C_{10}H_9O_2Cl$	61.1	4.6	60.8	4.6
2,4-Dichloro	15	77	145.5–147	146.5–147.5		$C_{10}H_8O_2Cl_2$	52.0	3.5	51.4	3.5
3,4-Dichloro	24	93	151 –152	151.5–152		$C_{10}H_8O_2Cl_2$	52.0	3.5	51.3	3.4
2,6-Dichloro	30	34[q]	154.5–155.5	156 –156.5		$C_{10}H_8O_2Cl_2$	52.0	3.5	51.8	3.4
4-Bromo	20	96	174 –175	174.5–175.5		$C_{10}H_9O_2Br$	49.8	3.8	49.6	3.8
2-Nitro	16	37[r]	196 –196.5	196 –196.5		$C_{10}H_9O_4N$	58.0	4.4	58.1	4.4
3-Nitro	9.5	98[s]	202 –203[t]		199.5–200.5[u,p]					
4-Nitro	24	89	205 –206.5	205.5–206.5[v]		$C_{10}H_9O_4N$	58.0	4.4	58.1	4.6
2,4,6-Trimethyl-3,5-dinitro	19	14	295	295[w]		$C_{13}H_{14}O_6N_2$	53.1	4.8	53.5	4.9
Furfural	20	61	114.5–115		116[x]					
1-Naphthaldehyde	34	71	155 –156	155.5–156	151[y]	$C_{14}H_{12}O_2$	79.2	5.7	79.1	5.7

[a] *Cf.* E. H. Rosenberg, footnote 2a. [b] K. v. Auwers, *Ann.*, **413**, 253 (1917). [c] W. H. Perkin, *J. Chem. Soc.*, **31**, 388 (1877). [d] No acidic material was isolated, and 2,4,6-trimethylbenzaldehyde could be recovered almost completely (98%) as its 2,4-dinitrophenylhydrazone derivative, m.p. 230–234°. Two crystallizations from absolute alcohol gave red crystals, m.p. 234–236° (preliminary softening at 230°). *Anal.* Calcd. for $C_{16}H_{16}N_4O_4$: C, 58.5; H, 4.9. Found: C, 58.4; H, 5.0. When malonic acid was substituted for methylmalonic in a 22-hour run, 80% of the calculated amount of carbon dioxide and 54% of a mixture of (*cis* and *trans*?) acids, m.p. 100–131°, were obtained. In another experiment with malonic acid, after 83 hours, 84% of carbon dioxide and 22% of thrice crystallized *trans*-2,4,6-trimethylcinnamic acid, m.p. 176–178°, were obtained [G. Lock and E. Beyer, *Ber.*, **72**, 1064 (1939); R. D. Kleene, F. H. Westheimer and G. W. Wheland, THIS JOURNAL, **63**, 791 (1941)]. [e] α-Methyl-2-methoxycinnamic acid, as a 1.1 × 10^{-5} *M* solution in 95% ethanol, showed absorption maxima at 266 mμ (ε 20,500) and at 306 mμ (ε 11,400). [f] E. H. Woodruff and T. W. Conger, THIS JOURNAL, **60**, 465 (1938). [g] Crystallized from ether–ligroin. [h] F. Tiemann and R. Kraaz, *Ber.*, **15**, 2070 (1882). [i] W. S. Ide and J. S. Buck, THIS JOURNAL, **62**, 425 (1940). [j] F. Tiemann and R. Kraaz, *Ber.*, **15**, 2059 (1882). [k] When equimolar amounts of salicylaldehyde and methylmalonic acid were allowed to react for 9 days at 50°, carbon dioxide (89%), α-methyl-2-hydroxycinnamic acid (68%) and 3-methylcoumarin (2%), m.p. 88–90°, were obtained; *cf.* W. H. Perkin, *J. Chem. Soc.*, **28**, 10 (1875). [l] K. Fries and W. Volk, *Ann.*, **379**, 90 (1911). [m] Crystallized from water. [n] Control experiments showed that under the conditions of its formation, approximately 10% of the α-methyl-4-hydroxycinnamic acid decomposed by decarboxylation. [o] The reaction mixture was acidified with acetic instead of hydrochloric acid. [p] W. v. Miller and Rohde, *Ber.*, **23**, 1895 (1890). [q] The yield of carbon dioxide was 88%. The same reaction with malonic acid used instead of methylmalonic acid gave 94% of the expected amount of carbon dioxide after 30 hours, together with a 34% yield of 2,6-dichlorocinnamic acid, m.p. 193–194° [G. Lock and E. Bayer, *Ber.*, **72**, 1064 (1939)]. Control experiments showed that the 2,6-dichlorobenzaldehyde starting material decomposes under the Doebner reaction conditions. [r] Very little evolution of carbon dioxide was noted in a control experiment in which α-methyl-2-nitrocinnamic acid was exposed to the conditions of its formation; 91% of the cinnamic acid could be recovered unchanged. The Doebner reaction using malonic acid instead of methylmalonic acid but otherwise the same conditions gave carbon dioxide in 103% of the calculated amount in 12 hours; however, 2-nitrocinnamic acid, m.p. 238–239°, was produced in only 36% yield; *cf.* I. Tanasescu, *Bull. soc. chim.*, [4] **41**, 1074 (1927). [s] When the ratio of 3-nitrobenzaldehyde to methylmalonic acid was 1 : 1, although evolution of carbon dioxide was quantitative after 6 hours, the yield of α-methyl-3-nitrocinnamic acid dropped to 62%. [t] α-Methyl-3-nitrocinnamic acid, as a 3.6 × 10^{-5} *M* solution in 95% alcohol, had an absorption maximum at 258 mμ (ε 22,400). [u] R. W. Maxwell and R. Adams, THIS JOURNAL, **52**, 2959 (1930). [v] Crystallized from absolute alcohol. [w] Purified by sublimation at 180–190° (0.01 mm.). [x] Kasiwagi, Beilstein's "Handbuch der Organischen Chemie," Series 4, Vol. 18 (second supplement), 1952, p. 274. [y] L. Rousset, *Bull. soc. chim.*, [3] **17**, 812 (1897).

