was then treated with decolorizing carbon and with attapulgus clay. Ether was removed at reduced pressure, keeping the temperature below 20°. The 34.5 g. (40%) of resulting oil VIII was rapidly colored by decomposition and could not be recrystallized.

2,2,2-Trichloro-1-(2-pyrryl)-ethyl Acetate.—Five grams of VIII was dissolved in 50 ml. of pyridine and 50 ml. of acetic anhydride. After three days the solution was poured into 1 l. of ice-water and the solid separated. Recrystallization from petroleum ether (b.p. 60–80°) yielded 4.5 g. (75%) of colorless needles, m.p. 69.8–70.8° dec.

Anal. Calcd. for $C_8H_8O_2NCl_3$: C, 37.46; H, 3.14. Found: C, 36.96; H, 3.07.

2,2,2-Trichloro-1-(N-methylpyrryl-2)-ethanol (IX).—As in the procedure used for VIII, 32.4 g. (0.4 mole) of N-methylpyrrole gave 40 g. of dark purple oil. This was dissolved in excess hot petroleum ether (b.p. 60–80°), treated with decolorizing carbon and attapulgus clay, then cooled by dry ice for 24 hours, then at 0° for 24 hours to yield 24 g. (26.5%) of colorless prisms, m.p. 58–60° dec. Two crystallizations from petroleum ether (b.p. 60–80°) raised the m.p. to 66.5–67.2° dec.

Anal. Calcd. for $C_7H_8ONCl_3$: C, 36.79; H, 3.53. Found: C, 36.99; H, 3.16.

2,2,2-Trichloro-1-(N-methylpyrryl-2)-ethyl Acetate.—By the procedure used for the acetate of VIII, 10 g. of the above carbinol yielded 8.5 g. (72%) of colorless prisms from petroleum ether (b.p. 30–60°), m.p. 63.0–64.0° dec.

Anal. Calcd. for $C_9H_{10}O_2NCl_3$: C, 39.95; H, 3.73. Found: C, 39.58; H, 4.01.

Acknowledgment.—The authors are indebted to Mr. Robert Carlson, Mrs. Margaret McConaghy and Mrs. Marian Sprott for carrying out the biological assays. Also, the authors wish to thank Mr. H. J. Barrett of E. I. du Pont de Nemours & Co. for supplying some of the starting chemicals used.

RIVERSIDE, CALIFORNIA

[CONTRIBUTION FROM HICKRILL CHEMICAL RESEARCH LABORATORY]

On the Reported Rearrangement of 2,4,7-Tribromotropone to 3,5-Dibromobenzamide

BY W. VON E. DOERING[1] AND ADNAN ABDUL-RIDA SAYIGH

RECEIVED JULY 27, 1953

The interesting report of Nozoe, *et al.*, that 2,4,7-tribromotropone is rearranged by ammonia to a mixture of 2,5- and 3,5-dibromobenzamide is incorrect. It is shown by infrared analysis that the mixture contains no appreciable amount of 3,5-dibromobenzamide and consists of the expected 2,4- and 2,5-dibromobenzamide in the approximate ratio of 1:2.

The aromatizing rearrangements of tropolone methyl ethers with methoxide ion and of 2-halotropones with hydroxide ion have been used by many workers in the field as the key reactions for determining the position of substituents in the tropolone ring system. It is therefore a matter for concern, particularly to us who have relied extensively on the rearrangement of halotropones,[2] when Nozoe, *et al.*,[3] asserts that 2,4,7-tribromotropone rearranges in methanolic ammonia to **3,5-dibromobenzamide**, that is, with simultaneous rearrangement of a bromine atom. That "this is a remarkable phenomenon that should be well-remembered[3]" seemed worthy of independent experimental investigation.

