

2,2'-Diduroylbibenzyl (VIII). A. From Duryl *o*-Tolyl Ketone.⁸—To a solution of 5.1 g. of duryl *o*-tolyl ketone in 60 ml. of anhydrous ether was added dropwise 25 ml. of a 1.05 *N* ethereal solution of *n*-butyllithium, while the temperature was maintained at -30° by means of a solid carbon dioxide-acetone bath. The addition, which required 10 minutes, was carried out under nitrogen and with constant stirring. The mixture was stirred at -30° for 1 hr. and then heated under reflux for 1.5 hr., while a stream of oxygen was allowed to pass slowly through it. After the mixture had been decomposed with dilute sulfuric acid, a white solid persisted between the ether and water layers. It was collected on a filter and dried, 0.37 g. (7.4%). After two recrystallizations of the solid from dimethylformamide, it was in the form of fine, colorless needles, m.p. 323.5 – 325.5° .

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 86.01; H, 7.62. Found: C, 85.82; H, 7.69.

The infrared spectrum contains bands attributable to a hindered, conjugated carbonyl group (1660 cm.^{-1}) and to *o*-disubstituted benzene (757 cm.^{-1}).

B. From *o*-Duroylbenzyl Bromide.—A solution of 1.5 g. of *o*-duroylbenzyl bromide in 20 ml. of anhydrous toluene and 20 ml. of anhydrous ether was added very rapidly to 6 ml. of an ethereal solution of 0.086 *N* *n*-butyllithium, main-

tained at -30° by means of a solid carbon dioxide-acetone bath. The addition was carried out with constant stirring in an atmosphere of nitrogen. The solution was stirred for one minute and then poured on a large excess of powdered solid carbon dioxide. After the mixture had come to room temperature, it was decomposed with dilute sulfuric acid. A nearly white solid, which persisted between the water and organic layers, was removed with the organic layer. This mixture was extracted three times with 5% sodium carbonate and washed with saturated sodium sulfate. No precipitate appeared when the sodium carbonate washings had been combined and acidified. The white solid was separated by filtration from the organic layer, which was dried over anhydrous magnesium sulfate. After two recrystallizations of the solid from dimethylformamide, 0.14 g. (12%) of colorless needles, m.p. 323 – 326° , was obtained.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 86.01; H, 7.62. Found: C, 85.62; H, 7.76.

A mixture melting point with a sample of the coupling product prepared by method A showed no depression, and the infrared spectra are identical. By removal of the solvent from the dried organic layer, 0.57 g. (38%) of the original bromoketone was recovered.

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[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE UNIVERSITY]

The Reaction of Acyl Halides with Cyclopropane

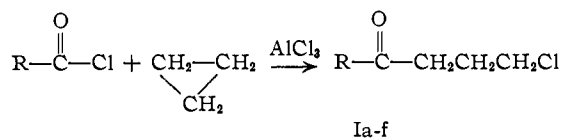
BY HAROLD HART AND OMER E. CURTIS, JR.

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Cyclopropane, with a homogeneous solution of $\text{RCOCl}:\text{AlCl}_3$ in chloroform, gave the unanticipated β -chloroketone $\text{RCOCH}(\text{CH}_2)\text{CH}_2\text{Cl}$ (II) as the major product, in addition to the expected γ -chloroketone $\text{RCO}(\text{CH}_2)_2\text{Cl}$ (I).

Attention often has been drawn¹⁻⁴ to the similarity between the cyclopropane ring and the olefinic double bond, both with regard to physical properties and chemical behavior. It is the purpose of this paper to describe results obtained from the Lewis-acid catalyzed reaction of cyclopropane with acyl halides; the corresponding reaction with olefins leads to β -chloroketones.⁵

It was anticipated that the products from acyl halides and cyclopropane would be γ -haloketones



R = a, CH_3 ; b, C_2H_5 ; c, *n*- C_3H_7 ; d, *i*- C_3H_7 ; e, cyclo- C_3H_5 ; f, C_6H_5

(1) For a general review, see R. A. Raphael in E. H. Rodd, "Chemistry of Carbon Compounds," Vol. IIa, Elsevier Publishing Co., Houston Texas, 1953, pp. 25-28.

(2) E. Vogel, *Fortschr. Chem. Forsch.*, **3**, 430 (1955).