TABLE II

α-ETHYLCINNAMIC ACIDS FROM THE REACTION OF ETHYLMALONIC ACID AND BENZALDEHYDES

Benzaldehyde	Reacn. time, hr.	Yield, %	M.p., °C.	M.p., °C., analytical sample	M.p., °C., reported	Formula	Analyses, % Calcd. C	H	Found C	H
Unsubstituted[a]	24	60	103–104		104[b]					
4-Isopropyl	43	40	126–126.5		123[c]					
2-Methoxy	24	55	110–110.5	110–110.5		$C_{12}H_{14}O_3$	69.9	6.8	70.1	6.9
4-Methoxy	36	43	131.5–133	132.5–133.5	123–124[c]	$C_{12}H_{14}O_3$	69.9	6.8	69.7	6.8
3,4-Methylenedioxy	48	30	130–131	131–131.5		$C_{12}H_{12}O_4$	65.4	5.5	65.3	5.5
2-Carboxy-3,4-dimethoxy	6	0[d]								
3-Nitro	48	64[e]	139–140	139–140		$C_{11}H_{11}O_4N$	59.7	5.0	59.4	5.0
4-Nitro	20	60	169–170		170[f]					

[a] Benzaldehyde and ethylmalonic acid reactants were taken here in a molar ratio of 4:1. [b] E. H. Rosenberg, footnote 2a. [c] W. H. Perkin, *J. Chem. Soc.*, **31**, 388 (1877). [d] This reaction between 2-carboxy-3,4-dimethoxybenzaldehyde (opianic acid) was carried out with the aldehyde and ethylmalonic acid in equimolar amounts. Fine light yellow needles separated on allowing the acidified reaction mixture to stand overnight. The solid, which was collected, washed on the funnel with water and air dried, proved to be the opianic acid starting material, m.p. 147–148°, in quantitative recovery. [e] In another run, when equimolecular amounts of ethylmalonic acid and 3-nitrobenzaldehyde were allowed to react for 19 hours at 100°, 98% of the calculated amount of carbon dioxide together with 48% of the calculated amount of α-ethyl-3-nitrocinnamic acid was obtained. [f] Vorländer, Beilstein's "Handbuch der Organischen Chemie," Series 4, Vol. 9 (first supplement), 1932, p. 259.

