These routes involve charge transfer by the classically accepted schemes of general acid–base catalysis. The route, C, F, G implies rate determination in G, the bimolecular reaction, after the formation of the ion pair. The route C, D, H implies rate determination in D or H, but since hydrogen ion concentration *per se* has little effect on the rate it is difficult to conceive of step H as rate determining. If this were so, increase in hydrogen ions would shift the equilibrium D to the right and lower the rate of product formation which is not in agreement with experiment.

Gold and Jefferson[33] also prefer a different mechanism of attack by hydroxyl ion than by carboxylate anion. A glance at the schemata shows a short cut, E, that results in the same fast-acting intermediate as through C and D. Direct nucleophilic attack by hydroxyl ion should have low energy and low entropy requirements.

The low heat of activation (9 kcal./mole) of aspirin anhydride is in accord with the effect of groups such as acetoxy, that will favor nucleophilic attack.[19,34] Its *o*-position should even increase its action in lowering the activation energy. The lower frequency factor is also consistent with Berliner and Altschul's premise[19] that groups favoring attack energetically withdraw electrons and lower the probability of the formation of the activated complex.

The lack of evidence for any acetylphenate ester hydrolysis concomitant with (or prior to) anhydride linkage hydrolysis in aspirin anhydride does not support an intramolecular condensation or cyclization with the *o*-groups in aspirin anhydride. The lack of significant acceleration of the anhydride linkage solvolysis by hydrogen ion does not support such mechanisms or intermediates in the anhydride hydrolysis.

The reaction rate of aspirin anhydride hydrolysis is fantastically enhanced by a relatively small decrease in dioxane concentration (from 10% dioxane), concomitantly with a very small increase in dielectric constant. A possible explanation consistent with the proposed hydrolysis mechanisms is that the activated complex has a high dipole moment. Reactions with such complexes should have rates accelerated by solvents of higher dielectric constant.[27,28]

Acknowledgment.—The author is greatly indebted to Mrs. Lillian G. Snyder for excellent technical assistance.

KALAMAZOO, MICH.

[34] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMICAL TECHNOLOGY, UNIVERSITY OF BOMBAY]

Reaction of Lithium Aluminum Hydride with Arylaminomethylenemalonate Esters and Related Compounds[1]

BY R. L. SHIVALKAR AND S. V. SUNTHANKAR[2]

RECEIVED MAY 19, 1959

A series of ethyl arylaminomethylenemalonates, ethyl arylaminomethylenecyanoacetates and arylaminomethylenemalononitriles has been prepared, and their reaction with lithium aluminum hydride has been studied. In the reduction of ethyl arylaminomethylenemalonates partial hydrogenolysis took place and the products obtained were 3-arylaminoallyl alcohols. In the case of ethyl arylaminomethylenecyanoacetate and arylaminomethylenemalononitrile cleavage took place, and the starting primary aromatic amines were obtained. The mechanism of the partial hydrogenolytic reduction is discussed.

In connection with some other studies, 2-(β-naphthylaminomethylene)-1,3-propanediol, was required. The most convenient method for the synthesis of this compound was thought to be the reduction of ethyl β-naphthylaminomethylenemalonate,[3] which was readily obtained in high yield by the condensation of diethyl ethoxymethylenemalonate and β-naphthylamine. However, the reduction, even under mild conditions, gave 3-(2-naphthylamino)-allyl alcohol (II) as the result of partial hydrogenolysis. Such a smooth hydrogenolytic reduction was of interest and, therefore, we studied this reaction more carefully. When ethyl β-naphthylaminomethylenemalonate was treated with excess of lithium aluminum hydride (4 moles) in ether for three and a half hours, allyl alcohol (II) was obtained in 90% yield. In order to see whether the excess of lithium aluminum hydride was responsible for hydrogenolysis, the reduction was carried out with one molar proportion of the reagent. However, the products obtained were the allyl alcohol and the unconverted ester, which during isolation by distillation under vacuum gave a benzoquinoline derivative[4] (III). Similarly ethyl anilinomethylenemalonate[5] gave the corresponding 3-anilinoallyl alcohol in 90% yield. Next ethyl N-ethylanilinomethylenemalonate was treated with excess of lithium aluminum hydride under similar conditions. However, cleavage took place and N-ethylaniline was recovered in 80% yield.

