intimately mixed, first mechanically and then by heating ten minutes in an oven at 100° (samples containing 90% or more of *cis*-cinnamic acid dibromide are completely molten at this temperature). Melting points were determined in capillary tubes. Since samples melt with some decomposition, the calibration curve is empirical and subject to variations in melting point technique and is, therefore, not given here. The two dibromides form a minimum melting mixture, perhaps a eutectic, of m.p. near 90°, containing about 92% *cis*-cinnamic acid dibromide. Unknown samples were analyzed by determining their melting points and then the melting point of a mixture with a small but measured quantity of pure *cis*-cinnamic acid dibromide in order to ascertain on which side of the minimum melting mixture the sample lay. The thermal analyses were probably accurate within one per cent. and were confirmed by the infrared analyses upon the β-bromostyrenes obtained from the cinnamic acid dibromides.

β-Bromostyrenes from Cinnamic Acid Dibromides.—All the samples of *cis*-cinnamic acid dibromide, unless otherwise indicated, were from a large well-mixed batch of *cis*-cinnamic acid dibromide of m.p. 88–92.5°, which was estimated by the melting point technique to contain 95.5% of *cis*-cinnamic acid dibromide. The decarboxylative eliminations were run in solvents ethanol and water as previously described[1] with the following exceptions. For the runs in absolute ethanol, 90 g. (0.292 mole) of *cis*-cinnamic acid dibromide and 140 g. (1.42 moles) of anhydrous potassium acetate oven dried one hour *in vacuo* (at 70°) were refluxed with stirring in 1000 ml. of absolute ethanol for three hours. For one run in water, 90 g. of *cis*-cinnamic acid dibromide suspended in one liter of water reacted with 1020 ml. (1.25 equiv.) of 1.23 *N* sodium hydroxide. The addition of sodium hydroxide was made slowly during heating of the solution; 1.5 hours were required to bring the solution up to 78 ± 2° and the solution was maintained at this temperature for 30 minutes. Phenolphthalein seems to be an unreliable indicator in this reaction mixture and excessive amounts of alkali were added relative to that used with *trans*-cinnamic acid dibromide.[1] Accordingly in a second run, 95 g. (0.308 mole) of *cis*-cinnamic acid dibromide (m.p. 86–96°, 91% *cis*-dibromide) was suspended in 400 ml. of water and 84 g. (1.0 mole) of sodium bicarbonate dissolved in 600 ml. of water was added in a period of 30 minutes to the slowly heated and stirred suspension of the dibromide. The reaction mixture attained a temperature of 75 ± 2° in 1.15 hours and was kept at this temperature for 20 minutes.

The decarboxylative eliminations in acetone were run according to the general procedure of Cristol and Norris.[3] Ninety grams (0.292 mole) of *cis*-cinnamic acid dibromide, 80 g. (0.955 mole) of sodium bicarbonate, and 1000 ml. of acetone (dried over anhydrous magnesium sulfate) were refluxed with stirring for eight hours. Most of the acetone was removed under reduced pressure and the β-bromostyrene separated as previously described,[1] *n*-pentane being used as the extraction liquid. *trans*-Cinnamic acid dibromide (100 g.) was similarly treated with sodium bicarbonate (90 g.) in two liters of acetone.

The yield and composition of the β-bromostyrenes obtained from these reactions are given in Table I.

Infrared Analyses.—A Perkin–Elmer, Model 21, double beam recording infrared spectrophotometer was used in the present work. The β-bromostyrene mixtures were analyzed as previously reported[1] except that the concentration of β-bromostyrene was one third that previously used. The lower concentration permits a more accurate analysis of samples composed largely of the *trans*-isomer. The average deviation of the individual values from the average of the four values (determined at the four wave lengths) was 0.8% or less; the maximum deviation of any of the individual values was 1.5%.

For analysis of mixtures of *cis*- and *trans*-cinnamic acids, 3 mm. rock salt cells were used and samples were dissolved in carbon disulfide. The extinction coefficients of such solutions were satisfactorily constant over a concentration range of 0.7 to 3 g. of sample per liter and analyses were made at the following wave lengths in microns, 10.13 (*trans*), 12.08 (*cis*), 14.13 (*trans*) and 14.44 (*cis*), which correspond to maxima of the *cis*- and *trans*-acids as labeled. The first two and then the last two wave lengths were used separately to calculate the *cis*–*trans* composition of irradiated cinnamic acid samples, the values were averaged, and the difference from 100% was assumed to correspond to the amount of by-product present in such samples. The method was probably accurate within 3 or 4% and the values reported are generally the average obtained from several different samples.

