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Decarboxylation Reactions. IV.[1] Reaction of Schiff Bases with Trichloroacetic Anhydride

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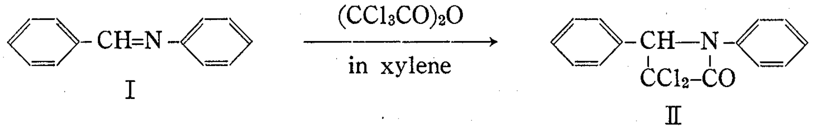
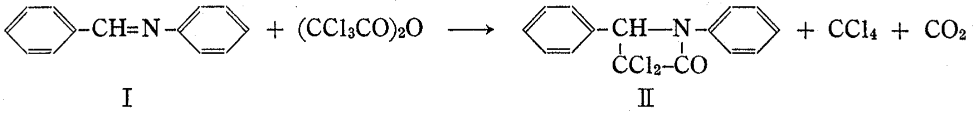
General 3,3-dichloro-2-azetidinone formation in good yield has now been realized by a new reaction of trichloroacetic anhydride with Schiff bases. Process of the reaction is characterized by the formation of carbon dioxide and carbon tetrachloride, mechanistically involving chlorine cation extraction from trichloroacetyl group by trichloromethyl anion.

While the reaction of Schiff bases with trichloro- and tribromoacetic acid has been exhibited[3] to give α-trihalomethyl-substituted amines with decarboxylation, a reaction of the same with trichloroacetic anhydride has now been found to result in the formation of 3,3-dichloro-2-azetidinones. N-Benzylideneaniline (I) was first allowed to react with trichloroacetic anhydride on heating their xylene solution at 135—137°. Process of the reaction was indicated by observation of carbon dioxide emission. Prisms, mp 161—162°, obtained as a product (83% yield) was assigned as 3,3-dichloro-1,4-diphenyl-2-azetidinone (II) by noting well correspondence of its infrared (IR) [$\nu_{\max}^{\mathrm{KBr}}$ 1768 cm^{-1} (β-lactam carbonyl)] and nuclear magnetic resonance (NMR) spectra with those of an authentic specimen prepared by another route.[4]



With interest in this finding we were tempted to elucidate its mechanistic path, because in the previous papers the formation of 3,3-dichloro-2-azetidinone derivatives from Schiff bases has been effected only by the reactions with dichloroacetyl reagents, *i.e.*, dichloroacetic anhydride,[5] dichloroacetyl chloride with triethylamine,[4] and dichloroacetic acid with phosphoryl chloride in dimethylformamide.[6]

In the course of the reaction by distilling off from the end of the condenser tube with the aid of a stream of air a volatile liquid was collected. By gas liquid chromatographic analysis this liquid was shown to be composed of carbon tetrachloride. Taking account of this carbon tetrachloride formation and the carbon dioxide emission overall sequence of the reaction can be represented as follows.



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[1] Part III: M. Sekiya, O. Matsuda, and K. Ito, *Chem. Pharm. Bull.* (Tokyo), **23**, 1579 (1975).

[2] Location: *2-2-1, Oshika, Shizuoka.*

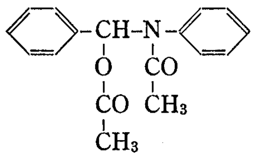
[3] A. Lukasiewicz, *Tetrahedron*, **20**, 1 (1964).

[4] F. Duran and L. Ghosez, *Tetrahedron Letters*, **1970**, 245.

[5] G. Sunagawa and N. Yoshida, *Yakugaku Zasshi*, **82**, 826 (1962); N. Yoshida, *ibid.*, **82**, 835 (1962); *idem, ibid.*, **82**, 841 (1962); *idem, ibid.*, **82**, 846 (1962); *idem, Ann. Sankyo Res. Lab.*, **18**, 38 (1966).

