[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE
POLYTECHNIC INSTITUTE OF BROOKLYN]

CONDENSATION OF ALIPHATIC ALDEHYDES WITH *p*-NITROPHENYLACETIC ACID. II. A STERIC EFFECT

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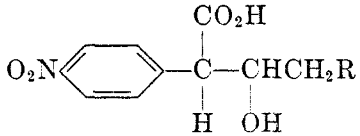
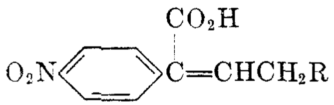
By a modification of the Perkin reaction aliphatic aldehydes may be condensed with *p*-nitrophenylacetic acid. At moderate temperatures (35–45°) employing the sodium salt and acetic anhydride in an inert solvent, this rather reactive acid combines readily with the carbonyl compounds to give fair yields of α,β-disubstituted acrylic acids which may be isolated with ease from the reaction mixtures and readily purified.

The applicability of this method of condensation to aliphatic carbonyl compounds in general has not been extensively investigated, acrolein being the only member of the series thus far employed (1). The mild conditions under which the condensation can be achieved appear to make it especially suitable for work with carbonyl compounds of sensitive character. Further investigation may well show that the method is useful in preparative work of a wider scope. The present work also throws some light on the limitations that are naturally expected to arise through steric hindrance offered by branched alkyl groups attached to the functional group.

Condensations were carried out with acetaldehyde, propionaldehyde, isobutyraldehyde, and trimethylacetaldehyde to give colorless products in 55, 49, 13, and 0% yield, respectively. The acids were identified by their neutral equivalents, ultimate analysis, and ultimate analysis of their *p*-bromophenacyl esters (Table I). However, the position of the double bond is not established by these data.

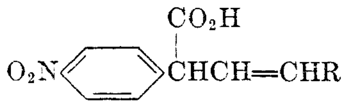
Since the intermediate in the condensation may undergo dehydration in two ways to give an α,β- or a β,γ-unsaturated acid, (a or b) there is no *prima facie* certainty regarding the position of the double bond. However, the fact that the





a

or



b

R = H or alkyl

acids resist the action of bromine as well as of potassium permanganate may be

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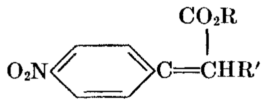
[1] Taken from a thesis submitted by W. H. H. to the Graduate School in partial fulfillment of the requirements for the degree of Master of Science.

TABLE I

2-(4'-NITROPHENYL)-3-ALKLYLACRYLIC ACIDS AND THEIR ESTERS



$O_2N-C_6H_4-C(CO_2R)=CHR'$

COMPOUND	R	R'	B.P., °C.	YIELD, %	FORMULA	NEUT. EQUIV.		CARBON		HYDROGEN		NITROGEN	
						Calc'd	Found	Calc'd	Found	Calc'd	Found	Calc'd	Found
1	H	CH_3	174–175[a]	55	$C_{10}H_9NO_4$	207	207	57.97	58.04	4.38	4.38	6.76	6.67
2	H	C_2H_5	156.5–157.5	49	$C_{11}H_{11}NO_4$	221	221	59.72	59.89	5.01	5.19	6.33	6.28
3	H	*iso*-C_3H_7	226.5–227.5	13	$C_{12}H_{13}NO_4$	235	236	61.27	61.44	5.57	5.63	5.95	5.90
4	*p*-$BrC_6H_4COCH_2$	CH_3	92–92.5	87	$C_{18}H_{14}BrNO_5$			53.48	53.62	3.49	3.66	3.47	3.39
5	*p*-$BrC_6H_4COCH_2$	C_2H_5	100–101	79	$C_{19}H_{16}BrNO_5$			54.56	54.61	3.86	3.96	3.34	3.30
6	*p*-$BrC_6H_4COCH_2$	*iso*-C_3H_7	139–139.5	82	$C_{20}H_{18}BrNO_5$			55.57	55.67	4.20	4.32	3.24	3.21

[a] Reported m.p. 173.5–174.5°, Ref. 6.

TABLE II

SPECTRAL CHARACTERISTICS OF 2-(4′-NITROPHENYL)-3-SUBSTITUTED ACRYLIC ACIDS AND THEIR *p*-BROMOPHENACYL ESTERS[a]

COMPOUND	λ_{min}	ϵ_{min} (molar)	λ_{max}	ϵ_{max} (molar)
1	245	4,500	282	9,600
2	245	5,000	282	9,900
3	—	—	282	10,100
4	232	11,000	260	26,900
5	232	12,100	260	27,100
6	232	12,400	260	27,300
p-Nitrophenyl-acetic acid	233	3,300	270	10,100

[a] The absorption spectra were determined in a Beckman quartz spectrophotometer, Model DU, using 1-cm. cells. The solvent was 95% ethanol and the concentration was 16 mg. per liter.