ATLANTA, GEORGIA

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

New Amebacides. II. The Preparation of Some N-Alkyl-N-benzylhaloacetamides

BY ALEXANDER R. SURREY AND MARCIA K. RUKWID[1]

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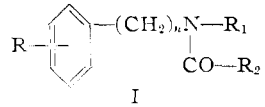
The preparation of a series of N-alkyl(aralkyl, cycloalkyl)-N-benzyldichloroacetamides is reported. Some monochloroacetamides and trichloroacetamides also are included. The use of methyl dichloroacetate as an acylating agent in the present work is discussed.

In the first paper in this series[2] we have reported the synthesis of some N-(substituted benzyl)-N-hydroxyalkyldihaloacetamides as part of an investigation of potential amebacidal agents derived from the general formula



I

The present communication deals with the preparation of a second series of compounds in which R = H, alkyl, alkoxy, chloro, dichloro and nitro; n = 1; R_1 = alkyl, aralkyl and cycloalkyl; and R_2 = CH_2Cl, $CHCl_2$ and CCl_3.

All of the N-alkyl-N-benzyldichloroacetamides in Table II as well as the monochloroacetamides and trichloroacetamides listed in Table III were prepared by acylation of the appropriate N-alkylbenzylamine with monochloroacetyl, dichloroacetyl and trichloroacetyl chloride in the presence of dilute sodium hydroxide solution. For the most part the yields ranged from 45–80%. About one-half of the dichloroacetamides were obtained as oils which were purified by distillation under reduced pressures.

The use of methyl dichloroacetate or ethyl dibromoacetate as the acylating agent which was successful with the N-(hydroxyalkyl)-benzylamines even under mild experimental conditions, was not satisfactory in most of the present work. Only in the case of the N-methylbenzylamines was it

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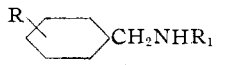
(2) A. R. Surrey, THIS JOURNAL, **76**, 2214 (1954).