(3) (a) C. D. Lawrence and C. F. H. Tipper, *J. Chem. Soc.*, 713 (1955); (b) C. F. H. Tipper, *ibid.*, 2045 (1955).

(4) See, however, G. S. Hammond and R. W. Todd, *THIS JOURNAL*, **76**, 4081 (1954), for the behavior of certain cyclopropane derivatives toward free radicals.

(5) For a review of earlier work, see C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941, Chapter 17. In early studies, considerable quantities of α,β -unsaturated ketones were formed with the expected β -haloketones, either directly or *via* decomposition of the latter. The technique for obtaining the β -haloketones was recently improved (see J. R. Catch, D. F. Elliott, D. H. Hey and E. R. H. Jones, *J. Chem. Soc.*, 278 (1948), and references cited there) so that the reaction has become synthetically useful. See, for example, F. Sondheimer and R. B. Woodward, *THIS JOURNAL*, **75**, 5438 (1953).

Opening of the cyclopropane ring here would be analogous to the formation of *n*-propyl esters from cyclopropane, acids and boron trifluoride.⁶ Since γ -haloketones are readily cyclized by base to cyclopropyl ketones,⁷ one would in effect have a two-step method for acylating cyclopropane. As it turned out, the anticipated reaction was accompanied by an unusual rearrangement, and the product was a mixture of two isomeric chloroketones.

The only previously reported use of cyclopropane as an acceptor in a Friedel-Crafts acylation is that of Krapivin in 1908.⁸ From acetyl bromide, aluminum bromide and cyclopropane in carbon disulfide, a 15-20% yield of a ketone $\text{C}_5\text{H}_8\text{O}$ was reported. It gave a semicarbazone, m.p. 169.5 – 170° , which on acid hydrolysis gave a ketone which polymerized readily and which gave a semicarbazone with a slightly higher melting point (177 – 178°). The product was not further characterized by Krapivin; its probable identity will be established below, but it might be noted here that the melting point of the semicarbazone does not correspond to the semicarbazones of any of the anticipated dehydrohalogenation products of Ia.

Our experimental procedure was similar to that used by Sondheimer and Woodward⁵ with ethylene.

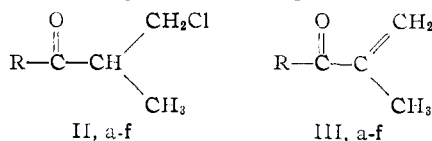
(6) T. B. Dorris and F. J. Sowa, *ibid.*, **60**, 358 (1938); see also ref. 3a.

(7) (a) See, for example, G. W. Cannon, R. C. Ellis and J. R. Leal, *Org. Syntheses*, **31**, 74 (1951); (b) also, H. Hart and O. E. Curtis, Jr., *THIS JOURNAL*, **78**, 112 (1956).

(8) S. Krapivin, *Bull. Soc. Imp. Nat. Moscow*, 1-176 (1908); *Chem. Zentr.*, **91**, I, 1335 (1910); *C. A.*, **6**, 1281 (1911). This article was available to us only as the abstract.

Cyclopropane was rapidly and exothermically absorbed by a solution of the 1:1 complex of aliphatic acid chlorides and aluminum chloride in chloroform at 0° (the reaction was rapid even at -40°). The reaction mixtures were homogeneous and only lightly colored. The yield of crude chloroketones was generally 60-80%. Benzoyl chloride reacted more slowly than aliphatic acid chlorides but also gave a good yield. The results of several experiments are summarized in Table I.

The minor product of the reaction was the expected γ -chloroketone I. The major product, in each case, was a β -chloroketone corresponding to structure II. With R = ethyl, isopropyl or phenyl, it was possible to separate the chloro-



ketones by efficient fractionation. In other cases, the crude chloroketone mixture was treated with sodium bicarbonate or carbonate, which selectively dehydrohalogenated II. The resulting α,β -unsaturated ketones III (Table I, column 8) were easily separable from I by fractional distillation. A summary of the physical constants, derivatives and analyses for the acylation products is given in Table II.