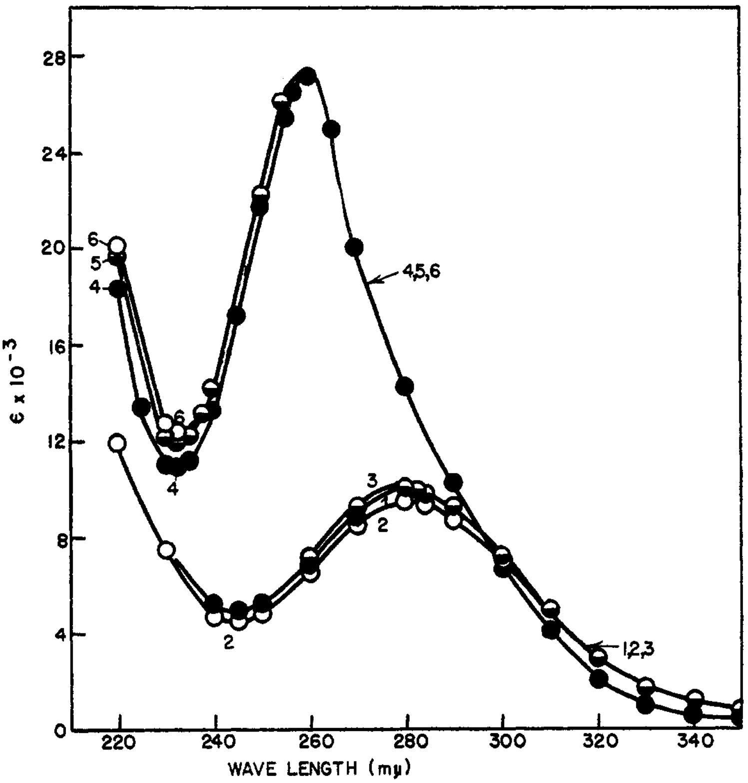


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF 2-(4′-NITROPHENYL)-3-ALKYLACRYLIC ACIDS (Curves 1, 2, and 3) AND THEIR *p*-BROMOPHENACYL ESTERS (Curves 4, 5, and 6)

taken to establish α,β-unsaturation. The failure of these 1,1-disubstituted olefins to add bromine is in accord with the fact that 2-(4′-nitrophenyl)-2,4-pentadienoic acid adds only two atoms of bromine (1). Comparison of the ultraviolet absorption spectra of *p*-nitrophenylacetic acid and 2-(4′-nitrophenyl)-2-butenoic acid (Table II and Figures 1 and 2) shows a bathochromic shift of 10 mμ in proceeding from the former to the latter. This is in accord with the expected result upon extension of the conjugated chain and supports the α,β-position of the double bond.

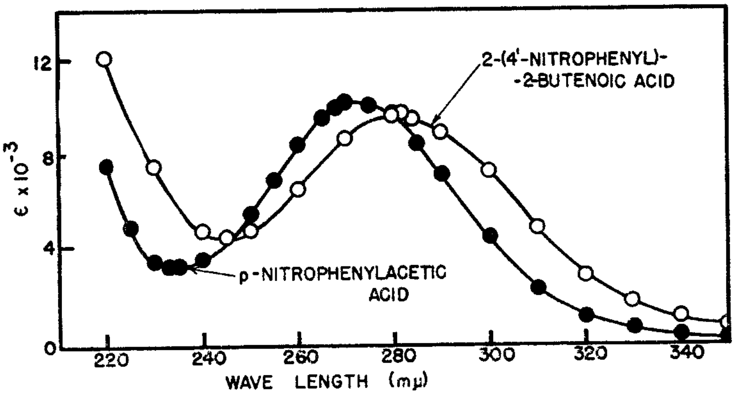
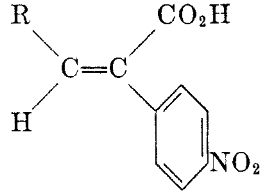


FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA OF *p*-NITROPHENYLACETIC ACID AND 2-(4′-NITROPHENYL)-2-BUTENOIC ACID

The spectra offer no basis for distinguishing between the two possible *cis*-



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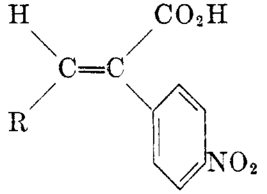

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and *trans*-structures which may have formed but in view of the close correlation of each set of curves, it may be surmised that each set of compounds is of the same type. Also, since the *p*-nitrophenyl group might be expected to offer greater steric hindrance than the carboxyl, it is probable that the whole series belongs to type "A".

