April, 1976] BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 49(4), 1105—1107 (1976) 1105

The Reaction of Anhydrochloralurethanes with Ketene Acetals

Tetsuo Akiyama, Nobuaki Urasato, Takeshi Imagawa, and Mituyosi Kawanisi
Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606

(Received October 6, 1975)

The reaction of anhydrochloralurethanes (I) with ketene acetals (II) has been found to give novel carbamate derivatives (III) in quantitative yield. The intermediacy of a cyclic intermediate, an oxazine derivative (IV), was confirmed by spectroscopic methods, although several attempts to isolate IV have been unsuccessful. The mechanism for formation of IV is discussed.

In 1968 Ulrich and coworkers[1)] established the structure and the synthetic method of *N*-(2,2,2-trichloroethylidene)alkoxycarbonylamine (I), commonly called anhydrochloralurethane. They also reported that the C=N double bond of I was highly reactive and easily attacked by several nucleophiles, such as water, alcohols, and amines.[1)]

In a previous report from this laboratory, we have demonstrated the potentiality of I as a dienophile in a Diels-Alder reaction.[2)]

A literature survey reveals that investigations about the reactivity of I have mainly noted the C=N double bond.[1–3)]

Since the CCl_3 group is equivalent to the CO_2H group, I might be valuable for constructing the α-amino acid skelton. However, the synthetic application of I is rather limited.[4)]

As judged from the structure of I, we have been intrigued with the supposition that I, as a heterodiene (C=N–C=O),[5)] might formally undergo a [4+2] Diels-Alder type reaction with inverse electron demand against an electron-abundant nucleophilic olefin to give an adduct.

In this report, we should like to present the results obtained in the reaction of I with ketene acetal (II) to give novel acyclic carbamates (III), and also convincing evidence for the intermediacy of cyclic oxazine derivatives (IV) which could arise from the abovementioned reaction.

Results and Discussion

When I ($R=C_2H_5$) and excess II ($R'=C_2H_5$) in benzene were heated under reflux for 15 h, a single product was obtained in a quantitative yield. Elementary analysis as well as spectral investigations established the structure as IIIa. Although its parent peak was missing, the mass spectrum had a peak corresponding to M^+-CCl_3 fragment ion as the base peak originating from the fragmentation β at the nitrogen atom. The NMR spectrum showed a typical ABX pattern corresponding to $-CH_2CH(CCl_3)-$, accompanied by the signals of NH and two $-OCH_2CH_3$.

A plausible mechanism for the formation of III is shown in Scheme 1:

A Diels-Alder type reaction between I and II in a sense of inverse electron demand affords a dihydro-1,3-oxazine (IV),[6)] hydrolysis (by atomospheric moisture or work-up) of which will give III.

Although the adduct (IV) was not obtained in a pure state, its existence was confirmed as follows. The crude product-mixture just after the reaction gave an additional peak in GLC along with that of III. Taking as an example the case of the reaction between Ia and IIa, in the mass spectrum [Fig. 1(a)], the parent peak

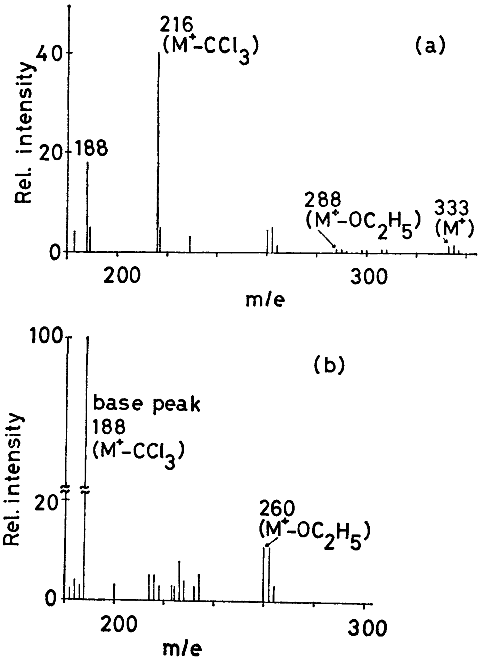
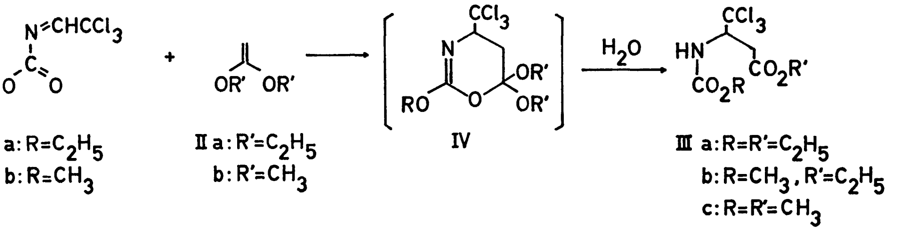
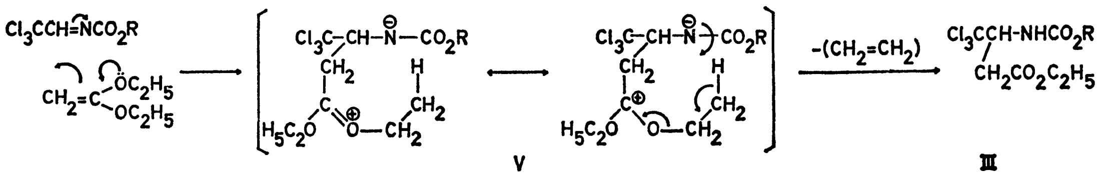