Dauben and Ringold[4] have communicated the preparation of 2,4,7-tribromotropone (I) by the reaction of bromine and 2-cyclohepten-1-one and have assigned its structure by isolation of 2,5-dibromobenzoic acid on treatment of I with ethanolic hydroxide ion. Nozoe, *et al.*,[5] have prepared I by the direct bromination of cycloheptanone and have confirmed its structure by rearrangement with hydroxide ion to 2,4- and 2,5-dibromobenzoic acids.[3] Unable to reproduce this latter preparation, presumably because of the inadequacy of the published experimental details, we have found that cycloheptanone can be converted quantitatively to a tribromo derivative[6] which when treated with bromine under more drastic conditions gives I in 41% yield.

The rearrangement of I was effected both in methanolic ammonia and liquid ammonia according to Nozoe, *et al.*[3] We likewise found the task of separation by crystallization difficult, although 2,5-dibromobenzamide could be isolated in pure form. The unpurified amides were hydrolyzed both with sulfuric acid according to Nozoe, *et al.*,[3] and with alkali, the product in both cases having identical infrared spectra. The unpurified mixture of dibromo acids was converted to the mixture of methyl esters with diazomethane. Comparison of the infrared spectrum of this mixture with the spectra of the pure methyl esters of 2,4- (II), 2,5- (III) and 3,5- (IV) dibromobenzoic acids (Table I) shows that both II and III are present and that IV is not detectable, even though the differences between the spectra are very favorable for the detection of IV. A small amount of unidentified material can be observed however. Either by calculation using the six wave numbers in bold-face type in Table I or by comparison with the infrared spectra of synthetic mixtures of II and III (40/60, 34/66 and 30/70), it appears that the mixture consists of about 1 part II and 2 parts III.

Contrary to the report of Nozoe, *et al.*,[3] the rearrangement of 2,4,7-tribromotropone with ammonia does not give 3,5-dibromobenzamide but

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(1) Sterling Chemistry Laboratory, Yale University, New Haven, Conn.

(2) (a) W. von E. Doering and L. H. Knox, THIS JOURNAL, **74**, 5683 (1952); (b) **75**, 297 (1953); (c) W. von E. Doering and J. R. Mayer, *ibid.*, **75**, 2387 (1953).

(3) T. Nozoe, Y. Kitahara, S. Masamune and S. Yamaguchi, *Proc. Japan Acad.*, **28**, 85 (1952).

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(6) According to O. Wallach, ***Ann.***, **418**, 36 (1919), cycloheptanone is converted to a dibromo derivative, m.p. 70–72°, in hot glacial acetic acid, whereas according to Nozoe, *et al.*,[5] in ice-cooled acetic acid it is converted to a tetrabromo derivative, m.p. 78°. It is under conditions identical with Nozoe's within the limits of the published description, that we obtain a tribromocycloheptanone, m.p. 71–72°.

proceeds normally giving 2,4- and 2,5-dibromobenzamide. Accordingly the structural reliability of the method need not be questioned.

Experimental[7]

Bromination of Cycloheptanone.—In an erlenmeyer flask equipped with a magnetic stirrer, thermometer and addition funnel, was placed 5.6 g. (0.05 mole) of cycloheptanone in 10 ml.of glacial acetic acid. Over a period of 45 min., 32 g. (0.2 mole) of bromine in 24 ml. of glacial acetic acid was added while the temperature was maintained below 8° by ice-cooling. The reaction mixture was placed in a refrigerator at 3–4° for 14 hr., after which it was stirred for an additional 4 hr. below 10°. At the end of this time, a light yellow solid precipitated. The mixture was poured into 400 ml. of ice-water and filtered; the tribromocycloheptanone obtained after drying in a desiccator over calcium chloride weighed 17.4 g. (100%) and melted at 71–72° after one or more crystallizations from either methanol or *n*-hexane.

Anal. Calcd. for $C_7H_9OBr_3$: C, 24.1; H, 2.6; Br, 68.7. Found: C, 24.3; H, 2.7; Br, 68.9.