The γ -chloropropyl ketones (I) were identified by cyclization to the corresponding cyclopropyl ketones.⁷ In one case (Ic) a synthesis (di-*n*-propyl-

TABLE I
ACYLATION OF CYCLOPROPANE WITH RCOCl^a

R	Moles of RCOCl	Solvent, ml.	Moles of cyclopropane	Total yield, % ^b	Yield of I, % ^c	Yield of II, % ^c	Yield of III, % ^{c,d}
CH ₃	2.0	1000	2.1	..	30	..	36
C ₂ H ₅	2.0	800	2.05	73	19	39	..
<i>n</i> -C ₃ H ₇	1.5	600	1.79	..	23	..	41
<i>i</i> -C ₃ H ₇	2.2	900	2.33	77	18	34	..
Cyclo-							
C ₃ H ₅	1.11	500	1.31	..	20 ^f	..	30
C ₆ H ₅ ^e	2.0	1100	2.38	64	14	32	..
C ₂ H ₅ ^g	0.5	300	0.5	30	..
C ₂ H ₅	0.5	300 ^h	0.57	9 ^f	..

^a Chloroform solvent, AlCl₃ and RCOCl in equimolar amounts, temperature 0° to room temperature, reaction time as short as cyclopropane could be added without allowing the temperature to rise above 25°. ^b Distilled product, but a mixture of I and II. ^c Fractionated product. ^d Not formed during the reaction but obtained after bicarbonate treatment (see Experimental) of the crude reaction mixture. ^e Not exothermic; stirred for 27 hr. at room temperature. ^f Grams, structure not proved. ^g Ferric chloride catalyst. ^h Nitromethane.

cadmium on cyclopropanecarbonyl chloride) independent of a base-catalyzed cyclization was used.

The carbon skeletons of II were proved in each case by dehydrohalogenation to III and hydrogenation to known isopropyl ketones. The position of the halogen (β not α) was established by independent synthesis in two cases. The action of formaldehyde and hydrogen chloride on diethyl ketone and propiophenone, respectively, gave products identical with those obtained from cyclo-

TABLE II
PROPERTIES AND DERIVATIVES OF THE ACYLATION PRODUCTS FROM RCOCl AND CYCLOPROPANE

R	Product ^a	B.p. °C.	Mm.	<i>n</i> _D ²⁰	Chlorine, %		2,4-Dinitrophenylhydrazones, ^d m.p., °C.	Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %	
					Calcd.	Found ^{b,c}		Calcd.	Found ^c	Calcd.	Found ^c	Calcd.	Found ^c	Calcd.	Found ^c
C H ₃	Ia	77-78	22	1.4368			126-127 ⁱ	43.9	44.1	4.3	4.7	18.6	18.4	11.7	11.6
	IIIa	45-46 ^f	98	1.4229			186-187 ^k								
C ₂ H ₅	Ib	52-53 ^g	3	1.4395	26.4	26.0	128-129	45.8	46.2	4.8	5.0	17.8	17.2	11.3	11.1
	IIb	46 ^h	4	1.4353	26.4	25.9	90-91 ^l	45.8	47.0	4.8	5.1	17.8	17.5	11.3	10.2
<i>n</i> -C ₃ H ₇	Ic	87	11	1.4408	23.9	23.4									
	IIIc	40	13	1.4303	75.0, 10.7 ^j	75.1, 10.4	156-157	53.5	53.2	5.5	5.6	19.2	19.0		
<i>i</i> -C ₃ H ₇	Id	54	3	1.4382	23.9	23.5	104-105	47.5	47.6	5.2	5.4	17.0	16.4	10.8	10.1
	IIId	41	3	1.4340	23.9	23.0	^m								
Cyclo-															
	C ₃ H ₅	Ie ^e	66-76	10	1.4592	24.2	21.3	124-125	47.8	48.0	4.6	4.8	17.1	16.2	10.9
	IIIe	57-58	21	1.4615	76.4, 9.1 ⁱ	74.5, 9.2 ^o	ⁿ								
C ₆ H ₅	If ^p	126-129	5	1.5490											
	IIIf	114	4	1.5425			142-143	52.9	54.5	4.1	4.5	15.4	14.2	9.7	7.2