Fig. 1. Mass spectra of the reaction products between Ia and IIa.



Scheme 1.



Scheme 2.

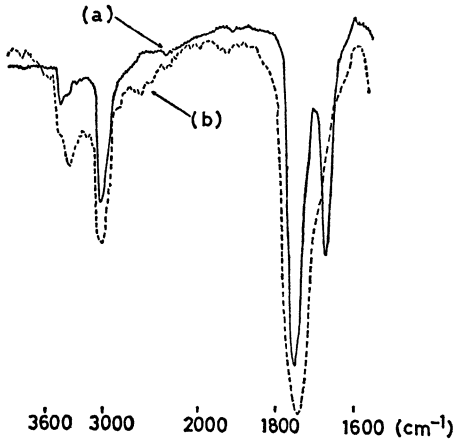


Fig. 2. IR spectra of the reaction products between Ia and IIa.
(a) For the crude products in the reaction of Ia and IIa. (b) For the analytically pure IIIa.

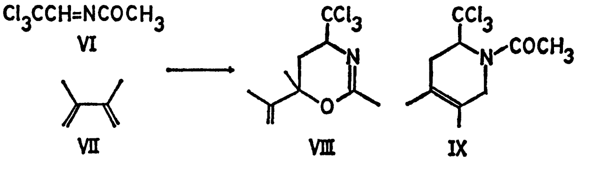
of IV ($R=R'=C_2H_5$), *m/e* 333, and the peak due to M^+-CCl_3 of IV, *m/e* 216, which were absent in the spectrum of IIIa [Fig. 1(b)], were clearly observed. The IR spectrum in CCl_4 solution [Fig. 2(a)] had only a small NH absorption band, which grew gradually significant after several hours in air, when the absorption band at 1680 cm^{-1} due to the C=N bond became disappeared. The crude reaction mixture was gradually hydrolyzed by atmospheric moisture. The intentional treatment of the reaction mixture with dil hydrochloric acid rapidly afforded III. It should be noted that the addition reaction giving IV is highly regioselective as far as the product is concerned.

An alternative path giving III from I and II may be the one shown in Scheme 2, in which a zwitterionic intermediate (V) would expel the neutral ethylene molecule as the leaving group. This mechanism could also explain the regioselectivity of the reaction.

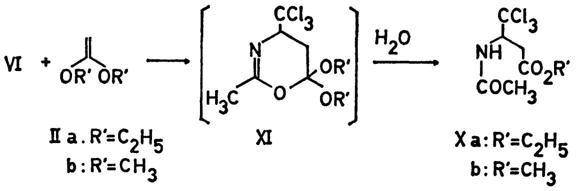
However, this scheme cannot be compatible with the spectral data mentioned above, and the fact that the reaction Ib with IIb gave a similar product IIIc cannot be adequately explained by this scheme (In this case a neutral molecule as a good leaving group cannot exist).