TABLE III

α-ALKYLCINNAMIC ACIDS FROM THE REACTION OF ALKYLMALONIC ACIDS AND BENZALDEHYDES

Benzaldehyde	Alkyl	Reacn. time, hr.	Yield, %	M.p., °C.	M.p., °C., analytical sample	Formula	Analyses, % Calcd. C	H	Found C	H
4-Isopropyl	Allyl[a]	24	24	82 - 84	86.5- 87	$C_{15}H_{18}O_2$	78.2	7.9	78.5	7.9
2-Methoxy	Allyl[a]	80[b]	46[c]	113 -114	114.5-115	$C_{13}H_{14}O_3$	71.5	6.5	71.4	6.5
3-Nitro	Allyl	25	67[d]	126 -128	129.5-130	$C_{12}H_{11}O_4N$	61.8	4.8	61.8	4.8
4-Isopropyl	Isopropyl	21	0[e]							
3-Nitro	Isopropyl	17	0[f]							
4-Isopropyl	Butyl	24	20	82 - 83.5	83.5- 84	$C_{16}H_{22}O_2$	78.0	9.0	77.9	9.0
2-Methoxy	Butyl	23	46	91.5- 92	91.5- 92	$C_{14}H_{18}O_3$	71.7	7.7	71.7	7.7
3-Nitro	Butyl	50[b]	53	105.5-106.5	107 -108	$C_{13}H_{15}O_4N$	62.6	6.1	62.7	6.3
4-Isopropyl	Undecenyl	27[g]	0[h]							
2-Methoxy	Undecenyl	24	26	67 - 69	69.5- 70	$C_{21}H_{30}O_3$	76.3	9.2	76.1	9.2
3-Nitro	Undecenyl	9	40[i]	79 - 81	82.5- 83.5	$C_{20}H_{27}O_4N$	69.5	7.9	69.4	7.9

[a] A 1:1 molar ratio of aldehyde and allylmalonic acid was used. [b] Evolution of carbon dioxide corresponded to 88% of the calculated amount. [c] α-Allyl-2-methoxycinnamic acid, as a 1.10×10^{-5} *M* solution in 95% alcohol showed absorption maxima at 266 mμ (ε 18,550) and 306 mμ (ε 10,450). [d] When 3-nitrobenzaldehyde and allylmalonic acid in 1:1 molar ratio were treated in the usual way for 5.5 hours, the yield of α-allyl-3-nitrocinnamic acid was 65%. The ultraviolet absorption curve for α-allyl-3-nitrocinnamic acid, as a 4.1×10^{-5} *M* solution in 95% alcohol, showed a maximum at 258 mμ (ε 20,400). [e] Unreacted 4-isopropylbenzaldehyde as its 2,4-dinitrophenylhydrazone derivative, m.p. 231–233°, was recovered in 98% yield. [f] Unreacted 3-nitrobenzaldehyde as its 2,4-dinitrophenylhydrazone derivative, m.p. 280.5–282° dec., was recovered in 98% yield. [g] The carbon dioxide evolution was 77% of that calculated. [h] Unreacted 4-isopropylbenzaldehyde as its 2,4-dinitrophenylhydrazone, m.p. 232–233°, was recovered quantitatively. [i] When 3-nitrobenzaldehyde and undecenylmalonic acid in 1:1 molar ratio were allowed to react for 24 hours, the yield of α-undecenyl-3-nitrocinnamic acid was 23%.

high as those reported for the corresponding cinnamic acids from the Doebner reaction with unsubstituted malonic acid. The mild conditions and the generally satisfactory results may warrant considering this the method of choice for the preparation of α-methylcinnamic acids. Application of the standardized procedure produced other α-alkylcinnamic acids (Tables II and III) for the most part in moderate but still useful yields. Actually, in all cases where comparison was possible with yields reported for specific α-alkylcinnamic acids prepared by other methods (*e. g.*, Perkin condensation, Reformatsky reaction, Claisen condensation, etc.[4]), the present Doebner method was superior.

In assessing the relation of structure to yield, the results obtained in forming α-methyl cinnamic acids from aldehydes having no substituent on the *o*-positions appeared significant. The average yield from the aldehydes in Table I substituted on the *m*- and/or *p*-positions with chloro, bromo or nitro groups is 95%. The average yield from the aldehydes in Table I substituted on the *m*- and/or *p*-positions with alkyl, methoxy, hydroxy or dimethylamino groups is 73%. Evidently electron-withdrawing groups favor, while electron-supplying groups retard, the reaction. Comparison of the results with 2,4,6-trimethylbenzaldehyde and with 2,4,6-trimethyl-3,5-dinitrobenzaldehyde (*cf.* Table I) is also pertinent. No condensation product with methylmalonic acid was obtained from the former aldehyde, 98% of the 2,4,6-trimethylbenzaldehyde being recovered. Steric as well as electronic factors might be expected to contribute to this result. In 2,4,6-trimethyl-3,5-dinitrobenzaldehyde steric hindrance to action at the aldehydic carbon atom must be at least as great as in 2,4,6-trimethylbenzaldehyde. Nevertheless, the dinitro compound reacted with methylmalonic acid to give cinnamic acid product. This contrasting behavior may be accounted for by the electron-with-

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[4] *Cf.* J. R. Johnson in R. Adams, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 210.

drawing effect of the two nitro groups. Whatever the detailed mechanism[2a] the aldehydic carbon atom appears to be involved as an electrophilic center, so that the greater the plus charge, the more effective the competition for the combining nucleophilic fragment.