2,4,7-Tribromotropone (I).—In a flask equipped with a condenser, 8.5 g. (0.02 mole) of tribromocycloheptanone in 20 ml. of glacial acetic acid was brominated by adding 6.4 g. (0.04 mole) of bromine in 20 ml. of glacial acetic acid, portionwise over a period of 15 min. The reaction mixture was heated at 96–98° for 18 hr., cooled to a solid mass, warmed to room temperature and filtered, affording 0.45 g. of yellow solid, m.p. 183–185°. The mother liquor was treated with 8 g. (0.05 mole) of bromine and heated to 105–110° for 6 hr. Similar treatment to that above afforded 2.63 g. of yellow solid, m.p. 183–185°. The mother liquor was evaporated to dryness *in vacuo*, giving a residue which was extracted with 100 ml. of hot chloroform. The chloroform solution was filtered while hot, extracted thoroughly with 1 *N* sodium bicarbonate, dried over magnesium sulfate, filtered and concentrated. The residue on sublimation afforded 0.2 g. of solid, m.p. 182–185°. The total amount of 2,4,7-tribromotropone (I) obtained was 3.3 g. (41% of theory), m.p. 184.5–185.5° after one crystallization from methanol (reported m.p. 184.5–185.0°[6] and 182.5–183.5°[4]).

Anal. Calcd. for $C_7H_3Br_3O$: Br, 69.9. Found: Br, 69.6.

Rearrangement of 2,4,7-Tribromotropone (I). (a) In Methanolic Ammonia.—A solution of 0.25 g. of I in 20 ml. of methanol was saturated with ammonia at room temperature and heated in a sealed tube at 134–136° for 15 hr. The ammonia and methanol were blown off by a stream of dry air, leaving a residue which was sublimed, affording 0.2 g. (96% of theory) of a mixture of dibromobenzamides, m.p. 155–168°. Fractional crystallization of the mixture from benzene and then from methanol yielded 2,5-dibromobenzamide, m.p. 180–181°; mixed m.p. with an authentic sample gave no depression, while mixed m.p. with either authentic 2,4-dibromobenzamide or 3,5-dibromobenzamide depressed.

(b) In Liquid Ammonia.—In a trap protected from moisture with a calcium chloride tube, and cooled with Dry Ice in acetone, 0.2 g. of I was dissolved in liquid ammonia by condensing about 20 ml. of ammonia. Cooling was stopped and the ammonia was allowed to evaporate, leaving a solid residue which, on sublimation, yielded 0.19 g. (90% of theory) of a mixture of dibromobenzamides, identical in infrared spectrum with that obtained from the rearrangement of I in methanolic ammonia.

Hydrolysis of the Mixed Dibromobenzamides. (a) With Hydroxide.—Refluxing a solution of 200 mg. of the mixed dibromobenzamides in 5.5 ml. of 10% sodium hydroxide and 2 ml. of ethanol for one hour, followed by evaporation of the ethanol, cooling, acidification of the solution with concentrated hydrochloric acid and filtration, afforded 190 mg. (95% of theory) of acidic material, m.p. 126–135° after one sublimation.

(b) With Acid.—The mixed dibromoamides (100 mg.) in 5 ml. of 75% sulfuric acid were heated at 160–170° for 6–7 hr. The reaction mixture was cooled, poured into a mixture of ice and water and filtered. The solid after drying weighed 90 mg. and melted at 126–132° after one sublimation. Its infrared spectrum was identical with that of the mixture of dibromo acids obtained from the alkaline hydrolysis.

Methyl 2,4-Dibromobenzoate (II).—Prepared from acetanilide[8a] *via* 2,4-dibromoacetanilide,[9] the acid had m.p. 172–172.5° (reported m.p. 173.5–174.5°[8a]; m.p. 169°[10]; m.p. 173.0–175°[11]); amide, m.p. 197–198° (reported m.p.