More recently, Arbuzov *et al.* reported[7] that the reaction between *N*-(2,2,2-trichloroethylidene)acetamide (VI) and 2,3-dimethylbutadiene (VII) gave an oxazine derivative (VIII) together with the normal Diels-Alder adduct (IX). The oxazine derivative (VIII) and its crystalline salt, on reaction with strong acids, were obtained in pure form (Scheme 3).

We expected similar oxazine derivatives to be isolable in the reaction between VI, instead of anhydrochloralurethane (I), with ketene acetal. However, also in this case the adduct (XI) was not stable toward any conventional methods of purification, and the hydrolyzed product X was again produced in quantitative yield (Scheme 4).



Scheme 3.



Scheme 4.

Based on these facts, we can safely conclude that the mechanism depicted in Scheme 1 is highly plausible.

In summary, a Diels-Alder type reaction with inverse electron demand between anhydrochloralurethane and ketene acetal takes place, giving novel carbamate derivatives. This reaction might emerge as a powerful synthetic route to α-amino acids. The investigation aiming at this point is currently under way in this laboratory.

Experimental

All the temperatures are uncorrected. The IR spectra were obtained on a Shimadzu IR-27 spectrometer. The mass spectra were taken by Hitachi RMS-4 Mass Spectrometer. The NMR spectra were obtained on a Varian EM-360 spectrometer, TMS being chosen as the internal standard.

Reaction of N-(2,2,2-Trichloroethylidene)ethoxycarbonylamine (Ia) with Ketene Diethyl Acetal (IIa). Refluxing a benzene (26 ml) solution of $CCl_3CH=NCO_2C_2H_5$ (Ia) (260 mg, 1.19 mmol) and ketene diethyl acetal (360 mg, 3.10 mmol) for 15 h gave a yellow oily mixture after evaporation of benzene and ketene diethyl acetal. After hydrolysis with dil hydrochloric acid, this mixture was distilled under vacuum to afford a quantitative yield (365 mg, 1.19 mmol) of IIIa, bp 100—104 °C/0.15 mmHg. IR (CCl_4): 3320, 1740 (broad) cm^{-1}. MS: *m/e* 260 (11%, $M^+-OC_2H_5$), 262 (11), 264 (3), 188 (100, M^+-CCl_3), 142 (33), 116 (41), 70 (36), 59 (81), 56 (37). NMR (CCl_4): δ 1.28 ppm (t, 6H, $-OCOCH_2-$

$\mathrm{C\mathbf{H}_3}$), 2.68 [dd, 1H, J=15.2, 3.6 Hz, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.18 [dd, 1H, J=15.2, 9.0 Hz, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 4.16 (q, 4H, $\mathrm{-OCOC\mathbf{H}_2CH_3-}$), 4.91 (m, 1H, $\mathrm{-CHCCl_3-}$), 5.48 (d, 1H, J=10.0 Hz, NH). Found: C, 34.82; H, 4.74; N, 4.60%. Calcd for $\mathrm{C_9H_{14}Cl_3NO_4}$: C, 35.26; H, 4.60; N, 4.57%.

Reaction of Ib with IIa. Refluxing a benzene (32 ml) solution of Ib (320 mg, 1.56 mmol) and an excess of IIa for 15 h gave an oily mixture. After being left at room temperature for several days, the reaction mixture turned into a white solid of IIIb (458 mg) quantitatively, mp 71.5—73.5 °C after recrystallization from hexane. IR (Nujol): 3300, 1750, 1710 cm^{-1}. MS: *m/e* 260 (3%, $\mathrm{M^+-OCH_3}$), 262 (3), 264 (1), 246 (11, $\mathrm{M^+-OC_2H_5}$), 248 (11), 250 (3), 174 (100, $\mathrm{M^+-CCl_3}$), 132 (30), 128 (52). NMR ($\mathrm{CCl_4}$): δ 1.27 ppm (t, 3H, $\mathrm{-OCH_2C\mathbf{H}_3}$), 2.69 (dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.07 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.71 (s, 3H, $\mathrm{-OCOCH_3}$), 4.18 (q, 2H, $\mathrm{-OCOC\mathbf{H}_2CH_3}$), 4.92 (m, 1H, $\mathrm{-CHCCl_3-}$), 5.50 (d, 1H, NH). Found: C, 32.74; H, 4.18; N, 4.80%. Calcd for $\mathrm{C_8H_{12}Cl_3NO_4}$: C, 32.85; H. 4.13; N, 4.79%.