Table IV lists percentage yields of α-alkylcinnamic acids from the condensation of various alkylmalonic acids with three substituted benzaldehydes. The yields with 3-nitrobenzaldehyde are seen to be greater than the yields with 4-isopropylbenzaldehyde. This comparison again indicates operation of an electronic effect, and is consistent with the conclusions reached in the last paragraph. For each of the aldehydes the trend is for lower yields with increasing bulk in the alkylmalonic acids. Three factors, all operating in the same direction, may account for this order. First, it is generally accepted that malonic acid enters into condensation reactions only after its α-hydrogen is removed. By virtue of the increased electron-donating inductive effect of the alkyl groups as they become larger (and possibly also because of greater hindrance to the approach of a proton acceptor), removal of the α-proton will be correspondingly more difficult. Accordingly less condensation will occur with the higher alkylmalonic acids. Second, a steric effect can be assumed in covalency formation between the moiety from the alkylmalonic acid and that from the aldehyde, so that the bulkier the alkyl group the lower the yield. This is particularly striking with isopropylmalonic acid, which gave no condensation products at all.[5] Third, a practical matter of isolating the cinnamic acid products tended to give higher yields with smaller alkyl groups. Since two moles of alkylmalonic acid were used per mole of aldehyde, at least one mole of the simple decarboxylation product was formed. With methyl, ethyl and allylmalonic acids, separation of the water-insoluble α-alkylcinnamic acids from the water-soluble decarboxylation acids was a simple matter. However, with butyl and undecenylmalonic acids, the condensation products and the simple decarboxylation acids were both water insoluble. Purification of these condensation products called for several recrystallizations, with concomitant decrease in yield.

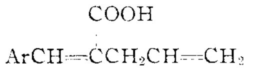
TABLE IV

COMPARISON OF YIELDS IN THE FORMATION OF α-ALKYLCINNAMIC ACIDS FROM THREE SUBSTITUTED BENZALDEHYDES AND SIX ALKYLMALONIC ACIDS

Benzaldehyde	Yield, % Methylmalonic	Ethylmalonic	Allylmalonic	Isopropylmalonic	Butylmalonic	Undecenylmalonic
2-Methoxy	85	55	46	..	46	26
3-Nitro	98	64	65	0	53	40
4-Isopropyl	77	40	24	0	20	0

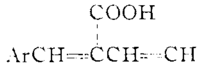
Structure of Products.—Several of the α-alkylcinnamic acids encountered in the present work (*e.g.*, α-methyl-, α-ethyl-, α,4-dimethyl-, α-methyl-2-methoxy, α-ethyl-2-methoxy- and α-methyl-4-methoxycinnamic acids) had been shown before to have the aryl and the carboxyl groups in the *trans* arrangements.[6-8] This, together with the production of *trans* products in the Doebner reaction with unsubstituted malonic acid,[9] is the basis for our provisional assignment of *trans* geometry to the other compounds of the series.

Another question of structure concerns the position of the double bonds in the α-allylcinnamic acids; that is, it was desirable to distinguish between the expected skipped diene system II and the two conjugated possibilities III and IV. The ultraviolet absorption of α-allyl- and that of α-methyl-3-nitrocinnamic acid were almost identical. The same was true of the ultraviolet absorption of the pair, α-allyl- and α-methyl-2-methoxy-cinnamic acid. This evidence, in showing that in at least two instances the chromophoric effect of α-methyl and α-allyl are the same, favors the allyl structure as in II over the other two possibilities. Further evidence against structure III for α-allyl-2-methoxycinnamic acid was obtained by ozonolysis, which furnished formaldehyde but no acetaldehyde.



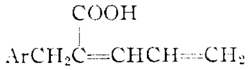
$ArCH{=}\overset{COOH}{C}CH_2CH{=}CH_2$

II



$ArCH{=}\overset{COOH}{C}CH{=}CHCH_3$

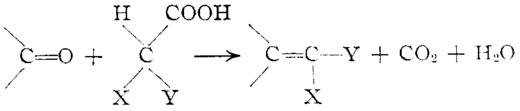
III



$ArCH_2\overset{COOH}{C}{=}CHCH{=}CH_2$

IV

Our experience with the reaction of alkylmalonic acids and aldehydes suggests investigation of a more general mode of decarboxylative condensation, that is, between a carbonyl compound and carboxylic acid V. As long as Y in compound V is any one of a number of familiar activating groups, X could represent almost any kind of organic radical. We hope to conduct further research on the preparative aspects of these decarboxylative condensations, as well as on the nature of the processes.