THE STERIC EFFECT

Although considerable work has been carried out on carbonyl condensations, the authors have not found a single set of reactions carried out under identical conditions which evaluate the steric effect, either in the carbonyl moiety or in the active methylene compound (2–5). In those reactions which at first hand may be cited, the variance in yield may be due to electronic or polar effects as well as steric factors. For example, in the Perkin reaction, benzaldehyde gives a 45–50% yield of cinnamic acid, 2-methylbenzaldehyde 15%, and 2,6-dimethylbenzaldehyde 0%. However, 2-chloro- and 2,4-dichloro-benzaldehyde give 71 and 82% yields, respectively. It is well known that the electropositive character of the methyl groups would render the carbonyl carbon less susceptible to attack by an anion while the polar effect of chlorine atoms would be the opposite. An effect which appears to be largely steric is manifest in the condensation of acetone and diethyl ketone with malonic acid. The yields are 60 and 30%, respectively, of the corresponding β,β-disubstituted acrylic acids.

In the experiments carried out here, a steric effect appears to be operative. As the hydrogens of acetaldehyde are replaced by methyl, the resistance offered by the methyl groups to the formation of the intermediate anion (2) in the transition state is increased greatly with consequent drop in yield. The small reduction in yield when one hydrogen is replaced by methyl as compared with the larger reductions evident in the replacement of two and three methyl groups again emphasize the essential steric nature of the effect.

TABLE III

REACTION CONDITIONS FOR CONDENSATION OF ALDEHYDES WITH *p*-NITROPHENYLACETIC ACID

SODIUM *p*-NITROPHENYLACETATE TAKEN		ALDEHYDE	GRAMS	MOLE	TEMP., °C.	TIME, DAYS	PRODUCT, G.
G.	Moles						
6.0	0.030	Acetaldehyde	1.6	0.036	35–40	3	I, 3.4
6.0	.030	Propionaldehyde	2.4	.043	40–45	3	II, 3.2
6.0	.030	Isobutyraldehyde	2.8	.040	40–45	3	III, 0.9
12.0	.060	Trimethylacetaldehyde	5.5	.064	40–45	3	[a]

[a] About 250 mg. of an impure acidic product which contained no nitrogen was obtained. In this experiment 200 ml. of isopropyl ether was taken.

EXPERIMENTAL

Starting materials. p-Nitrophenylacetic acid (m.p. 153–154°) was prepared by nitration of phenylacetic acid (7). Acetaldehyde was freshly prepared by depolymerizing paraldehyde. Propionaldehyde (b.p. 49.5°, n_D^{21} 1.3631) and isobutyraldehyde (b.p. 63–64°, n_D^{20} 1.3726) were distilled before use. Trimethylacetaldehyde was prepared from *tert*-butylmagnesium chloride and methyl formate (8) and distilled before use (b.p. 72–75°, n_D^{25} 1.3773).

Acids. The procedures employed in each case were similar. Table III lists the quantities taken; the condensation with acetaldehyde is described in detail. A mixture of sodium *p*-nitrophenylacetate (6.0 g.), redistilled acetic anhydride (30 ml.), acetaldehyde (1.6 g.), and 100 ml. of dry, peroxide-free isopropyl ether was stirred for three days at 35–40°. At the end of this period 5 ml. of water was added to hydrolyze excess anhydride and stirring was continued for two hours. Addition of 2 ml. of 6 *N* hydrochloric acid to the mixture was followed by pouring the mixture into 100 ml. of water and extracting thoroughly with ethyl ether. The ether solution was in turn extracted with 5% sodium carbonate and the product precipitated by adding 6 *N* hydrochloric acid. The crude material was freed from unreacted *p*-nitrophenylacetic acid by suspension in hot water and filtration, redissolved in hot 5% sodium carbonate (charcoal), acidified, and recrystallized once from a 3:1 mixture of naphtha (b.p. 104–116°) and benzene, and once from chloroform to give 3.4 g. (55%) of product, m.p. 174–175°.

Raising the temperature to 80–110° and shortening the reaction time to 18–20 hours gave the same quantity of product, but with a lower melting point.

The pure acids are fine white powders, insoluble in water and naphtha, moderately soluble in benzene, and very soluble in ethanol.

A few drops of a 2.5% solution of bromine in carbon tetrachloride were added to a solution of 0.1 g. of the acid in 3 ml. carbon tetrachloride. An equal quantity (0.1 g.) of acid in 2 ml. of acetone was treated in the same manner with a 2% solution of potassium permanganate. In neither case was the color discharged. Warming and prolonged standing were without effect.

Preparation of the p-bromophenacyl esters. A single experiment is described. A suspension of the 2-(4′-nitrophenyl)-2-butenoic acid (1.0 g., 4.8 mmole) in water was neutralized with 10% sodium hydroxide solution, made just acid with 6 *N* hydrochloric acid and then, after the addition of 30 ml. of ethanol containing 1.4 g. (5.0 mmole) of *p*-bromophenacyl bromide, refluxed for one hour. The pure derivative, recrystallized from ethanol, weighed 1.7 g. (4.2 mmole, 87%).

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SUMMARY

Acetaldehyde, propionaldehyde, and isobutyraldehyde condense with *p*-nitrophenylacetic acid in a modified Perkin reaction to give the corresponding α,β-unsaturated acids in yields of 55, 49, and 13%, respectively. Trimethylacetaldehyde failed to react.

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