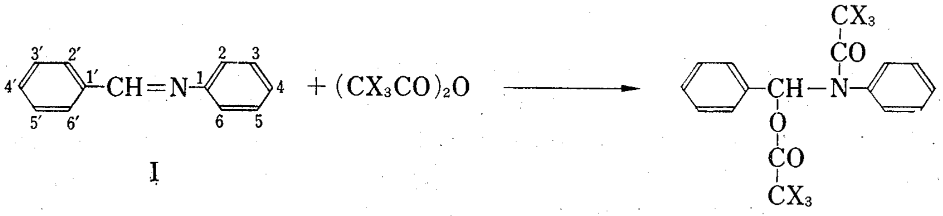
[6] E. Ziegler, Th. Wimmer, and H. Mittelbach, *Monatsh. Chem.*, **99**, 2128 (1968).

It has been reported[7] that I reacts with acetic anhydride in the presence of acetic acid to give the crystalline adduct, N-(α-acetoxybenzyl)acetanilide (III). On referring to this fact it seemed very likely that the reaction may be initiated by a similar adduct formation. A clear evidence of this adduct (IV) formation was provided by IR and NMR measurements of a solution of I and trichloroacetic anhydride in 1: 1 molar proportion. These spectral data are summarized in Table I. Its IR spectrum in chloroform was very similar to that of III exhibiting two carbonyl absorptions, 1775 cm^{-1} and 1700 cm^{-1}. Their higher wave numbers were consistent with the contributions of the neighboring electron-attracting trichloromethyl groups. Also in its NMR spectrum in deuterochloroform the existence of IV would allow the assignment of the band at δ 8.16 to the methine hydrogen similarly to that of III.



III

Table I. Spectral Data of I, III, and IV



I

III or IV

Compound	IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}		NMR[a] δ (in $CDCl_3$)	
I	1628(C=N)		8.32(1H, s, -CH=)	7.6 —8.0 (2H, m, $H_{(2')}$ and $H_{(6')}$) 7.0 —7.55(8H, m, ar H)
III (X=H)	1748(O-C=O)	1670(N-C=O)	8.17(1H, s, ⟩CH-)	6.65—6.9 (2H, m, $H_{(2)}$ and $H_{(6)}$) 7.0 —7.3 (8H, m, ar H)
IV (X=Cl)	1775(O-C=O)	1700(N-C=O)	8.16(1H, s, ⟩CH-)	6.8 —7.8 (10H, m, ar H)

a) abbreviations: s=singlet, m=multiplet, ar=aromatic

When we speculate on a mechanism of the formation of II from the adduct a path shown in Chart 1 seems very probable, in which trichloroacetate ion liberated from the adduct undergoes decarboxylation and the resulting trichloromethyl anion extracts a chlorine cation from N-trichloroacetyl group so as to give II and carbon tetrachloride. Mechanistically this reaction would be therefore distinguished from the previously reported reactions with the dichloroacetyl reagents. While the latter involves the proton extraction from N-dichloroacetyl group of the adduct by the bases, the former is unique in the chlorine cation extraction from N-trichloroacetyl group by trichloromethyl anion. No such chlorine cation extraction has appeared in literature other than that arising in the reaction between pyridine N-oxide and trichloroacetic anhydride.[8]

The reaction was extensively examined with a number of N-benzylideneanilines possessing one substituent in each of them. The reactions were processed under the conditions similar to those carried out with I at the temperatures effecting considerable emission of carbon dioxide. Results are summarized in Table II yielding the corresponding 3,3-dichloro-1,4-diaryl-2-azetidinones in good yields in all the runs. Substituent effect can be deduced from these data indicating that electron-releasing substituents accelerate the reaction. Additionally the reaction with N-benzylidene-1-naphthylamine was carried out to give the corresponding

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[7] H.R. Snyder, D.B. Bright, and J.C. Lorenz, *J. Am. Chem. Soc.*, 73, 1836 (1951); A.W. Burgstahler, *ibid.*, 73, 3021 (1951).

[8] T. Koenig and J. Wieczorek, *J. Org. Chem.*, 35, 508 (1970).