TABLE I

N-ALKYL-N-BENZYLAMINES 

R	R_1	B.p., °C.	Mm.	$n^{25}D$	Yield, %	Formula	Nitrogen, % Calcd.	Found
3-CH_3	Methyl	90–92	0.15	1.5170	70	$C_9H_{13}N$	10.36	10.27
4-CH_3	Methyl	92–94	.15	1.5162	57	$C_9H_{13}N$[a]	10.36	10.21
4-*i*-C_3H_7	Methyl	102–107	.15		49	$C_{11}H_{17}N$	8.60	8.42
4-OC_4H_9	Methyl	149–150	.11	1.5091		$C_{12}H_{19}NO$	7.25	7.20
2,4-Cl_2	Methyl	121–123	.13	1.5527	47	$C_8H_9Cl_2N$	7.37	7.29
H	Ethyl	86–88[b]	.15	1.5109	68	$C_9H_{13}N$	[c]	
2-OCH_3	Ethyl	147–149[d]	.40	1.5208	62	$C_{10}H_{15}NO$	8.48	8.13
2,3-$(OCH_3)_2$	Ethyl	115–117	.2	1.5188	57	$C_{11}H_{17}NO_2$	7.17	6.97
3,4-Cl_2	Ethyl	85–95	.8	1.5420	40	$C_9H_{11}Cl_2N$	6.86	6.48
H	Propyl	47–55	.2	1.5301	55	$C_{10}H_{15}N$	9.40	9.33
2,4-Cl_2	Propyl	152	.15			$C_{10}H_{13}Cl_2N$	6.42	6.18
H	*i*-Propyl	50–55[e]	.8	1.5000	73	$C_{10}H_{15}N$	9.40	9.33
4-CH_3	*i*-Propyl	55–57	.5	1.4990	65	$C_{11}H_{17}N$	8.59	8.52
4-*i*-C_3H_7	*i*-Propyl	82–85	.65	1.4968	60	$C_{13}H_{21}N$	7.34	6.96
3,4-O_2CH_2	*i*-Propyl	95–100	.3	1.5220	60	$C_{11}H_{15}NO_2$	7.25	7.17
4-OC_4H_9	*i*-Propyl	117–120	.4	1.4960	65	$C_{14}H_{23}NO$	6.34	6.36
2-Cl	*i*-Propyl	70	.9	1.5180	57	$C_{10}H_{14}ClN$	7.63	7.36
4-Cl	*i*-Propyl	70–74	.9	1.5490	72	$C_{10}H_{14}ClN$	[f]	
2,4-Cl_2	*i*-Propyl	126–127	.7	1.5320	71	$C_{10}H_{13}Cl_2N$	6.42	6.15
3,4-Cl_2	*i*-Propyl	90–94	.4	1.5329	59	$C_{10}H_{13}Cl_2N$	6.42	6.31
4-NO_2	*i*-Propyl	[g]			75	$C_{10}H_{14}N_2O_2$		
H	Butyl	50–55	.1	1.5035	60	$C_{11}H_{17}N$[h]	8.60	7.55
2,4-Cl_2	Butyl	100–105	.1	1.5290	74	$C_{11}H_{15}Cl_2N$	6.03	5.84
3,4-Cl_2	Butyl	105	.25	1.5310	68	$C_{11}H_{15}Cl_2N$	6.03	5.92
3,4-Cl_2	*s*-Butyl	96	.3	1.5300	82	$C_{11}H_{15}Cl_2N$	6.03	5.83
3,4-Cl_2	*i*-Butyl	95	.2	1.5275	72	$C_{11}H_{15}Cl_2N$	6.03	5 92
2,4-Cl_2	*t*-Butyl	85–92	.1	1.5265	53	$C_{11}H_{15}Cl_2N$	[i]	
2,4-Cl_2	$C_6H_5CH_2$	141–145	.01	1.5903	75	$C_{14}H_{13}Cl_2N$	5.26	5.42
3,4-Cl_2	$C_6H_5CH_2CH_2$	155	.25	1.5810	60	$C_{15}H_{15}Cl_2N$	5.00	5.04
2,4-Cl_2	Cyclopentyl	127	.9	1.5510	48	$C_{12}H_{15}Cl_2N$	5.74	5.76
2,4-Cl_2	Cyclohexyl	128–132	.1	1.5485	41	$C_{13}H_{17}Cl_2N$	5.43	5.37

[a] Hydrochloride, m.p. 176–177°, R. Baltzly and P. B. Russell, THIS JOURNAL, **72**, 3410 (1950). [b] B.p. 198° (750 mm.), P. C. Young and R. Robinson, *J. Chem. Soc.*, 275 (1933). [c] Hydrochloride, m.p. 180–182°. Calcd.: Cl^-, 20.65. Found: Cl^-, 21.02. [d] B.p. 238°, H. Wojahn and K. Erdelmeier, *Arch. Pharm.*, **280**, 215 (1942). [e] E. A. Steck, L. L. Hallock and C. M. Suter, THIS JOURNAL, **70**, 4063 (1948). [f] Hydrochloride, m.p. 195–196°. Calcd.: Cl^-, 16.14. Found: Cl^-, 15.97. [g] The crude product was used directly. [h] Hydrochloride, m.p. 242°, C. Mannich and O. Hieronimus, *Ber.*, **75**, 49 (1942). [i] Hydrochloride, m.p. 245–246°. Calcd.: Cl^-, 13.21. Found: Cl^-, 13.21.

found possible[3] to effect dichloroacylation with the dichloroacetic acid ester. For example, when a mixture of methyl dichloroacetate and N-methyl-4-isopropylbenzylamine was allowed to stand at room temperature for 24 hours a 70% yield of N-(4-isopropylbenzyl)-N-methyldichloroacetamide was obtained and 30% of the starting amine was recovered. With N-methyl-4-butoxybenzylamine the yield of the dichloroacetamide was 78% after standing at room temperature for four days. The yield with N-methyl-2,4-dichlorobenzylamine was only 47% after three days. When a mixture of the latter amine was heated with methyl dichloroacetate at 45–50° for 18 hours the yield of N-(2,4-dichlorobenzyl)-N-methyldichloroacetamide was 30%. Under these same conditions with N-ethylbenzylamine, N-propylbenzylamine and N-isopropylbenzylamine little if any reaction occurred with methyl dichloroacetate. Most of the starting amines were recovered. The failure to react in these cases is probably due to steric hindrance.