IIIc was similarly obtained from Ib and IIb (15 h; 100%), mp 96—99 °C (hexane). IR (Nujol): 3350, 1760, 1730 cm^{-1}. MS: *m/e* 246 (8%, $\mathrm{M^+-OCH_3}$), 248 (7.5), 250 (2), 160 (100, $\mathrm{M^+-CCl_3}$), 138 (80). NMR ($\mathrm{CCl_4}$): δ 2.69 ppm [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.08 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.70 (s, 6H, $\mathrm{-OCOCH_3}$), 4.88 (m, 1H, $\mathrm{-CHCCl_3-}$), 5.50 (d, 1H, NH). Found: C, 30.24; H, 3.64; N, 5.04%. Calcd for $\mathrm{C_7H_{10}Cl_3NO_4}$: C, 30.19; H, 3.62; N, 5.03%.

Reaction of N-*(2,2,2-Trichloroethylidene)acetamide (VI) with Ketene Acetals (II).* In a manner similar to the above, Xa was obtained from VI and IIa (15 h at 80 °C, 100%), mp 61.5—63.0 °C (hexane). IR (Nujol): 3300, 1740, 1680 cm^{-1}. MS: *m/e* 230 (9%, $\mathrm{M^+-OC_2H_5}$), 232 (9), (9), 234 (3), 158 (44, $\mathrm{M^+-CCl_3}$), 116 (100). NMR ($\mathrm{CCl_4+CDCl_3}$): δ 1.27 ppm (t, 3H, $\mathrm{-OCH_2C\mathbf{H}_3}$), 2.08 (s, 3H, $\mathrm{-COCH_3}$), 2.72 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.13 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 4.17 (q, 2H, $\mathrm{-OC\mathbf{H}_2CH_3}$), 5.32 (m, 1H, $\mathrm{-CHCCl_3-}$), 6.43 (d, 1H, NH). Found: C, 34.49; H, 4.44; N, 5.28%. Calcd for $\mathrm{C_8H_{12}Cl_3NO_3}$: C, 34.75; H, 4.37; N, 5.06%.

Similarly, Xb was obtained from VI and IIb (15 h at 80 °C, 100%), mp 132.0—132.5 °C from hexane and benzene (1 : 1). IR (Nujol): 3300, 1760, 1680 cm^{-1}. MS: *m/e* 230 (4%, $\mathrm{M^+-OCH_3}$), 232 (4), 234 (1), 144 (33, $\mathrm{M^+-CCl_3}$), 102 (100). NMR ($\mathrm{CCl_4+CDCl_3}$): δ 2.09 ppm (s, 3H, $\mathrm{-COCH_3}$), 2.73 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.10 [dd, 1H, $\mathrm{-C\mathbf{H}_2CH(CCl_3)-}$], 3.73 (s, 3H, $\mathrm{-OCOCH_3}$), 5.27 (m, 1H, $\mathrm{-CHCCl_3-}$), 6.27 (d, 1H, NH). Found: C, 32.13; H, 3.85; N, 5.36%. Calcd for $\mathrm{C_7H_{10}Cl_3NO_3}$: C, 32.03; H, 3.84; N, 5.34%.

References

1) H. Ulrich, B. Tucker, and A. A. R. Sayigh, *J. Org. Chem.*, **33**, 2887 (1968).

2) T. Imagawa, K. Sisido, and M. Kawanisi, *Bull. Chem. Soc. Jpn.*, **46**, 2922 (1973).

3) M. S. Raasch, *J. Org. Chem.*, **40**, 161 (1975).

4) C. Kashima, Y. Aoki, and Y. Omote, The 32th Annual Meeting of the Chemical Society of Japan, Tokyo 1G34 (1975).

5) a) W. Seeliger and W. Diepers, *Justus Liebigs Ann. Chem.*, **697**, 171 (1966). b) R. R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, **4**, 241 (1965); *ibid.*, **8**, 602 (1969).

6) It is not implied that the formation of IV from I and II should follow a concerted pathway. We feel it to be probable to allot a polar transition state for this reaction. However the precise mechanism is still undetermined.

7) Y. A. Arbuzov, E. I. Klimova, N. D. Autonova, and Y. V. Tomilov, *Zh. Org. Khim.*, **10**, 1164 (1974).