3. An interesting similarity in aroma is shown by 2-phenyl-, 2-α-furyl-, and 2-α-thienyl-benzothiazoles.

NEW YORK, N. Y.

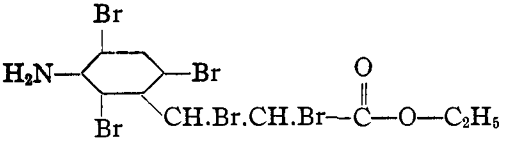
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

REACTIONS OF ETHYL AMINOCINNAMATES WITH BROMINE[1]

BY H. W. UNDERWOOD, JR., AND E. L. KOCHMANN

RECEIVED SEPTEMBER 3, 1925 PUBLISHED JANUARY 8, 1926

Since ethyl *m*-aminocinnamate contains a double bond in the side chain and one ring hydrogen atom *para* to the amino group as well as two atoms of hydrogen in *ortho* positions, treatment of this ester with an excess of bromine might yield a derivative containing three atoms of halogen in the nucleus and two in the side chain,



Possibly a study of the compound obtained by the use of bromine and the ester in molecular proportions would show whether substitution of halogen in the ring preceded addition to the ethylene linkage. The esters of *o*- and *p*-aminocinnamic acids offer analogous possibilities, except that each of these compounds contains only two sensitive aromatic hydrogen atoms. This paper is an account of results obtained in an investigation of reactions in this series. Since chloroform is not readily brominated and apparently does not cause side reactions it has been employed as a solvent and diluent.

Discussion of Experiments and Interpretation of Results[2]

Nitration of Cinnamic Acid and Esterification of the *o*- and *p*-Nitro Derivatives.—The procedure employed was essentially that given by Müller.[3] For the removal of nitrocinnamic and nitrobenzoic acids from ethyl *o*-nitrocinnamate cold, concd. sodium carbonate solution was used; crystals of the *ortho* ester were obtained from alcohol. Yields are recorded in the summary.

Ethyl *m*-Nitrocinnamate.—A 43.8% yield of *m*-nitrocinnamic acid was obtained from 100 g. of technical *m*-nitrobenzaldehyde by the usual method.[4] The average of the yields in several esterifications was 92%.

---

[1] The experimental results described in this paper are taken from a thesis submitted to the Faculty of the Massachusetts Institute of Technology by E. L. Kochmann in partial fulfilment of the requirements for the degree of Master of Science.

[2] All the temperatures given are uncorrected.

[3] Müller, *Ann.*, **212,** 124 (1882).

[4] Schiff, *Ber.*, **11,** 1782 (1878). Tiemann and Oppermann, *Ber.*, **13,** 2060 (1880).

Reduction of Ethyl Nitrocinnamates.—Miller and Kinkelin[5] described a process for the reduction of ethyl *p*-nitrocinnamate by means of tin and hydrochloric acid. We used this procedure for the *o*-, *m*- and *p*-nitro esters. In the treatment of the *ortho* compound the reaction mixture was diluted with 500 cc. of water and 100 cc. of 95% ethyl alcohol (for 25 g. of ester); evaporation to dryness of the liquid obtained from the reduction of ethyl *p*-nitrocinnamate after the removal of tin sulfide gave the hydrochloride of *p*-aminocinnamic acid, which was subsequently esterified.[6] Yields of the amino ester are recorded in the summary.

Bromination of Ethyl Aminocinnamates

Chloroform was used as a solvent (5 cc. for 1 g. of amino compound) in the bromination experiments. Weighed amounts of a 15% solution of bromine in chloroform were slowly added during stirring. During the course of each experiment, which was carried out in ordinary diffused light, the reaction mixture was kept cold by surrounding the beaker with cracked ice. In some cases evolution of hydrogen bromide occurred. Subsequently, the reaction mixture was allowed to stand under a hood until partial or complete evaporation of the chloroform had taken place. The solid thus secured was air-dried and purified, if necessary, by crystallization from appropriate solvents. The results obtained are given below.

TABLE I

RESULTS

Expt.	Amino ester		Bromine atomic equivalents	Products				
		G.		G.	M. p., °C.	Calcd. for formula	Br, %	Found, %
1	*ortho*	4	8	..	235–239	$C_{11}H_{11}O_2NBr_7$:	74.73	74.50; 74.61
2	*ortho*	4	8	4	251–253	$C_{11}H_{11}O_2NBr_4$:	62.82	62.00; 62.15
3	*ortho*	4	2	as described in Expt. 2				
4	*meta*	8	8	16.7	145	$C_{11}H_{10}O_2NBr_5$:	67.98	68.10; 68.21
5	*meta*		2	..	110	$C_{11}H_{10}O_2NBr_3$:	56.03	55.85; 55.86
6	*para*	4	8	6	..	$C_{11}H_{12}O_2NBr_5$:	67.75	67.71
7	*para*	4	8	..	112.5	$C_{11}H_{12}O_2NBr_3$:	55.76	55.51; 55.58
8	*para*	2	2	tar; no compound isolated				

The figures given under bromine refer to the number of atoms of halogen for one molecule of amino ester. The compound obtained by partial evaporation of the solvent in Expt. 1 was a dark red, crystalline solid; results of analyses indicated that it was a perbromide. Upon standing overnight this substance became yellowish-brown, and after three crystallizations from glacial acetic acid and two from alcohol, it was light yellow, weighed 4 g., and melted incompletely at 251–253°; this is the material described in Line 2. Ethyl alcohol was employed for crystallizing com-

---

[5] Miller and Kinkelin, *Ber.*, **18**, 3234 (1885).