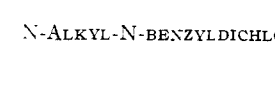
These observations are consistent with some recent work of Joullié and Day[4] who showed that ethyl trichloroacetate reacts with relatively unhindered secondary amines such as piperidine, morpholine, pyrrolidine and dimethylamine to yield urethans. However, with more hindered amines such as diethylamine and α-methylpiperidine no reaction occurred. The splitting out of chloroform in the case of trichloroacetate and of methanol in the case of methyl dichloroacetate can be reconciled by a comparison of the relative ease of anion formation one would expect with trichloromethyl, dichloromethyl and methoxide groups, $CCl_3 > OCH_3 > CHCl_2$.

The secondary amines employed in the present work (Table I) were prepared (a) by treating an excess of the alkylamine with a chlorobenzyl or dichlorobenzyl or nitrobenzyl chloride and (b) by reductive alkylation of the alkylamine with a substituted benzaldehyde. In the case of methylamine and ethylamine aqueous solutions were used.

The amides listed in Tables II and III were screened in hamsters for their effectiveness in the treatment of intestinal amebiasis. Most of the compounds showed fair antiamebic activity (ED_{50} 40–150 mg./kg). In general, the most active compounds were those in which R is 4-butoxy, 2,4-

(3) C. Mannich and R. Kuphal, *Arch. Pharm.*, **250**, 539 (1912).
(4) M. M. Joullié and A. R. Day, THIS JOURNAL, **76**, 2990 (1954).