^a Products of structure I and II were obtained by fractional distillation of the mixed chloroketones; products with structure III were obtained indirectly, by selective dehydrohalogenation of the crude chloroketone mixture, followed by fractional distillation. ^b The haloketones, especially β , decomposed on standing; analyses were usually low, even in freshly distilled samples. Fractions from the distillations were stored at Dry Ice temperature. ^c See footnote 10. ^d All DNP's prepared according to G. D. Johnson, THIS JOURNAL, 73, 5888 (1951), and recrystallized from methanol. ^e The structure of this product was not proved. ^f Cf. J. H. Brant, THIS JOURNAL, 64, 2224 (1942). ^g Cf. H. Normant, Compt. rend., 232, 1942 (1951); H. Wohlgenuth, *ibid.*, 159, 80 (1914). ^h Cf. J. Colonge, Bull. soc. chim., [5] 3, 2116 (1936). ⁱ Percentage C and H, respectively. ^j The semicarbazone melted at 103-104°. I. A. D'yachonov, J. Gen. Chem. (U.S.S.R.), 10, 414 (1940); C. A., 34, 7861 (1940), reports 91-92° for the semicarbazone. Authentic 5-chloro-2-pentanone (ref. 7a) gave identical derivatives as the acylation product. ^k The semicarbazone melted at 174-175° (cf. ketone C₆H₅O in ref. 8); literature values for physical constants and derivatives of methyl isopropenyl ketone vary considerably, but our values agree well with those obtained in a particularly careful study by E. M. McMahon, J. N. Roper, Jr., W. P. Utermohlen, Jr., R. H. Hasek, R. C. Harris and J. H. Brant, THIS JOURNAL, 70, 2971 (1948), who report 184-186° for the DNP and 172.6-173.5° for the semicarbazone. Furthermore, authentic 3-methyl-3-butene-2-one, prepared according to E. Landau and E. P. Irany, J. Org. Chem., 12, 422 (1947), gave derivatives which showed no m.p. depression when mixed with those of IIIa. ^l Resolidified and remelted at 130°. ^m Gave no crystalline DNP on two attempts. ⁿ Derivative turned from red to brown at 150-170° and melted with decomposition at 170-175°. ^o It was later learned that this analysis had been performed on a white amorphous powder; apparently the ketone had polymerized before analysis. ^p J. B. Cloke, THIS JOURNAL, 51, 1174 (1929); also J. B. Couant, J. B. Segur and W. R. Kirner, *ibid.*, 46, 1882 (1924).

propane (IIb and IIc). It will be noted that the product described by Krapivin (*vide supra*) corresponds (see Experimental for details) to the α,β -unsaturated ketone IIIa.

We prefer to postpone a discussion of the mechanism by which II is formed until experiments now in progress are completed. It can be said at this point, however, that the γ -chloroketones I do not rearrange to II under the reaction conditions, that alkyl cyclopropyl ketones are not intermediates and that propylene, which might conceivably arise by arrangement of cyclopropane, gives β -chloroketones of structure R-C-CH₂CHClCH₃.



Extension of this reaction to other acyl halides, other sources of acyl ions, to certain alkyl carbonyl ions and to substituted cyclopropanes will be reported later.⁹

Experimental¹⁰

Acylation Reaction.—The following details for the reaction of propionyl chloride with cyclopropane illustrate the general acylation procedure. To a cooled (ice-bath) suspension of 266 g. (2.0 moles) of anhydrous aluminum chloride in 800 ml. chloroform, there was added (15 minutes) 186 g. (2.0 moles) of propionyl chloride. The mixture was stirred until a homogeneous solution was obtained. Cyclopropane gas (86 g., 2.05 moles) was bubbled in, using a gas delivery tube with a fritted disk. The reaction was exothermic, and the rate of addition controlled so that all the gas was absorbed and the temperature remained below 20° (ice-bath). After the gas was added, stirring was continued for 1 hr. The solution was poured slowly onto a mixture of 1500 g. of cracked ice and 800 ml. of concentrated hydrochloric acid. The chloroform layer was separated, washed successively with water, 10% sodium bicarbonate, water and dried over calcium chloride at 0°. The solvent was removed *in vacuo*; the residue which boiled at 50–60° at 5 mm., was refractionated through an efficient column.

In cases where separation of the isomeric chloroketones was not feasible by fractional distillation, the crude product was refluxed with 20% sodium bicarbonate (for a 1.5-mole run, 500 ml. of aqueous bicarbonate was used) until the rate of CO₂ evolution diminished sharply. The organic layer and ether extracts of the aqueous phase were combined, dried over potassium carbonate and, after removal of the solvent, fractionated to give III followed by I.