TABLE I

INFRARED SPECTRA[a] OF THE METHYL ESTERS OF DIBROMOBENZOATES

II		III		IV		Mixture[b]	
Cm.$^{-1}$	T, %	Cm.$^{-1}$	T, %	Cm.$^{-1}$	T, %	Cm.$^{-1}$	T, %
						3480	92
						3340	90
3060	91	3055	93	3050	87	3060	92
2975	85	2960	89	2968	72	2975	87
2930	74	2920	79			2925	75
2828	90	2820	94			2820	92
1730	8	1737	9	1721	4	1733	8
						[1691	57][c]
						[1604	72]
1575	17[d]	1577	86			1575	41
1548	65	1553	86	1557	30	1548	74
				1477	81		
1468	42	1460	48	1466	75	1465	50
1435	31	1438	33	1441	71	1436	30
				1427	40		
				1418	37		
		1384	**50**	1378	59	1382	56
1367	41			1368	51	1367	65
		1335	83			1330	82
1285	5	1285	5			1285	4
1270	29	1260	37	1264	2	1260	38
1245	11	1245	9			1244	7
1193	56	1193	66			1192	57
				1176	71		
1147	52					1146	50
1140	54	1137	48	1131	30	1140	49
1126	20	1125	42			1123	31
1115	15	1113	29			1112	24
1086	43	1090	44	1100	43	1087	42
1039	12	1033	19	1022	45	1033	25
965	86	**970**	49			969	55
				910	81		
		896	83	899	75	893	84
875	64			875	43	874	82
		845	81			845	80
827	**38**					827	67
				717	73		
680	80					680	88
				662	67		
656	87	657	87			655	81

[a] The infrared spectra were taken in a Perkin–Elmer Model 21 Recording Infrared Spectrophotometer using a sodium chloride prism and a 0.104-mm. cell and 0.3 *M* solutions of the esters in carbon tetrachloride. [b] The mixture of methyl esters obtained by hydrolysis and diazomethane esterification of the crude rearrangement product of I. [c] The wave numbers in brackets are those which are not present in the spectra of II, III or IV. [d] The wave numbers in bold-faced type are those used in the quantitative estimation of the composition of the mixture.

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(7) All melting points are corrected. Analyses were performed by the Schwarzkopf Microanalytical Laboratories, 56-19—37th Avenue, Woodside 17, New York.

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195°[12b]; m.p. 198°[11]); methyl ester by diazomethane esterification and crystallization from *n*-pentane at −40°, m.p. 34° (reported m.p. 33°[12b]).

Methyl 2,5-Dibromobenzoate (III).—The acid was prepared from 2,5-dibromotoluene by oxidation with nitric acid,[10] m.p. 151–152° (reported m.p. 153°[10]); amide, m.p. 182–183° (not reported); methyl ester (prepared as above), m.p. 40–41°.

Methyl 3,5-Dibromobenzoate (IV).—Prepared from anthranilic acid by the method of Bogert and Hand,[13] 3,5-dibromobenzoic acid melted at 217–218° (reported m.p. 219–220°[13]; m.p. 218.5–219.5°[8b]); amide, m.p. 185–186° (reported[10,12a] m.p. 187°); methyl ester, m.p. 51–52°.

Analysis of the Mixed Methyl Esters by Infrared Spectroscopy.—Treatment of the mixed dibromo acids with diazomethane without purification yielded an oil whose infrared spectrum was determined and compared with the spectra of the pure esters (Table I). Quantitative comparison could not be expected to give excellent results because the mixture of methyl esters contains at least one unidentified substance in addition to II and III. In Table II the results of estimating the relative amounts of II and III are shown using six appropriate bands. There is 33.5 ± 8% of II and 66.5 ± 8% of III neglecting the impurities. By way of confirmation the spectrum of a mixture of II and III (34/66) agreed better with the unknown than 30/70 or 40/60 synthetic mixtures.