V

Experimental[10]

Alkylmalonic Acids.—Methylmalonic acid was prepared from diethyl methylmalonate. Diethyl methylmalonate in turn was obtained by the decarbonylation of ethyl ethoxalylpropionate,[11] which was either synthesized[12] or purchased.[13] Saponification of diethyl methylmalonate was

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[5] Since the Doebner condensation is competing with simple decarboxylation of the alkylmalonic acid, the effect of the alkyl group on the rate of simple decarboxylation—and, thereby, on the extent of the competing condensation process—will eventually have to be taken into account.

[6] R. Stoermer and G. Voht, *Ann.*, **409**, 36 (1915).

[7] R. Fusco and S. Rossi, *Gazz. chim. ital.*, **78**, 524 (1948) [*C. A.*, **43**, 1744 (1949)].

[8] W. H. Perkin, *J. Chem. Soc.*, **39**, 409 (1881).

[9] *Cf.* W. M. Lauer and W. J. Gensler, THIS JOURNAL, **67**, 1171 (1945); R. D. Kleene, F. H. Westheimer and G. W. Wheland, *ibid.*, **63**, 791 (1941); W. J. Gensler, *Chem. Revs.*, **57**, 224 (1957).

[10] Melting points and boiling points are uncorrected. The elementary analyses were performed by Carol K. Fitz, 115 Lexington Ave., Needham Heights, 94, Mass.

[11] R. F. B. Cox and S. M. McElvain, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 279.

[12] R. F. B. Cox and S. W. McElvain, *ibid.*, p. 272.

[13] Winthrop–Stearns, Inc., 1450 Broadway, New York 18, N. Y.

carried out by one or the other of the following methods: (1) A mixture of 120.5 g. of diethyl methylmalonate (0.718 mole), 120.5 g. of potassium hydroxide (2.16 moles) and 120.5 ml. of water was boiled for 14 hours. If the reaction in its initial stages was too vigorous, the mixture was cooled. Water (50–100 ml.) was added, and the solution was distilled until the temperature of the distillate reached 100°. The cooled alkaline solution was washed with two 50-ml. portions of ether, and then acidified with cold 18% hydrochloric acid to *p*H 2. The methylmalonic acid was collected by continuous ether extraction for 50 hours. The ether extract, after drying over calcium sulfate, was warmed on the steam-bath to remove solvent, and the residue crystallized from benzene–ether. Methylmalonic acid (69.0 g. or 85%) was obtained with m.p. 133–134° dec.

(2) A convenient modification proceeded by the dropwise addition of 260 g. (1.42 moles) of diethyl methylmalonate to a stirred solution of 260 g. (4.65 moles) of potassium hydroxide in 260 ml. of water at a rate sufficient to maintain a gentle reflux. The addition required one hour. The mixture was boiled thereafter for 2 hours, and then distilled until the vapor temperature reached 100°. Product was isolated essentially the same as before, except that the extraction was continued for 7 days instead of 2 days. Crystallized methylmalonic acid was obtained in 89% yield (158 g.).

Ethylmalonic acid was prepared from commercially available diethyl ethylmalonate[14] essentially according to the first set of directions given above for methylmalonic acid. After crystallization from benzene, ethylmalonic acid, m.p. 110.5–112°, was obtained in 45% yield.

Allylmalonic acid was prepared from diethyl allylmalonate[14] by saponification according to method 2 for methylmalonic acid. There was no need for continuous extraction here, since most of the allylmalonic acid was removed from the aqueous acid mixture by several batch extractions with ether. Allylmalonic acid, after crystallization from ether–benzene, showed m.p. 101–102.5°. The yield was 51%.

Isopropylmalonic acid was prepared from its ester[15] in a manner similar to that given above for allylmalonic acid. Solvent was removed from the dry ethereal solution by evaporation under a stream of dry nitrogen. Crystallization from chloroform gave isopropylmalonic acid, m.p. 87.5–88.5°, in 34% yield.

Butylmalonic acid, m.p. 99–101°, was obtained from student preparation material by recrystallization from benzene–ether.