The amounts of materials, yields and properties of products are described in Tables I and II.

Structure Proof of I.—The γ -chloroketones were dehydrohalogenated to alkyl cyclopropyl ketones by refluxing with 10% sodium hydroxide for 15 minutes.¹¹ The ketone was then steam distilled, the upper layer and ether extracts of the aqueous layer dried over potassium carbonate. The solvent was stripped and the residue fractionated. Yields and physical constants (Table III) are for pure product; derivatives are also given in Table III.

Authentic *n*-Propyl Cyclopropyl Ketone.—The filtered Grignard reagent from 93 g. (0.74 mole) of *n*-propyl bromide and 18 g. (0.75 mole) of magnesium in 400 ml. of ether was treated at 0° with 0.27 mole of anhydrous cadmium chloride. After 1 hr., 51 g. (0.5 mole) of cyclopropane carbonyl chloride in 100 ml. of anhydrous ether was added and the solution refluxed for 4 hr. After workup, there was obtained 26.0 g. (47%) of *n*-propyl cyclopropyl ketone, b.p. 62° at 25 mm., *n*_D²⁰ 1.4300. The infrared spectrum was identical with that of the material obtained by dehydrohalogenation of Ic. Authentic 2-ethylcyclopentanone was prepared for comparison. Its infrared spectrum was different in many respects from that of *n*-propyl cyclopropyl ketone, showing that Ie, with base, closed only on the near side of the carbonyl group.

(9) Unpublished work with George Levitt.

(10) Carbon, hydrogen and nitrogen analyses by Clark Micro-analytical Laboratories, Urbana, Ill. Halogen analyses by Clark and by O. E. C., Jr.

(11) This is a modification of the procedure described in ref. 7a.

TABLE III
DEHYDROHALOGENATION PRODUCTS FROM Ia-e

R	Yield of alkyl cyclopropyl ketone, %	B.p. of prod.		<i>n</i> _D ²⁰	2,4-DNP m.p., °C.	
		°C.	mm.		Found	Literature
CH ₃	71	110–111	745	1.4222	147	149–150 ^a
C ₂ H ₅	68	48–51	35	1.4229	161–162	161 ^b , 170 ^c
<i>n</i> -C ₃ H ₇	53	63	27	1.4304	151–152	165 ^b , ^d
<i>i</i> -C ₃ H ₇	84	64	40	1.4263	^d	^d
C ₆ H ₅	61	88–90	3	1.5515	149–150 ^b	151, ^f 211–213 ^g

^a J. D. Roberts and C. Green, THIS JOURNAL, 68, 214 (1946). ^b V. A. Slabey and P. H. Wise, *Nat. Advisory Comm. Aeronaut.*, Tech. Note No. 2398, 22 pp., 1951; *C. A.*, 46, 5535 (1952). ^c H. Normant, *Compt. rend.*, 232, 1358 (1951). ^d The DNP melted at 171–175° after the first recrystallization from methanol and at 164–165° after the second and third recrystallizations from the same solvent. This behavior was reproducible. V. A. Slabey (THIS JOURNAL, 74, 4963 (1952)) reported 188° for this DNP. Our sample gave analytical values which agree with the formula C₁₃H₁₆N₄O₄: Calcd.: C, 53.5; H, 5.5; N, 19.2. Found: C, 53.6; H, 5.47; N, 19.2. Infrared on the original ketone was consistent with the structure isopropyl cyclopropyl ketone. ^e Authentic *n*-propyl cyclopropyl ketone, prepared as indicated in detail in the Experimental, gave a DNP m.p. and mixed m.p. 151–152°. ^f C. F. H. Allen and R. Boyer, *Can. J. Research*, 9, 159 (1933). ^g R. P. Mariella and R. R. Raube, THIS JOURNAL, 74, 521 (1952). ^h The semicarbazone melted at 180–181°; lit. value 182–183° (second reference in footnote *g* of Table II).