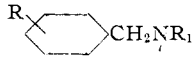
TABLE II

N-ALKYL-N-BENZYLDICHLOROACETAMIDES 

R	R_1	M.p. or b.p., °C.	Mm.	Yield, %	Formula	Analyses, % C (Calcd.)	H (Calcd.)	Cl (Calcd.)	C (Found)	H (Found)	Cl (Found)
3-CH_3	Methyl	128	0.4	78	$C_{11}H_{13}Cl_2NO$	53.69	5.32	28.81	53.38	5.56	29.18
4-CH_3	Methyl	84.1–85.5		69	$C_{11}H_{13}Cl_2NO$	53.69	5.32	28.81	53.68	5.25	29.26
4-*i*-C_3H_7	Methyl	49.1–50.8		44	$C_{13}H_{17}Cl_2NO$	56.94	6.25	25.86	57.13	5.68	25.30
4-OC_4H_9	Methyl	43.7–45.9		78	$C_{14}H_{19}Cl_2NO_2$	55.28	6.29	23.30	55.45	6.14	24.02
2,4-Cl_2	Methyl	130	0.001	30	$C_{10}H_9Cl_4NO$	39.89	3.01	47.12	40.23	2.96	47.77
H	Ethyl	128	.04	37	$C_{11}H_{13}Cl_2NO$	53.67	5.32	28.81	53.52	5.62	28.53
2-OCH_3	Ethyl	135	.03	53	$C_{12}H_{15}Cl_2NO_2$	52.18	5.47	25.67	52.40	5.61	25.25
2,3-$(OCH_3)_2$	Ethyl	157–158	.06	52	$C_{13}H_{17}Cl_2NO_3$	51.01	5.60	23.17	50.96	5.75	22.98
3,4-Cl_2	Ethyl	77.2–83.2		66	$C_{11}H_{11}Cl_4NO$	41.94	3.52	22.52	41.93	3.67	22.26
H	Propyl	110–115	.02	54	$C_{12}H_{15}Cl_2NO$	55.41	5.81	27.26	55.41	5.77	27.0
2,4-Cl_2	Propyl	150	.05	45	$C_{12}H_{13}Cl_4NO$	43.79	3.98	21.55[a]	43.49	4.24	21.26
H	*i*-Propyl	120–125	.01	52	$C_{12}H_{15}Cl_2NO$	55.39	5.81	27.25	55.10	6.05	27.74
4-CH_3	*i*-Propyl	120	.05	37	$C_{13}H_{17}Cl_2NO$	56.90	6.26	25.90	57.13	6.26	25.99
4-*i*-C_3H_7	*i*-Propyl	125–130	.05	60	$C_{15}H_{21}Cl_2NO$	59.61	7.00	23.50	59.70	7.12	23.53
3,4-O_2CH_2	*i*-Propyl	158–165	.01	80	$C_{13}H_{15}Cl_2NO_3$	51.34	4.97	23.31	51.42	4.95	23.48
4-OC_4H_9	*i*-Propyl	167–170	.01	26	$C_{16}H_{23}Cl_2NO_2$	57.83	6.97	21.34	57.67	7.11	21.20
2-Cl	*i*-Propyl	71.7–76.1		74	$C_{12}H_{14}Cl_3NO$	48.92	4.79	36.10	48.60	4.90	36.20
4-Cl	*i*-Propyl	89.7–93.1		61	$C_{12}H_{14}Cl_3NO$	48.92	4.79	24.00[a]	48.70	4.68	24.11
2,4-Cl_2	*i*-Propyl	71.9–73.8		60	$C_{12}H_{13}Cl_4NO$	43.79	3.98	21.55[a]	44.34	3.74	21.67
3,4-Cl_2	*i*-Propyl	71.8–75.6		47	$C_{12}H_{13}Cl_4NO$	43.79	3.98	43.09	43.84	4.08	42.51
4-NO_2	*i*-Propyl	100.8–103.3		65	$C_{12}H_{14}Cl_2N_2O_3$	47.24	4.62	9.18[b]	47.44	4.65	8.90[b]
H	Butyl	120–125	.02	64	$C_{13}H_{17}Cl_2NO$	56.95	6.25	25.87	56.95	6.09	26.1
2,4-Cl_2	Butyl	147–149	.05	55	$C_{13}H_{15}Cl_4NO$	45.51	4.40	41.34	45.30	4.30	41.04
3,4-Cl_2	Butyl	59.2–60.2		35	$C_{13}H_{15}Cl_4NO$	45.51	4.40	20.67[a]	45.62	4.67	20.85
3,4-Cl_2	*s*-Butyl	155	.06	50	$C_{13}H_{15}Cl_4NO$	45.51	4.40	41.34	45.21	4.90	41.23
3,4-Cl_2	*i*-Butyl	81.8–84.6		58	$C_{13}H_{15}Cl_4NO$	45.51	4.40	41.34	45.63	4.82	40.92
2,4-Cl_2	*t*-Butyl	95.9–114.1		25	$C_{13}H_{15}Cl_4NO$	45.51	4.40	41.34	45.83	3.99	41.00
H	Benzyl	56.4–58.3		83	$C_{16}H_{15}Cl_2NO$	62.34	4.91	23.01	62.53	4.78	22.95
2,4-Cl_2	Benzyl	186–189	0.01	35	$C_{16}H_{13}Cl_4NO$	50.97	3.47	37.62	50.97	3.43	37.80
3,4-Cl_2	Phenethyl	60.2–63.3		23	$C_{17}H_{15}Cl_4NO$	52.21	3.86	36.26	52.13	4.22	36.27
2,4-Cl_2	Cyclopentyl	82.4–85.2		57	$C_{14}H_{15}Cl_4NO$	47.76	4.29	20.14	47.69	4.29	19.81
2,4-Cl_2	Cyclohexyl	83.1–84.9		32	$C_{15}H_{17}Cl_4NO$	48.81	4.64	19.21	48.47	4.76	19.25

[a] Determination of readily hydrolyzable chlorine. [b] Nitrogen.