In order to verify that the partial hydrogenolysis is not due to the α,β-unsaturated character of the compounds but due to the β-amino group, ethyl benzalmalonate[6] was reduced under similar conditions. The product isolated in this case was the

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[1] A preliminary report of this work has appeared; K. S. Sardesai, R. L. Shivalkar and S. V. Sunthankar, *J. Sci. Industr. Res.*, **17**, 282 (1958).

[2] To whom correspondence concerning this article should be addressed.

[3] Robert E. Foster, *et al.*, THIS JOURNAL, **68**, 1327 (1946).

[4] K. S. Sardesai and S. V. Sunthankar, *Cur. Sic.*, **26**, 250 (1957).

[5] Byron Riegel, *et al.*, THIS JOURNAL, **68**, 1264 (1946).

[6] *Org. Syntheses*, **25**, 42 (1945).

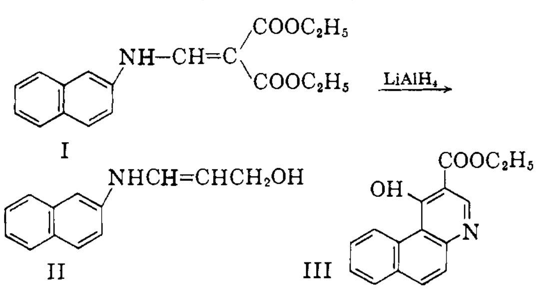
TABLE I

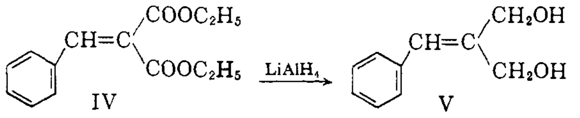
ARYLAMINOMETHYLENEMALONATE ESTERS AND RELATED COMPOUNDS

Condensed product	M.p., °C.	Crystalline nature and solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Ethyl benzylaminomethylenemalonate	74	Colorless ndls. from petr. ether (40–60°)	$C_{15}H_{19}NO_4$	65.0	65.0	6.9	7.2	5.0	5.2
Ethyl N-ethylanilinomethylenemalonate	50	Colorless ndls. from petr. ether (40–60°)	$C_{16}H_{21}NO_4$	66.0	66.1	7.2	6.9	4.8	4.5
Ethyl N-ethylanilinomethylenecyanoacetate	78	Colorless ndls. from aq. ethanol	$C_{14}H_{16}N_2O_2$	68.9	68.9	6.5	6.9	11.5	11.0
Ethyl anilinomethylenecyanoacetate	108	Colorless ndls. from ethanol	$C_{12}H_{12}N_2O_2$	66.7	66.8	5.5	5.4	13.0	13.1
Ethyl β-naphthylaminomethylenecyanoacetate	170	Colorless ndls. from ethanol	$C_{15}H_{14}N_2O_2$	72.2	72.0	5.3	5.3	10.5	10.4
β-Naphthylaminomethylenemalononitrile	253	Colorless ndls. from ethanol	$C_{14}H_9N_3$	76.7	76.9	4.1	4.1	19.2	19.2
Ethyl 2-pyrimidylaminomethylenemalonate[a]	113	Yell. ndls. from ligroin (80–110°)	$C_{12}H_{15}N_3O_4$	54.4	54.4	5.6	5.2	15.9	16.4

[a] Condensation was done in phenyl ether. In all cases yields are above 80% of theory.

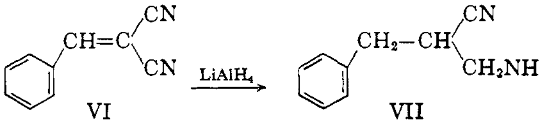
corresponding diol V. The reduction of ethyl benzylaminomethylenemalonate under similar conditions gave a partially hydrogenolyzed reduced product, *i.e.*, 3-benzylaminoallyl alcohol. Apparently, the benzene ring directly attached to the nitrogen does not influence the hydrogenolytic reduction.





In order to investigate the scope of such hydrogenolysis, the reaction of lithium aluminum hydride with related compounds was next studied. Ethyl arylaminomethylenecyanoacetates on treatment with lithium aluminum hydride gave the starting primary aromatic amines.