[6] The reduction of ethyl *o*- and *p*-nitrocinnamates is described in Beilstein, but the preparation of ethyl *m*-aminocinnamate (by the use of tin and acid) is not mentioned. Beilstein contains no reference to ethyl *p*-aminocinnamate.

pounds given under Expts. 4 and 5; the material referred to in Expt. 6 was not crystallized. The substance described in Expt. 7 was obtained by crystallizing the compound having the composition $C_{11}H_{12}O_2NBr_5$ twice from glacial acetic acid; during this operation hydrogen bromide was evolved. Analyses reported are percentages of bromine. Amounts of products given are the weights before purification.

Investigations of the Structure of the Brominated Compounds

Since ethyl *o*-aminocinnamate contains two sensitive ring hydrogen atoms and an unsaturated side chain, it might be inferred that the tetrabromo derivative contained two atoms of halogen in the ring and two in the side chain. Evidence in support of this idea was secured by heating a 0.15g. sample of the compound for one hour with an excess (calcd. amt. × 10) of a 1% solution of silver nitrate in alcohol. The weight of bromine in the silver bromide formed was found to be 30.6% of the weight of the sample; two atoms of bromine in the tetrabromo compound constitute 31.33% of its molecular weight.

By use of the procedure described above, a value of 26.48% for the pentabromo *m*-amino compound was secured; two atoms of bromine in the substance constitute 27.19% of its molecular weight.

One g. of ethyl tribromo-*m*-aminocinnamate was added to 27.6 g. of 10% solution of potassium hydroxide (about seven times the amount necessary to saponify the ester and remove two molecules of hydrogen bromide) in ethyl alcohol, and the material heated for 1.5 hours on a water-bath. After the reaction mixture had been poured into water, it was filtered and the clear liquid acidified with hydrochloric acid. The solid thus obtained was collected on a filter, dried and crystallized from alcohol. Results of analyses showed that the compound contained three atoms of bromine. Evidently treatment with alcoholic potassium hydroxide hydrolyzed the ester but did not remove any bromine; this indicates that the halogen atoms are in the ring.

Anal. Calcd. for $C_9H_6NBr_3$: Br, 59.96. Found: 59.71, 59.80.

Treatment of 1.1 g. of ethyl tribromo-*p*-aminocinnamate with an excess of alcoholic potassium hydroxide solution (approximately six times the amount necessary to hydrolyze the ester and to remove two molecules of hydrogen bromide) in the manner previously described produced a white solid, which melted with some decomposition after thorough washing with water and drying.

Anal. Calcd. for $C_9H_7O_2NBr_2$: Br, 49.80. Found: 49.00, 49.18.

Evidently one of the halogen atoms is in the side chain and two are in the ring.

Summary

When cinnamic acid is nitrated a mixture of the *o*- and *p*-mononitro derivatives is obtained; the isomeric esters produced by treating the product with absolute ethyl alcohol can be separated by crystallization. If it is assumed that the esterification reactions give quantitative results, the yields of *o*- and *p*-nitrocinnamic acids are approximately 17 and 43%. Reduction of ethyl *o*-, *m*- and *p*-nitrocinnamates by means of tin and hydrochloric

acid produces the corresponding amino esters in 45, 60 and 52% yields, respectively.

Treatment of ethyl *o*-aminocinnamate with quantities of bromine which correspond to eight and to two atoms for one molecule of ester yields a compound containing four atoms of bromine, two of which are apparently in the side chain.

Upon reaction with an amount of bromine sufficient to saturate the double bond and to replace all sensitive hydrogen atoms in the ring, ethyl *m*-aminocinnamate is transformed into a compound in which five atoms of bromine are present; reactions of this derivative indicate that two atoms of bromine are in the side chain and three in the aromatic nucleus. The use of one molecule of halogen for one of ester yields a tribromo derivative, in which all three halogen atoms are aromatic. Apparently, substitution of bromine in the ring precedes addition to the double bond.

If the ethyl ester of *p*-aminocinnamic acid is treated with an excess of bromine a compound containing three atoms of halogen is secured; only one of the bromine atoms is in the side chain. A plausible explanation of this result may be found by assuming that bromine first enters the ring and that the hydrogen bromide thus formed adds to the aliphatic unsaturated linkage. If two atoms of bromine for one molecule of ester are employed a tarry mixture is secured; no pure compound was obtained from this material.

CAMBRIDGE A, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

SOME ETHER-SUBSTITUTED DERIVATIVES OF DIETHYL MALONATE AND BARBITURIC ACID

BY ARTHUR J. HILL AND DEWITT T. KEACH[1]

RECEIVED SEPTEMBER 9, 1925 PUBLISHED JANUARY 8, 1926

Since the preparation of 5,5-diethylbarbituric acid (Veronal or Barbital) by Fischer and von Mering, and the subsequent discovery of its hypnotic properties, a large amount of research has been carried out with a view to securing hypnotics superior to this substance.

In general these attempts have centered on substitution in Position 5, in which the effect of a very large number of organic radicals has been investigated. Among these, ether groups[2] of the types represented by $—OC_6H_5$ and $—CH_2CH_2.OR$ have been introduced, and their physiological effects studied. In connection with these, it is interesting to note that the

---

[1] From a part of the dissertation presented by DeW. T. Keach to the Faculty of the Graduate School of Yale University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Dox and Yoder, THIS JOURNAL, **44**, 1578 (1922). Ger. pat. 285,636 (1915); 295,492 (1917). U. S. pat. 1,217,446; 1,217,447 (1917).