Undecenylmalonic acid was obtained by saponifying the ester[16] essentially according to method 2 described for methylmalonic acid. Acidification of the alkaline solution precipitated the product, which was removed by filtration. Undecenylmalonic acid after crystallization from alcohol–water had m.p. 110–110.5° and was obtained in 91% yield.

Aromatic Aldehydes.—The following aldehydes were either used as received from commercial suppliers or were purified by crystallization or distillation: 2-methylbenzaldehyde ($n^{25}\mathrm{D}$ 1.5300), 4-methylbenzaldehyde ($n^{25}\mathrm{D}$ 1.5412), 4-isopropylbenzaldehyde ($n^{25}\mathrm{D}$ 1.5289), 2-methoxybenzaldehyde (m.p. 3–4°), 4-methoxybenzaldehyde (m.p. 0.5–2°), 2,3-dimethoxybenzaldehyde (m.p. 51–52°), 3,4-dimethoxybenzaldehyde (m.p. 43–44°), 3,4-methylenedioxybenzaldehyde or piperonal (m.p. 36–37°), 3-methoxy-4-hydroxybenzaldehyde or vanillin (m.p. 81–82.5°), 2-hydroxybenzaldehyde or salicylaldehyde (b.p. 193–193.5°, $n^{25}\mathrm{D}$ 1.5708), 3-hydroxybenzaldehyde (m.p. 102–104°), 4-hydroxybenzaldehyde (m.p. 115–117°), 4-dimethylaminobenzaldehyde (m.p. 73–74.5°), 2-chlorobenzaldehyde (m.p. 10.5–11.5°), 4-chlorobenzaldehyde (m.p. 45–46.5°), 2,4-dichlorobenzaldehyde (m.p. 71–72°), 3,4-dichlorobenzaldehyde (m.p. 42–43°), 4-bromobenzaldehyde (m.p. 55.7–57°), 2-nitrobenzaldehyde (m.p. 43.5–44°), 3-nitrobenzaldehyde (m.p. 58–59°), 4-nitrobenzaldehyde (m.p. 105–106.5°), furfural (b.p. 159–161°) and 1-naphthaldehyde ($n^{21.8}\mathrm{D}$ 1.6508).

Benzaldehyde was washed free of acids with bicarbonate solution, dried, distilled under nitrogen, and the fraction boiling at 176–176.5° collected and stored under nitrogen away from light.

2-Carboxy-3,4-dimethoxybenzaldehyde or opianic acid, m.p. 145–146°, was made available through the courtesy of Dr. A. L. Bluhm of these laboratories.[17]

3-Methylbenzaldehyde, b.p. 197–198° and $n^{25}\mathrm{D}$ 1.5370, was obtained in 45% yield by the Stephen reduction of *m*-toluonitrile.[18] 2,4,6-Trimethylbenzaldehyde, synthesized from mesitylene according to published directions,[19] showed b.p. 237–240° and $n^{23.5}\mathrm{D}$ 1.5484. Nitration of 2,4,6-trimethylbenzaldehyde gave 2,4,6-trimethyl-3,5-dinitrobenzaldehyde, m.p. 163–164°.[20] Methylation of 3-hydroxybenzaldehyde with methyl iodide furnished 3-methoxybenzaldehyde, b.p. 232–233°.[21] 3-Chlorobenzaldehyde, b.p. 74–76° (4 mm.), $n^{24}\mathrm{D}$ 1.5263, was prepared from 3-nitrobenzaldehyde.[22] 2,6-Dichlorobenzaldehyde was in part purified from commercially available material[23] and in part prepared[24] from α,α,2,6-tetrachlorotoluene.[23] 2,6-Dichlorobenzaldehyde on crystallization from alcohol–water melted at 70.5–71.5°, and on crystallization from petroleum ether (b.p. 30–60°) at 70–71°.

Pyridine and Piperidine.—Eastman Kodak Co. white label pyridine was boiled with anhydrous barium oxide for one hour. Distillation from barium oxide through a 30-cm. Vigreux column gave a 113–114° boiling fraction, which was stored over potassium hydroxide pellets.

Eastman Kodak Co. practical piperidine was boiled with sodium for 2 hours, and then distilled from sodium through a 15-cm. Vigreux column. The fraction with b.p. 104.5–105.5°, $n^{25}\mathrm{D}$ 1.4500, was taken as piperidine, and was stored over potassium hydroxide pellets.