Since complete cleavage took place at reflux temperature, in one experiment the reduction of ethyl anilinomethylenecyanoacetate was carried out at −10°. The product obtained was the starting material, indicating that no reduction took place at this low temperature. Ethyl N-ethylanilinomethylenecyanoacetate, also, on treatment with lithium aluminum hydride at the reflux temperature of ether gave N-ethylaniline. Anilinomethylenemalononitrile[7] and β-naphthylaminomethylenemalononitrile obtained, respectively, by the reaction of aniline and β-naphthylamine with ethoxymethylenemaloninitrile were next reduced. Because these products were insoluble in ether, they were allowed to react with lithium aluminum hydride in tetrahydrofuran at reflux temperature (64°). Again the products obtained were aniline and β-naphthylamine, respectively. However, the reduction of the benzalmalononitrile[8] in refluxing ether under similar condition gave α-cyano-β-phenylpropylamine (VII), formed by the reduction of one nitrile group as well as α,β-unsaturation.



Similarly, ethyl 2-pyridylaminomethylenemalonate and ethyl 2-pyrimidiylaminomethylenemalonate were cleaved by lithium aluminum hydride, and 2-aminopyridine and 2-aminopyrimidine, respectively, were recovered from the reaction mixtures.

In order to ascertain that the hydrogenolytic product II has the above structure and that no rearrangement has taken place during reduction, further confirmatory evidence was obtained. For example, compound II coupled readily with a diazonium salt and gave a negative diazotization reaction, indicating that the α-position is free and the primary amine group is absent. Zerewitinoff test indicated the presence of two active hydrogens in product II and the catalytic reduction of II gave 3-(2-naphthylamino)-propanol. The product (II) showed strong bands in the infrared at 3.04 μ (OH) and 3.1 μ (NH). Similarly, the compound VII gave a negative test for unsaturation and the infrared spectrum of it gave a double peak at 2.9 μ for NH$_2$ and at 4.55 μ for CN.

Only a few cases of hydrogenolysis of esters have been reported in the literature,[9] and in the majority of such cases the carbethoxy group is reduced to a methyl group; that is the carbon oxygen bond undergoes hydrogenolysis. Moreover, such hydrogenolytic reductions are generally effected at elevated temperatures or extended reaction periods.[10,11]

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(7) Charles C. Price and Virgil Boekelheide, THIS JOURNAL, **68**, 1246 (1946).

(8) U. S. Patent 2,347,573, April 15, 1944; *C. A.*, **39**, 150 (1945).

(9) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, Chapters 9 and 16.

(10) Lloyd H. Conover and D. S. Tarbell, THIS JOURNAL, **72**, 3586 (1950).

(11) R. H. Baker and A. H. Schlesinger, *ibid.*, **68**, 2009 (1946).

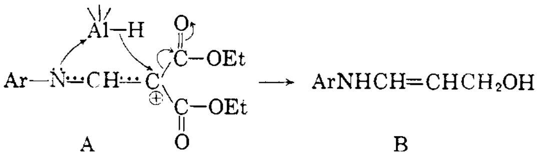
TABLE II

REDUCTION OF ARYLAMINOMETHYLENEMALONATE ESTERS AND RELATED COMPOUNDS WITH LITHIUM ALUMINUM HYDRIDE

Starting material	Reduction product	M.p., °C.[c]	B.p. °C.	B.p. Mm.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Ethyl anilinomethylenemalonate	3-Anilinoallyl alcohol[b]		100–105	0.5	$C_9H_{11}NO$	72.5	72.8	7.4	7.7	9.4	9.3
Ethyl β-naphthylaminomethylenemalonate	3-(2-Naphthylamino)-allyl alcohol[b]	108			$C_{13}H_{13}NO$	78.4	78.8	6.5	6.4	7.0	6.9
Ethyl *o*-aminoanilinomethylenemalonate	*o*-Aminoanilinoallyl alcohol[b]	119			$C_9H_{12}N_2O$	65.9	66.3	7.3	7.6	17.0	16.6
Ethyl benzylaminomethylenemalonate	3-Benzylaminoallyl alcohol[b]		100–105	1.5	$C_{10}H_{13}NO$	..	..	..	..	8.6	8.4
Ethyl benzalmalonate	2-Benzal-1,3-propane diol[a]		90–95	1.5	$C_{10}H_{12}O_2$	73.2	73.6	7.3	7.7	..	..
Benzalmalononitrile	α-Cyano-β-phenyl propylamine[b]	79			$C_{10}H_{12}N_2$	75.0	75.5	7.5	7.0	..	..
Ethyl anilinomethylenecyanoacetate	Aniline[a]		115–120	2.0		Acetyl derivative					
Ethyl β-naphthylaminomethylenecyanoacetate	β-Naphthylamine[a]	112			$C_{10}H_9N$	83.9	83.5	6.3	6.2	9.8	10.3
Ethyl N-ethylanilinomethylenemalonate	N-Ethylaniline[a]		55–60	0.5	$C_8H_{11}N$	79.3	79.1	9.0	9.0	11.5	11.4
Ethyl N-ethylanilinomethylenecyanoacetate	N-Ethylaniline[b]		55–60	0.5		Picrate derivative					
Anilinomethylenemalononitrile	Aniline[a]		115–120	2.0		Acetyl derivative					
β-Naphthyaminomethylenemalononitrile	β-Naphthylamine[a]	112			$C_{10}H_9N$	83.9	83.7	6.3	6.1	9.8	9.3
Ethyl 2-pyrimidylaminomethylenemalonate	2-Aminopyrimidine[a]	125	..		..	..	..	..	..	..	..
Ethyl 2-pyridylaminomethylenemalonate	2-Aminopyridine[b]	54	...			..	..	..	..	..	..