TABLE III

N-ALKYL-N-BENZYLCHLORO(AND TRICHLORO)-ACETAMIDES 

R	R_1	Yield, %	M.p. or b.p., °C.	Mm.	Formula	Analyses, % C (Calcd.)	H (Calcd.)	Cl (Calcd.)	C (Found)	H (Found)	Cl (Found)
					Z = CH_2Cl						
H	*i*-Propyl	71	100–103	0.1	$C_{12}H_{16}ClNO$	63.85	7.13	15.71	63.85	7.20	15.80
3,4-Cl_2	*i*-Propyl	37	167	.01	$C_{12}H_{14}Cl_3NO$	48.92	4.79	12.10[a]	48.85	4.61	12.32
H	Benzyl	29	165–166	.05	$C_{16}H_{16}ClNO$	70.18	5.89	12.95	70.13	5.99	13.20
2,4-Cl_2	Benzyl	77	74.9–76.2		$C_{16}H_{14}Cl_3NO$	56.08	4.12	31.04	56.22	4.13	31.00
					Z = CCl_3						
2,4-Cl_2	Propyl	60	76.3–79.7		$C_{12}H_{12}Cl_5NO$	39.57	3.31	48.69	39.82	3.61	48.18
H	*i*-Propyl	61	96.6–98.4		$C_{12}H_{14}Cl_3NO$	48.92	4.79	36.10	49.00	4.46	36.20
4-CH_3	*i*-Propyl	39	80.0–82.3		$C_{13}H_{16}Cl_3NO$	50.58	5.22	34.46	50.86	4.96	34.18
3,4-Cl_2	*i*-Propyl	55	102.1–105.3		$C_{12}H_{12}Cl_5NO$	39.57	3.31	48.69	39.77	2.98	48.48
2,4-Cl_2	Butyl	42	158	0.06	$C_{13}H_{14}Cl_5NO$	41.36	3.73	46.96	41.39	3.74	46.36
3,4-Cl_2	*s*-Butyl	48	150–160	0.05	$C_{13}H_{14}Cl_5NO$	41.36	3.73	46.96	41.30	3.94	46.66
3,4-Cl_2	*i*-Butyl	45	118.0–118.8		$C_{13}H_{14}Cl_5NO$	41.36	3.73	46.96	41.49	3.71	46.55
H	Benzyl	47	64.5–66.2		$C_{16}H_{14}Cl_3NO$	56.08	4.12	31.04	56.30	4.31	30.60
2,4-Cl_2	Benzyl	78	112.4–114.3		$C_{16}H_{12}Cl_5NO$	46.70	2.94	43.08	46.92	2.85	42.80

[a] Determination of readily hydrolyzable chlorine.

dichloro and 3,4-dichloro; R_1 is isopropyl and R_2 is $CHCl_2$. The ED_{50} for these dichloroacetamides is similar to that found for the corresponding N-(2-hydroxyethyl)-dichloroacetamides.[2]

Replacing the isopropyl group by *n*-propyl or by higher alkyl groups resulted in a sharp drop in activity. The same was found true for the benzyl, cyclopentyl and cyclohexyl groups. The order of amebacidal activity with variation in R_2 is similar to that found in several other series, $CHCl_2 > CCl_3 > CH_2Cl$. The compounds substituted in the phenyl ring, (*e.g.*, R = dichloro or 4-butoxy) were considerably more active than the unsubstituted derivatives where R = H.

Acknowledgment.—The authors wish to thank Mr. M. E. Auerbach and Mr. K. D. Fleischer and staffs for the analytical data and corrected melting points recorded. The authors are indebted also to the Biology Division and especially to Dr. D. A. Berberian for the screening data.

Experimental[5]

N-Alkylbenzylamines (Table I).—The following examples illustrate the procedures employed for the preparation of these compounds.

2,4-Dichlorobenzyl chloride (39.4 g.) was added dropwise with stirring to 72 g. of isopropylamine over a period of 1 hour. After standing at room temperature overnight the mixture was warmed on a steam-bath, poured into water, sodium hydroxide solution added, and the oil which separated was extracted with benzene. After drying the combined extracts, the benzene was removed by distillation and the product was fractionally distilled.

A mixture of 26.7 g. of 4-butoxybenzaldehyde and 9 g. of isopropylamine was warmed on a steam-bath for 30 minutes and then dissolved in 125 ml. of ethanol and reduced catalytically with palladium-on-charcoal catalyst. After filtering off the catalyst and removing the solvent the product was fractionally distilled.

N-Alkyl-N-benzylhaloacetamides (Tables II and III).—The following example illustrates the general procedure for the preparation of these compounds.