General Directions for the Doebner Condensation of Aromatic Aldehydes and Alkylmalonic Acids.—A mixture of aldehyde, alkylmalonic acid (2 molar quantities) and piperidine (2 molar quantities) in pyridine solvent (12.5 ml. for 0.01 mole of aldehyde) was heated on the steam-bath for the length of time given in the tables. As a rule, either 0.01 mole or 0.02 mole of aldehyde was used together with the corresponding 0.02 mole or 0.04 mole, respectively, of malonic acid. The flask, fitted to a vertical water-cooled condenser, was swept with "oil-pumped" nitrogen that had been bubbled through sulfuric acid at the rate of about a bubble every 2 seconds. The nitrogen and evolved gases passed up the condenser, through an empty safety flask, then through two flasks containing concentrated sulfuric acid, and finally into an absorption bulb containing sodium hydroxide on asbestos (Ascarite). The gain in weight of the absorption tube served as a measure of the carbon dioxide evolved. In all cases at the end of the stated reaction time, 90–108% of the expected amount of carbon dioxide, calculated on the basis of 1 mole per mole of alkylmalonic acid, had been given off. The extent of carbon dioxide evolution at intermediate periods was not measured, so that it is entirely possible that some of the reactions were unduly prolonged.

The cooled reaction mixture was added to a mixture of 25 ml. of concentrated hydrochloric acid and 50 g. of ice for every 12.5 ml. of pyridine. If an oil appeared, the acid mixture was extracted with two 100-ml. portions of ether, and the ether extracted with a total of 50 ml. of 5% sodium hydroxide solution for every 0.01 mole of starting aldehyde. Sodium bicarbonate (5%) solution was used when phenolic aldehydes were involved. If a precipitate formed in the acidified mixture, it was filtered and, to ensure complete recovery of product, the filtrate was extracted with two 100-ml. portions of ether. The ether extract together with the

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(14) Matheson, Coleman and Bell Division, East Rutherford, N. J.

(15) C. S. Marvel and V. du Vigneaud, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 93; R. Adams and O. Kamm, "Organic Syntheses," Coll. Vol. I, second edition, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 250.

(16) W. J. Gensler, E. M. Behrmann and G. R. Thomas, THIS JOURNAL, **73**, 1071 (1951).

(17) *Cf.* A. Matthiessen and G. C. Foster, *J. Chem. Soc.*, **16**, 342 (1863); C. Liebermann and C. Chojnacki, *Ann.*, **162**, 321 (1872).

(18) H. Stephen, *J. Chem. Soc.*, **127**, 1874 (1925); J. B. Bowen and E. M. Wilkinson, *ibid.*, 750 (1950).

(19) R. C. Fuson, E. C. Horning, S. P. Rowland and M. L. Ward, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 549.

(20) L. E. Hinkel, E. E. Ayling and W. H. Morgan, *J. Chem. Soc.*, 1170 (1931).

(21) R. Pschorr and B. Jaekel, *Ber.*, **33**, 1826 (1900).

(22) *Cf.* J. S. Buck and W. S. Ide, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 130.

(23) Eastman Organic Chemicals, Rochester 3, N. Y.

(24) *Cf.* L. F. Fieser and M. Fieser, "Organic Chemistry," second edition, D. C. Heath and Co., Boston, Mass., 1950, p. 715.

precipitate was treated with 50 ml. of 5% sodium hydroxide solution (or 5% bicarbonate solution) to take up the acids. In either case the aqueous alkaline solution was added dropwise with stirring to a mixture of 50 ml. of concentrated hydrochloric acid and 100 g. of ice. The precipitate was collected by filtration, crystallized from alcohol–water, and dried. The percentage yields given in the tables as well as the melting points refer to this product. Where a sample for analysis was desired, the product was recrystallized, usually from alcohol–water, and finally dried *in vacuo*.

In some cases a measure of unreacted aldehyde was found by examining the ethereal solution from which acids had been removed with aqueous alkali. When benzaldehyde was used, unreacted aldehyde was oxidized with alkaline permanganate and the benzoic acid collected and weighed. In other cases the aldehyde was recovered as the 2,4-dinitrophenylhydrazone.

Ozonolysis of α-Allyl-2-methoxycinnamic Acid.—Ozonized oxygen was bubbled into a solution of 0.436 g. (2.00 millimoles) of α-allyl-2-methoxycinnamic acid in 30 ml. of ethyl acetate at −80°. When 2.00 millimoles of ozone had been absorbed (after 4–5 minutes) the reaction was interrupted, and the ethyl acetate removed by evaporation in a stream of nitrogen. Zinc dust (0.65 g.) and ice-water (50 ml.) was added to the residual oil, and the mixture was stirred for 30 minutes. More water (200 ml.) was added and the mixture was distilled directly into a solution of 0.56 g. (4 millimoles) of dimethyldihydroresorcinol in 200 ml. of water. After 3 days in the refrigerator, the separated solids were collected and air-dried. The derivative (0.28 g., m.p. 158–170°) after three crystallizations from alcohol–water weighed 0.08 g. (14%) and melted at 185–186.5°. The mixture melting point with the same derivative of formaldehyde (m.p. 187.5–188.5°) was 186–187°.