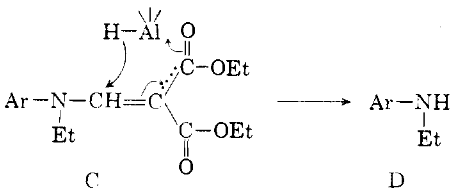
[a] 70–80% yield. [b] 80–90% yield. [c] Melting points are uncorrected.

The above hydrogenolytic reactions can be explained according to the generalized concepts of reduction with lithium aluminium hydride. In the reduction of ethyl arylaminomethylenemalonate, the reactive metal hydride fragment (AlH_4^-) probably coördinates with amide ion initially formed in the reaction; and in such a complex, by a process of concerted type of reaction, the hydride ion brings about the nucleophilic displacement of the carbethoxy group as



A B

In the case of ethyl N-ethylanilinomethylenemalonate the reducing agent probably forms a complex (C) with carbonyl oxygen of the ester group. The hydride ion is then transferred to the β-carbon atom. The reversal of the Michael addition takes place during hydrolysis and the product obtained is N-ethylaniline resulting from the cleavage of the carbon–nitrogen bond.



C D

In a similar way, the reduction of ethyl arylaminomethylenecyanoacetates and arylaminomethylenemalononitrile can be explained.

On the other hand, in the case of ethyl benzalmalonate no coördinative group is attached to the β-carbon atom and it undergoes normal reduction to the diol. In the case of benzalmalononitrile, however, lithium aluminum hydride probably coordinates with one nitrile group. The hydride ion is transferred to the β-carbon atom and, therefore, on hydrolysis the product obtained is α-cyano-β-phenylpropylamine.

Experimental

Arylaminomethylenemalonate Esters and Related ComA—pounds. mixture of amine (0.01 mole) and ester (0.01 mole) in benzene (20 ml.) was heated on a water-bath for 2.5 hours. The benzene was removed after the reaction was over. The residue on cooling gave a solid mass, which was crystallized from an appropriate solvent.

Reduction of Arylaminomethylenemalonate Esters and Related Compound.—A solution of lithium aluminum hydride (4 moles) in 30 cc. of dry ether was treated with ethyl arylaminomethylenemalonate (0.02 mole) in dry ether (40 cc.), introduced at a rate such as to produce gentle reflux. After complete addition, the stirring was continued for 3.5 hours. The reaction mixture was hydrolyzed with ice-cold water. The inorganic precipitate was then filtered off. The ethereal layer was extracted with 2 *N* hydrochloric acid; the acid extract was neutralized with 10% sodium hydroxide and extracted with ether. After evaporation of the ethereal layer, the products obtained were purified.

Hydrogenation of 3-(2-Naphthylamino)-allyl Alcohol.—3-(2-naphthylamino)-allyl alcohol (0.700 g.) was catalytically hydrogenated with platinum oxide catalyst in ethyl acetate. The required amount of hydrogen (1 mole, 90 cc.) was absorbed in six hours. Evaporation of ethyl acetate gave a semi-solid (0.680 g.) which on crystallization from benzene gave 3-(2-naphthylamino)-propanol as white needles, m.p. 77°.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.6; H, 7.5; N, 7.0. Found: C, 78.0; H, 8.0; N, 6.8.