TABLE IV
SUMMARY OF EVIDENCE FOR STRUCTURAL ASSIGNMENTS TO IIa-f AND IIIa-f

R	Product isolated ^a	Dehydrohalogenation product	M.p., °C. of the 2,4-DNP of	
			Found	Literature
CH ₃	IIIa		119–120 ^c	117 ^b
C ₂ H ₅	IIb ^o	IIIb ^d	111–112 ^f	111–113 ^e
<i>n</i> -C ₃ H ₇	IIIc		118–119 ^g	119 ^h
<i>i</i> -C ₃ H ₇	IId	IIId ⁱ	94–95 ^j	95 ^k
Cyclo-C ₃ H ₅	IIIe		1	
C ₆ H ₅	IIIf ^p	IIIIf ^m	157–158 ⁱ	163 ⁿ

^a For derivatives of these products, see Table II. ^b I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. III, Eyre and Spottiswoode, London, 1953, p. 447. ^c The *p*-nitrophenylhydrazone melted at 105–106°; Heilbron, ref. *b*, gives 107°. ^d B.p. 40–41° at 29 mm., *n*_D²⁰ 1.4263; semicarbazone m.p. 158–159° (*J. Colonge, Bull. soc. chim.*, [5] 3, 2116 (1936), reported 161°). The 2,4-DNP melted at 147–148°. *Anal.* Calcd. for C₁₂H₁₄N₄O₄: C, 51.7; H, 5.0; N, 20.1. Found: C, 51.7; H, 5.28; N, 20.2. ^e Heilbron, ref. *b*, Vol. II, 1953, p. 513. ^f Semicarbazone m.p. 94–95°; lit. value (footnote *e*) 95°. ^g Semicarbazone. ^h H. Meerwein, *Ann.*, 419, 121 (1919). ⁱ B.p. 52° at 39 mm., *n*_D²⁰ 1.4248, *p*-nitrophenylhydrazone m.p. 89–90°, semicarbazone m.p. 94–95°. ^j E. E. Blaise and I. Herman, *Compt. rend.*, 146, 700 (1908), reported 89 and 90°, respectively. ^k No depression on mixture with an authentic sample. ^l R. L. Shriner, R. C. Fuson and D. Y. Curtin "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 316. ^m The infrared spectrum and m.p. of derivatives of the hydrogenated IIIe were identical with those of isopropyl cyclopropyl ketone obtained by dehydrohalogenation of Id (see Table III). ⁿ Phenylhydrazone m.p. and mixed m.p. 121–122°; J. H. Burckhalter and R. C. Fuson, THIS JOURNAL, 70, 4184 (1948), reported 119–121°. ^o D. P. Evans, *J. Chem. Soc.*, 785 (1936). ^p Identical (infrared, DNP) with authentic material prepared from formaldehyde, 3-pentanone and hydrogen chloride (*J. Colonge, footnote d*). ^q An authentic sample was prepared in 40% yield by heating (stirred) propiophenone (98 g.) and formalin (80 ml., 30%) containing 36 g. of hydrogen chloride in a pressure bottle for 3 hr. at 100°.

Structure Proof of II and III.—If the β -chloroketone II was obtained pure, it was dehydrohalogenated to the corresponding III by refluxing with 25% aqueous sodium bicarbonate for 2 hr. The resulting III, or III obtained by dehydrohalogenation of the crude mixture (*vide supra*), was derivatized, hydrogenated over Raney nickel at room temperature and three atmospheres pressure to the corresponding isopropyl ketone and the latter also derivatized. Yields of III from II were 60–85%; hydrogenations were essentially quantitative. The results are given in Table IV.

Miscellaneous.—In one experiment with ferric chloride in place of aluminum chloride, propionyl chloride gave only

the rearranged chloroketone IIb (Table I). With nitromethane as solvent, the propionyl chloride–aluminum chloride complex did not form a homogeneous solution, and even after a 10-hr. reaction period, only 9 g. of product, b.p. 52–67° at 5 mm., was obtained. It was obviously a mixture of chloroketones and was not investigated further. The reaction between phosgene, aluminum chloride and cyclopropane gave a complex mixture which requires further examination.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Fischer Indole Synthesis. IV. Halogen Interchange during the Zinc Halide Induced Fischer Reactions of Acetophenone 2,6-Dihalophenylhydrazones¹