TABLE II

Cm.$^{-1}$	II, %	III, %
1575	46	
1384	[27]	73
1367	36	
970	[20]	80
875	37	
827	35	

KATONAH, NEW YORK

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF KANSAS]

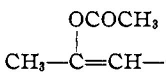
Mechanism of the O-Benzoylation of Ethyl Benzoylacetate in Pyridine

BY WILLIAM R. GILKERSON,[1] WILLIAM J. ARGERSINGER, JR., AND WILLIAM E. MCEWEN

RECEIVED AUGUST 3, 1953

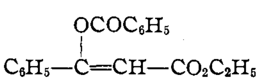
The rate of formation of ethyl β-benzoxycinnamate (II) from benzoyl chloride and ethyl benzoylacetate in pyridine solution at 25° has been measured. The rate data are best interpreted as indicating an initial condensation reaction between the benzoylpyridinium cation (VIII) and the enol form of ethyl benzoylacetate to give both ethyl benzoyl-(1-benzoyl-1,4-dihydro-4-pyridyl)-acetate (XA) and ethyl benzoyl-(1-benzoyl-1,2-dihydro-2-pyridyl)-acetate (XIA). The latter rearranges *via* a quasi six-membered ring transition to give pyridine and ethyl β-benzoxycinnamate (II).

The present study was undertaken in an effort to determine the mechanism of the reaction of an acid chloride with a β-ketoester in pyridine solution. This reaction represents a well known synthetic method for the preparation of the O-acyl derivative. Examples include the preparation of ethyl O-acetylacetoacetate (I) from ethyl acetoacetate and acetyl chloride,[2] and of ethyl β-benzoxycinnamate (II) from ethyl benzoylacetate and benzoyl chloride.[3,4] The yields of the O-acyl derivatives, I and II, are excellent, and there is no evidence that either of the isomeric C-acyl derivatives, ethyl diacetylacetate (III) and ethyl dibenzoylacetate (IV), respectively, is formed in the reaction.



$$CH_3-\overset{\overset{\displaystyle OCOCH_3}{|}}{C}=CH-CO_2C_2H_5$$

I



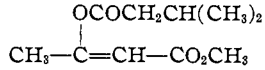
$$C_6H_5-\overset{\overset{\displaystyle OCOC_6H_5}{|}}{C}=CH-CO_2C_2H_5$$

II

$(CH_3CO)_2CHCO_2C_2H_5$
III

$(C_6H_5CO)_2CHCO_2C_2H_5$
IV

The situation with respect to the use of other tertiary amines as the solvent is somewhat confused. Claisen and Haase[5] reported that the use of dimethylaniline and antipyrine led to the formation of O-acyl derivatives, but they gave no experimental details. Bouveault and Bongert[6] prepared methyl O-isovalerylacetoacetate (V) in 55% yield by the reaction of isovaleryl chloride with methyl acetoacetate in diethylaniline, but they did not indicate whether any of the C-acyl derivative also was formed. They did make a qualitative statement, however, to the effect that the conversion to the O-acyl derivative is more nearly complete in pyridine solution than in diethylaniline.



$$CH_3-\overset{\overset{\displaystyle OCOCH_2CH(CH_3)_2}{|}}{C}=CH-CO_2CH_3$$

V

The main result of the reaction of the sodium salt of a β-ketoester with an acid chloride in an inert solvent is C-acylation. Small amounts of the O-acyl derivatives are sometimes isolated in these reactions.[7-11] The observation by Claisen and Haase[8] that ethyl O-acetylacetoacetate (I) was isomerized to ethyl diacetylacetate (II) by the action of the sodium salt of ethyl acetoacetate led these workers to suggest that the O-acyl derivative is an intermediate in the formation of the C-acyl derivative. This suggestion has been refuted by Dieckmann and Stein[12] and also by Michael and Carlson,[11] who demonstrated that the reaction of the sodium salt of a β-ketoester with an acid chloride can give the C-acyl derivative under conditions which do not permit the isomerization of the O-acyl derivative to the C-acyl derivative. In other words, they

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(1) Atomic Energy Commission Fellow, 1951–1953.

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