Acknowledgments.—The authors wish to thank Dr. T. S. Gore for the microanalysis and the Kay-Fries Chemicals, Inc., West Haverstraw, N. Y., for the valuable gift of diethyl ethoxymethylenemalonate and other chemicals.

MATUNGA, BOMBAY 19, INDIA

[CONTRIBUTION FROM THE ETHYL CORPORATION]

Sodium β-Sodiomethacrylate, A New Sodium Organic with Possible Cyclic Structure

BY D. O. DEPREE

RECEIVED JUNE 8, 1959

A new organosodium compound, sodium β-sodiomethacrylate, may be prepared by the reaction of sodium amide with sodium methacrylate in an open system at about 200°. Proof of its β-sodio substitution has been afforded by its ready reaction with carbon dioxide to give disodium itaconate and reaction with dimethyl sulfate to give sodium ethacrylate. A cyclic structure for the compound is proposed as an explanation of its high thermal stability. The infrared spectrum of the compound is consistent with such a structure. A mechanism of formation is proposed.

The synthesis of sodium α-sodioacetate by the reaction of sodium amide with sodium acetate was described in a previous publication.[1] The remarkably high thermal stability (decomposition at 280°), as well as the inertness of this compound to air oxidation, was explained on the basis of the formation of a resonance hybrid involving distribution of the negative charge between the α-carbon and the carbonyl groups. This work suggested that lower thermal stability and higher reactivity could be expected if one were to metalate an organic acid salt in which there could be no resonance stabilization involving the carbonyl group.

To test this hypothesis, sodium methacrylate was metalated with sodium amide by the same technique at 200°. It was anticipated that the β-sodio derivative would decompose below its synthesis temperature, because the compound would be expected to have the lower stability of an allylic sodium compound with no resonance contribution available from the carboxyl portion of the molecule. Unexpectedly, the compound had a high thermal stability and formed readily.

$$CH_2C(CH_3)CO_2Na + NaNH_2 \longrightarrow CH_2C(CH_2Na)CO_2Na + NH_3 \quad (1)$$

Preparation.—Equimolar quantities of sodium amide and anhydrous sodium methacrylate were carefully blended and then added gradually to a heated vessel (180–220°). The evolution of ammonia was immediate and steady. The mixture was heated until evolution of ammonia ceased.

The product of this reaction is a tan solid, insoluble in hydrocarbons. The material reacts slowly with dry air at room temperature and shows only slight thermal instability at temperatures up to 290°, where it darkens without evolution of gas. Decomposition occurs very slowly at 250° on prolonged heating. The product softens but does not melt at temperatures below its decomposition temperature. It does not sublime at temperatures up to 200° under vacuum.

Chemical Properties.—When the reaction product is added to water, heat is evolved and sodium methacrylate and sodium hydroxide are formed by the hydrolysis

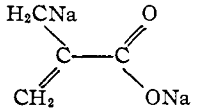
$$CH_2C(CH_2Na)CO_2Na + H_2O \longrightarrow CH_2C(CH_3)CO_2Na + NaOH \quad (2)$$

A study of the reactions of the β-sodio compound with carbon dioxide and with dimethyl sulfate provides proof of its identity. Carboxylation with carbon dioxide at room temperature yields disodium itaconate, and methylation with dimethyl sulfate yields sodium ethacrylate.

$$CH_2C(CH_2Na)CO_2Na \xrightarrow{CO_2} CH_2C(CH_2CO_2Na)CO_2Na \quad (3)$$

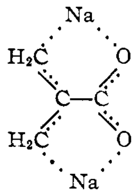
$$CH_2C(CH_2Na)CO_2Na \xrightarrow{(CH_3)_2SO_4} C_2H_4C(CH_2)CO_2Na \quad (4)$$

Probable Structure.—A study of the reactions carried out with sodium β-sodiomethacrylate leads to the conclusion that substitution consistently occurs in the β-position. This indicates the structure



(5)

However, the high thermal stability suggests greater stabilization than that afforded by the allylic portion of the molecule. Accordingly, the following cyclic structure is proposed for the compound



(6)

This structure is a hybrid in which both the allylic structure and the carbonyl portion of the molecule can contribute to its stabilization. Furthermore, a high degree of symmetry is provided which also contributes to the stability. These considerations would also explain the ease of formation of the com-

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[1] D. O. DePree and R. D. Closson, THIS JOURNAL, 80, 2311 (1958).