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Acetophenone 2,6-dibromophenylhydrazone, when heated with zinc chloride, yields a mixture containing about equimolar amounts of 2-phenyl-5,7-dibromoindole (II) and of 2-phenyl-5-chloro-7-bromoindole (III) plus a trace of 2-phenyl-7-bromoindole (I). Acetophenone 2,6-dichlorophenylhydrazone, when heated with zinc bromide, behaves similarly; the products are 2-phenyl-5,7-dichloroindole (IV) and 2-phenyl-5-bromo-7-chloroindole (V) in about 1:3 molar ratio. The four 2-phenyl-5,7-dihaloindoles II-V all have closely similar melting points, and mixtures show slight or no melting point depressions. Separation of mixtures is not practicable by any of the methods tried. The four pure indoles II-V were synthesized from the corresponding acetophenone 2,4-dihalophenylhydrazones and their infrared spectra measured. Characteristic differences in the spectra, particularly in the 13–14 μ region, were used as the means of identification of the components of the mixtures obtained from the 2,6-dihalophenylhydrazones. A mechanism featuring an intermediate (*e.g.*, VI) having an allylic halide structural sequence is proposed to account for the observed halogen interchange; the "positive halogen" hypothesis seems inadequate to account for the interchange. Cyclohexanone 2,6-dibromophenylhydrazone, heated with zinc chloride, yields, after chloranil dehydrogenation of the product, an unknown monobromocarbazole.

Investigations of the Fischer indole transformations of 2,6-dichlorophenylhydrazones have disclosed that 5,7-dichloroindoles are formed in the presence of zinc chloride but that 7-monochloroindoles are the products when stannous chloride is the promoter.³ A mechanism was proposed^{3b} to account for the behavior of these 2,6-dichlorophenylhydrazones in the Fischer reaction which included as an essential feature the migration or reductive removal of "positive" chlorine. To provide evidence bearing on the general validity of this proposed mechanism, a study of 2,6-dibromophenylhydrazones in the Fischer reaction was undertaken, and this paper reports the reactions of acetophenone 2,6-dibromophenylhydrazone with zinc chloride and with zinc bromide. Since the reaction of acetophenone 2,6-dichlorophenylhydrazone with zinc chloride already was known,^{3a} the series could be completed by carrying out the reaction of this dichlorophenylhydrazone with zinc bromide. The latter reaction also is reported in this paper.

In a preliminary investigation, Fisher⁴ found that acetophenone 2,6-dibromophenylhydrazone, when heated with zinc chloride in nitrobenzene, was converted to a crystalline product, m.p. 139°, that gave a positive Ehrlich test. The product was shown to be related to 2-phenylindole, for it

afforded this compound on catalytic reductive dehalogenation. That it was not 2-phenyl-5,7-dibromoindole was shown by preparation of the latter, m.p. 149°, from acetophenone 2,4-dibromophenylhydrazone. Elementary analysis of the material of m.p. 139° suggested that it might be a mixture of 2-phenyl-5,7-dibromoindole and 2-phenyl-7-bromoindole. There was reason to suppose that mixtures of halogen-substituted 2-phenylindoles showed little or no melting point depression and that they often melted sharply. Fisher's investigations were abandoned when efforts to effect separations of the material of m.p. 139° into its components by fractional crystallization, by high vacuum sublimation, by liquid–liquid extraction and by chromatography on alumina all failed.

Inasmuch as the yield of the material of m.p. 139° from acetophenone 2,6-dibromophenylhydrazone was only about 5%, quite large amounts of the dibromo phenylhydrazone had to be prepared if a detailed study of the product was to be carried out. The first problem encountered, then, was the preparation of substantial amounts of 2,6-dibromoaniline, the precursor of the corresponding phenylhydrazone. In our hands the preparative method for this compound described in "Organic Syntheses"⁵ led to erratic results; all too often the procedure afforded quite low yields of a product containing too much tribromoaniline to be useful in our work. More consistent yields of a superior product were realized when 2,6-dibromoaniline was prepared from sulfanilic acid through the barium dibromosulfanilate, following the general procedure given

(1) Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Carnegie Institute of Technology.

(2) Allied Chemical and Dye Corp. Fellow, 1952–1953.

(3) (a) R. B. Carlin and E. E. Fisher, *THIS JOURNAL*, **70**, 3421 (1948); (b) R. B. Carlin, J. G. Wallace and E. E. Fisher, *ibid.*, **74**, 990 (1952).

(4) E. E. Fisher, Ph.D. Thesis, Carnegie Institute of Technology, 1948.

(5) M. K. Seikel, "Org. Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 261.