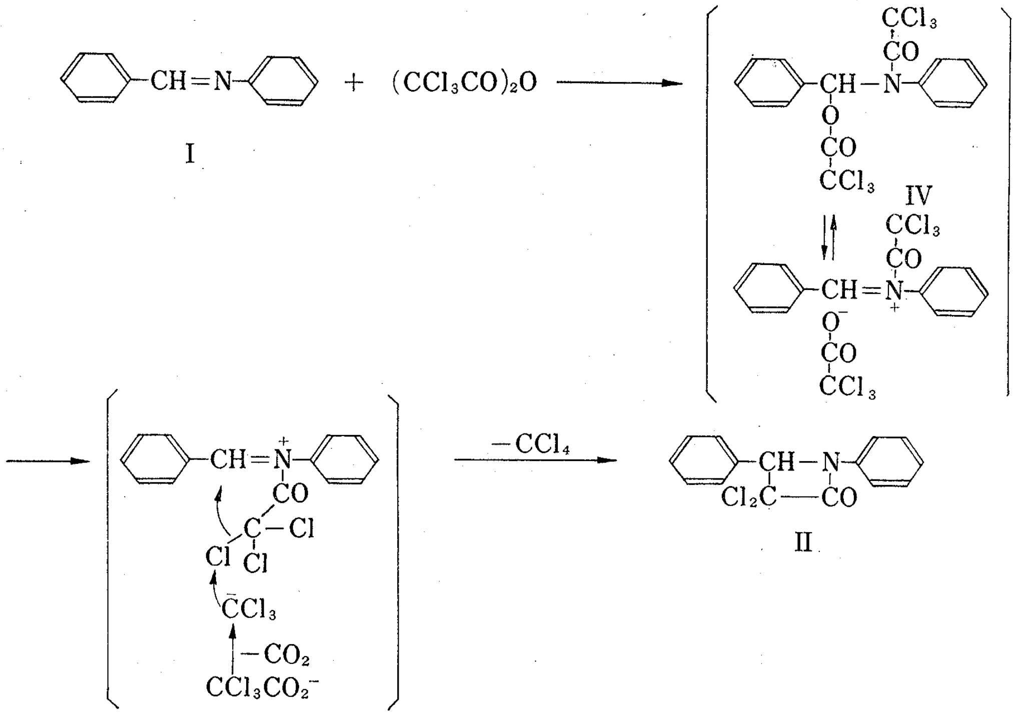
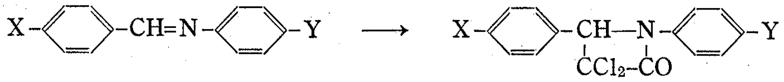


Chart 1

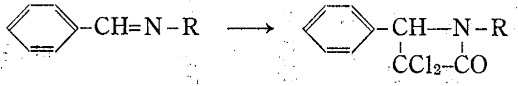
Table II. Reaction[a] with N-Benzylideneanilines Possessing Varied Ring-substituents



X	Y	Reaction temp. (°C)	Reaction time (hr)	Yield[b] (%)
H	H	135—137	3	83
H	Cl	143—145	3	73
H	CH_3O	135—140	1.5	96
H	NO_2	145—148	8	51
Cl	H	138—145	3	87
CH_3O	H	125—128	1.2	92
$(CH_3)_2N$	H[c]	80— 82	2	30
NO_2	H	140—142	6	55

[a] molar ratio: Schiff base (0.03 mole)/trichloroacetic anhydride=1/1.3; solvent: xylene (30 ml)
[b] based on the product isolated
[c] solvent: dioxane (30 ml)

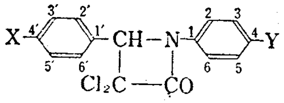
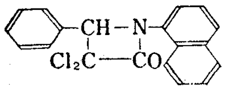
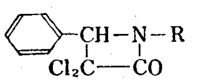
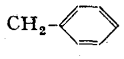
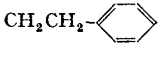
Table III. Reaction[a] with N-Benzylidenealkylamines



R	Reaction temp. (°C)	Reaction time (hr)	Yield[b] (%)
CH_3	137—140	2.2	80
CH_2- 	143—145	6	84
CH_2CH_2- 	131—135	1.2	89
	135—137	1	97
α-$C_{10}H_7$	140—144	4	87