Dichloroacetyl chloride (7.5 g.) was added dropwise with stirring at 0° to a mixture of 10.9 g. of N-(2,4-dichlorobenzyl)-isopropylamine, 100 ml. of ethylene dichloride and 50 ml. of 1 *N* sodium hydroxide solution. After the addition was completed the mixture was allowed to warm up to room temperature and stirring was continued for one hour. The organic layer was separated, washed with 1 *N* hydrochloric acid, then water, and dried. The ethylene dichloride was removed by distillation and the residue which solidified was recrystallized from Skellysolve A.

Most of the other amides were recrystallized either from Skellysolve B or C.

Reaction of N-Methyl-4-isopropylbenzylamine with Methyl Dichloroacetate.—The reactions with methyl dichloroacetate were carried out in the following manner.

A mixture of 8.15 g. of N-methyl-4-isopropylbenzylamine and 7.35 g. of methyl dichloroacetate was allowed to stand at room temperature for 24 hours. (In those cases where a product was obtained a slightly exothermal reaction occurred when the reactants were mixed.) The material was dissolved in benzene and washed several times with 1 *N* hydrochloric acid, water, 2.5% sodium hydroxide solution and then water. After drying, the benzene was removed by distillation to give 9.5 g. (70%) of N-(4-isopropylbenzyl)-N-methyldichloroacetamide.

The acid washings were combined, made basic and the resulting oil was taken up in ethylene dichloride to give 2.5 g. (30%) of N-methyl-4-isopropylbenzylamine.

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(5) All melting points are corrected.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

Ortho Esters, Imidic Esters and Amidines. VI. Two General Methods of Synthesis of N-Phenylformimidic Esters Involving Transesterification[1,2]

BY ROYSTON M. ROBERTS, THOMAS D. HIGGINS, JR., AND PAUL R. NOYES

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The reaction of alkyl orthoformates with aniline in the presence of acid catalyst to produce alkyl N-phenylformimidates has been shown to be general. Higher alkyl orthoformates can be obtained readily from methyl and ethyl orthoformates by acid-catalyzed transesterification. Combination of these two reactions leads to a synthesis of N-phenylformimidic esters from methyl and ethyl orthoformates. The same over-all result has been attained by the transesterification of methyl and ethyl N-phenylformimidates by the common alcohols. The second method has been found to be more generally useful.

In earlier papers in this series[3,4] we reported the synthesis of ethyl N-phenylformimidate by the reaction of ethyl orthoformate with aniline. The present communication describes the extension of this synthesis to methyl N-phenylformimidate and to several higher alkyl N-phenylformidates using methyl orthoformate or one of the higher alkyl orthoformates (equation 1) and introduces an efficient and practical method of synthesis of some of the higher alkyl N-phenylformimidates *via* the transesterification of methyl or ethyl N-phenylformimidate (equation 2).

$$C_6H_5NH_2 + CH(OR)_3 \rightleftharpoons C_6H_5N{=}CH{-}OR + 2ROH \quad (1)$$

$$C_6H_5N{=}CH{-}OR + R'OH \rightleftharpoons C_6H_5N{=}CH{-}OR' + ROH \quad (2)$$

(1) Paper V, THIS JOURNAL, **76**, 4379 (1954).

(2) Taken in part from the M.A. theses of Thomas D. Higgins, Jr. (1954) and Paul R. Noyes (1952), the University of Texas.

(3) R. M. Roberts, THIS JOURNAL, **71**, 3848 (1949).

(4) R. M. Roberts and R. H. DeWolfe, *ibid.*, **76**, 2411 (1954).

Recently, Alexander and Busch[5] described a convenient method of preparing higher orthoformic esters by the transesterification of ethyl orthoformate, although they were unable to obtain interchange using isopropyl or *t*-butyl alcohols. By substituting methyl orthoformate for ethyl orthoformate we have succeeded in effecting interchange with isopropyl alcohol. The interchange was, however, quite slow. The addition of a small amount of concentrated sulfuric acid markedly increased the rate of removal of methyl alcohol and ultimately a yield of 75% of isopropyl orthoformate was realized in a reasonable period of time.

The use of acid catalysis was found to be advantageous also in the transesterification of ethyl orthoformate by all of the primary and the low-boiling secondary alcohols studied. The yields of alkyl orthoformates were equal to or higher than those reported by Alexander and Busch, and the time required for removal of ethyl alcohol was

(5) E. R. Alexander and H. M. Busch, *ibid.*, **74**, 554 (1952).