When allylmalonic acid was ozonized in a similar manner, formaldehyde as its dimethyldihydroresorcinol derivative was obtained in 34% yield.

BOSTON, MASS.

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Ionic Fission of the O–O Bond in *t*-Butyl Arylpersulfonates[1]

BY PAUL D. BARTLETT AND BAYARD T. STOREY

RECEIVED MAY 3, 1958

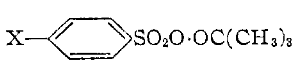
t-Butyl benzenepersulfonate, a new class of perester, and four *p*-substitution products have been prepared. These decompose quantitatively in methanol to give acetone and arylsulfonic acid by ionic cleavage of the peroxide bond. Kinetic studies of the decomposition of *t*-butyl pertosylate in methanol and aqueous methanol have been carried out. The reaction is subject to unusual salt effects which show pronounced maxima with salt concentration and which disappear almost completely with the addition of water to the methanol. In contrast to 9-decalyl perbenzoate, *t*-butyl pertosylate shows strong negative deviation from the Grunwald–Winstein equation near the methanol end of a series of methanol–water mixtures, but obeys this equation over the rest of the range. A mechanistic interpretation of this behavior is offered.

Introduction

Peresters derived from *t*-butyl hydroperoxide usually decompose by cleavage to radicals. One exception discovered recently[2a,b] is *t*-butyl trifluoroperacetate, which seems to decompose in part by ionic cleavage. This suggested that a *t*-butyl perester derived from a sufficiently strong acid might well undergo ionization of the oxygen–oxygen bond to the exclusion of homolytic cleavage. The strongest organic acids available are the sulfonic acids and so the possibility of preparing *t*-butyl persulfonates was investigated.

Products of Decomposition

Five *t*-butyl arylpersulfonates were prepared: the *p*-methoxybenzene, *p*-toluene, benzene, *p*-chlorobenzene and *p*-bromobenzene peresters, Ia-e.



Ia, X = CH_3O
b, X = CH_3
c, X = H
d, X = Cl
e, X = Br

The first two are relatively stable, decomposing exothermically (and usually quite violently) at room temperature after about 5–10 minutes. The benzenepersulfonate is of intermediate stability, and the *p*-chloro and *p*-bromo compounds are quite unstable and hard to handle. (All may be left from two to four weeks in the freezer.) The *p*-nitro compound could not be prepared. The order of stability indicates that decomposition of these peresters is favored by anionic stability of the sulfonate group.

Determination of the products of decomposition of the peresters in methanol at room temperature confirms the ionic mechanism in this solvent. Only two products are isolated and these in quantitative yield: acetone and the appropriate arylsulfonic acid. Acetone was determined gravimetrically as the 2,4-dinitrophenylhydrazone. Yields ranged from 95 to 99% and the purity of the unrecrystallized material gave no suggestion of side products. The sulfonic acid was determined both by titration and by isolating and weighing the sodium salt. Yields were consistently 100 ± 1%. *t*-Butyl pertosylate gave the same result in aqueous methanol (mole fraction of water 0.1 and 0.2.). As a control, *t*-butyl hydroperoxide was decomposed at 100° in methanol, conditions which should give *t*-butoxy radicals. Formaldehyde was isolated as the 2,4-dinitrophenylhydrazone in 65–70% yield, presumably from attack by *t*-butoxy radicals on the solvent. No formaldehyde was present in the products of the persulfonate decompositions.

Kinetic Evidence

In the radical-producing thermal decomposition

II

of *t*-butyl perbenzoates II,[3] the Hammett equation[4] is obeyed, a plot of log *k* against σ having a slope

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(1) This paper was presented at the Spring Meeting of the National Academy of Sciences, Washington, D. C., April 29, 1958.

(2) (a) P. D. Bartlett and R. R. Hiatt, THIS JOURNAL, **80**, 1398 (1958); (b) P. D. Bartlett, *Experientia*, Suppl. VII, 275 (1957).

(3) A. T. Blomquist and I. A. Berstein, THIS JOURNAL, **73**, 5546 (1951).

(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 186.