[a] molar ratio: Schiff base (0.03 mole)/trichloroacetic anhydride=1/1.3; solvent: xylene (30 ml)
[b] based on the product isolated

TABLE IV. 3,3-Dichloro-1,4-disubstituted-2-azetidinones

			Appearance (recryst. solvt.)	mp (°C)	Formula	Analysis (%) Calcd. (Found)			IR ν_{max}^{KBr} cm^{-1} (C=O)	NMR^a) δ (*ca.* 10% soln. in CDCl$_3$) *J*=Hz		
						C	H	N		>CH (1H, s)	Aromatic H	Other H
	X	Y										
	H	H	prisms (EtOH)	161—162^b)	$C_{15}H_{11}ONCl_2$	61.65 (61.85)	3.79 (3.81)	4.79 (4.80)	1768	5.45	7.0—7.5(10H, m)	
	H	Cl	prisms (EtOH)	131—132^c)	$C_{15}H_{10}ONCl_3$	55.16 (55.17)	3.09 (3.11)	4.29 (4.42)	1790	5.41	7.1—7.5(9H, m)	
	H	CH_3O	needles (iso-propyl ether)	110.5—112^d)	$C_{16}H_{13}O_2NCl_2$	59.65 (59.79)	4.07 (4.01)	4.35 (4.48)	1780	5.43	6.6—6.9 (2H, d, *J*=8, H$_{(3)}$ and H$_{(5)}$) 7.0—7.5(7H, m)	3.70(3H, s, OC**H**$_3$)
	H	NO_2	prisms (EtOH)	138—139	$C_{15}H_{10}O_3N_2Cl_2$	53.43 (53.70)	2.99 (3.09)	8.31 (8.75)	1792	5.52	7.2—7.5(7H, m) 8.0—8.2 (2H, d, *J*=8, H$_{(3)}$ and H$_{(5)}$)	
	Cl	H	prisms (EtOH)	130—131^e)	$C_{15}H_{10}ONCl_3$	55.16 (55.36)	3.09 (3.20)	4.29 (4.24)	1773	5.42	7.0—7.5(9H, m)	
	CH_3O	H	prisms (EtOH)	154—155	$C_{16}H_{13}O_2NCl_2$	59.65 (59.76)	4.07 (3.97)	4.35 (4.21)	1767	5.39	6.7—7.3(9H, m)	3.77(3H, s, OC**H**$_3$)
	$(CH_3)_2N$	H	prisms (AcOEt)	164—165	$C_{17}H_{16}ON_2Cl_2$	60.91 (60.75)	4.81 (4.79)	8.36 (8.46)	1768	5.34	6.5—6.7 (2H, d, *J*=8, H$_{(3')}$ and H$_{(5')}$) 6.9—7.3(9H, m)	2.90(6H, s, N(C**H**$_3$)$_2$)
	NO_2	H	prisms (EtOH)	150—151^f)	$C_{15}H_{10}O_3N_2Cl_2$	53.43 (53.56)	2.99 (3.03)	8.31 (8.38)	1773	5.60	7.05—7.4(5H, m) 7.46 (2H, d, *J*=8, H$_{(2')}$ and H$_{(6')}$) 8.19 (2H, d, *J*=8, H$_{(3')}$ and H$_{(5')}$)	
			prisms (EtOH)	138.5—139	$C_{19}H_{13}ONCl_2$	66.68 (66.74)	3.83 (3.77)	4.09 (4.07)	1787	5.83	7.0—8.75(12H, m)	
	R											
	CH_3		prisms (iso-propyl ether–*n*-hexane)	88—89.5	$C_{10}H_9ONCl_2$	52.20 (52.40)	3.94 (4.12)	6.09 (6.08)	1790	4.97	7.0—7.5(5H, m)	2.86(3H, s, C**H**$_3$)
			prisms (iso-propyl ether–petr.ether)	45—46	$C_{16}H_{13}ONCl_2$	62.76 (62.97)	4.28 (4.32)	4.58 (4.67)	1787	4.77	6.9—7.5(10H, m)	3.89(1H, d) 4.88(1H, d, *J*=13.8, C**H**$_2$)
			prisms (petr.ether)	41—42	$C_{17}H_{15}ONCl_2$	63.76 (63.58)	4.72 (4.66)	4.37 (6.35)	1790	4.65	6.9—7.4(10H, m)	2.70—4.05 (4H, m, C**H**$_2$C**H**$_2$)
			leaflets (*n*-hexane)	98—98.5	$C_{15}H_{17}ONCl_2$	60.42 (60.65)	5.75 (5.75)	4.70 (4.98)	1785	4.99	7.2—7.5(5H, m)	0.8—2.3 (10H, m, (C**H**$_2$)$_5$) 3.0—3.6 (1H, m, >C**H**)

a) The following abbreviations are used: s=singlet; d=doublet; m=multiplet *b*) lit.[6] mp 164° *c*) lit.[6] mp 136° *d*) lit.[6] mp 118° *e*) lit.[6] mp 135° *f*) lit.[6] mp 158°

3,3-dichloro-2-azetidinone in a excellent yield. Furthermore it was also realized that several N-benzylidenealkylamines reacted smoothly to give the corresponding 3,3-dichloro-1-alkyl-4-phenyl-2-azetidinones as shown in Table III. Appearances of β-lactam carbonyl absorption at 1767—1792 cm^{-1} in their IR spectra evidenced the 3,3-dichloro-2-azetidinone structures.

Experimental9)

Reaction of Schiff Bases with Trichloroacetic Anhydride——General Procedure: The following thirteen Schiff bases used (see Table II and III) as substrates of the reaction of trichloroacetic anhydride were synthesized, showing melting and boiling points as in the parentheses; N-benzylideneaniline (mp 46—67°), N-benzylidene-*p*-chloroaniline (mp 60—61°), N-benzylidene-*p*-anisidine (mp 68—69°), N-benzylidene-*p*-nitroaniline (mp 115—116°), N-*p*-chlorobenzylideneaniline (mp 60—61°), N-*p*-methoxybenzylideneaniline (mp 59—60°), N-*p*-dimethylaminobenzylideneaniline (mp 97—98°), N-*p*-nitrobenzylideneaniline (mp 88—89°), N-benzylidene-1-naphthylamine (mp 71—72°), N-benzylidenemethylamine [bp 92—93° (34 mmHg)], N-benzylidenebenzylamine [bp 147—148° (6 mmHg)], N-benzylidene-β-phenethylamine (mp 33—34°), N-benzylidenecyclohexylamine [bp 154° (21 mmHg)].

To a solution of each 0.03 mole of the Schiff bases in 30 ml of dry xylene was added 0.039 mole of trichloroacetic anhydride and the mixture was heated with constant stirring in a stream of dry air free from CO_2 in order to check emitting CO_2 by $Ba(OH)_2$ solution. The reaction temperature was maintained at 125—148° effecting considerable emission of CO_2 for several hours. The run with N-*p*-dimethylaminobenzylideneaniline is an exception of the above procedure, which was processed at 80—82° using dioxane in place of xylene. After subsidence of the CO_2 emission the reaction solution was concentrated under reduced pressure. The evaporated residue was crystallized in most cases and the crystals were collected by filtration after digested with isopropyl ether, or when oily residue was obtained it was digested with a small amount of isopropyl ether or petr. ether and cooled to give crystals. The resulting crystals were recrystallized from appropriate solvent.

By the above procedure the corresponding 3,3-dichloro-2-azetidinones were obtained as listed in Table IV with their physical and analytical data. Reaction conditions and yield of each of the runs are recorded in Table II and III.

Acknowledgement The authors are indebted to the members of Analysis Center of this college for microanalyses.

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9) All melting and boiling points are uncorrected. IR spectra were determined on a Hitachi EPI-G2 spectrophotometer. NMR spectra were taken at 60 MHz with a Hitachi R-24 spectrometer using tetramethylsilane as an internal standard.