CHEMISTRY LETTERS, pp. 487-490, 1987.

Synthesis of 2a-Substituted Dichlorocyclobuta[c]quinolin-3-one and 3-(Trichloroethenyl)-2-quinolone through the Cross Photocycloadduct of 2-Quinolone and Tetrachloroethylene

Shinji NONOYAMA, Noriyuki YONEZAWA, Kazuhiko SAIGO, Tsuneo HIRANO,* and Masaki HASEGAWA*

Department of Synthetic Chemistry, Faculty of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

2a-Substituted dichlorocyclobuta[c]quinolin-3-one was obtained from the cross photocycloadduct of 2-quinolone and tetrachloroethylene by the reaction with bases or nucleophiles via cyclobutene formation and intermolecular S_N2' displacement along with trichloroethenyl-2-quinolone via [2+2] cycloreversion of the cyclobutene intermediate.

In the recent papers,[1] we have shown unique reaction behaviors of the photocycloadduct of coumarin and tetrachloroethylene, namely, the ring contraction from a [4,6,6]- to [4,5,6]-fused ring system through lactone-opening, cyclobutene formation, and intramolecular S_N2' displacement, and [2+2] cycloreversion of the cyclobutene intermediate to yield trichloroethenylcoumarin. In our continuing study on compounds having [4,6,6]-fused ring system,[2] we investigated the reaction of 1,1,2,2-tetrachloro-1α,2α,2aα,3α,4α,8bα-hexahydrocyclobuta[c]quinolin-3-one (**1**).[3] Contrary to our expectation based on the results for the reaction of the cycloadduct of coumarin,[1] **1** gave no ring-contracted product but new cyclobutene compounds and trichloroethenyl-2-quinolone. In this communication we wish to report the reaction of **1** with nucleophiles or bases and the structural investigation on the product by means of two-dimension (2D) NMR method.

The synthetic procedure for cycloadduct **1** is as follows: 5.81 g (40.0 mmol) of 2-quinolone and 1.24 g (6.8 mmol) of benzophenone were dissolved in a mixture of 1327.9 g (8.0 mol) of tetrachloroethylene and 1000 ml of dichloromethane. The solution was irradiated with the light of a 500-W high-pressure mercury lamp through a Pyrex filter for 87 h. After concentration of the reaction mixture under reduced pressure, silica-gel column chromatographic separation (Wako C-200) using benzene as an eluent followed by recrystallization from dichloromethane gave 5.64 g (43.9%) of pure **1**. The present procedure gives a higher yield than the method reported by Evanega and Fabiny.[3]

Treatment of **1** with an alkali in methanol gave two products, but neither of them was the expected compound having a [4,5,6]-fused ring system; one was a cyclobutene compound containing a methoxy group and the other was trichloroethenyl-2-quinolone. As conventional spectroscopic analyses could not

specify the position of the methoxy group in the former compound, we explored Nuclear Overhouser Effect (NOE) by 2D NMR spectroscopy to reveal the exact structure of it. 2D NMR (COSY and NOESY) spectra were recorded on a JEOL GX-400 at 400 MHz with 3.1 s recycle time, 8 transitions correlated for each t_1 value, and accumulations of 512 spectra each consisting of 2048 data points. The resulted NOESY contour plot is illustrated in Fig. 1. In the COSY spectrum, no J_H coupling except for aromatic protons could be observed. The correlation between 3.5 and 4.2 ppm in the NOESY spectrum manifests that the distance between the cyclobutene ring proton and the methoxy protons is very short. The cross peak between 4.2 and 7.2 ppm indicates that the cyclobutene proton and one of the aromatic protons are also located closely. Furthermore, a correlation was also observed between the methoxy protons and the amide proton. If the methoxy group was situated in C_1, C_2, or C_{8b}, one or more of the above NOE cross peaks must be absent.[4] Based on these considerations it is unambiguous that the methoxy group is situated at the carbonyl α position, consequently 3a was confirmed to be 1,2-dichloro-2a-methoxy-2aα,3α,4α,8bα-tetrahydrocyclobuta[c]quinolin-3-one.

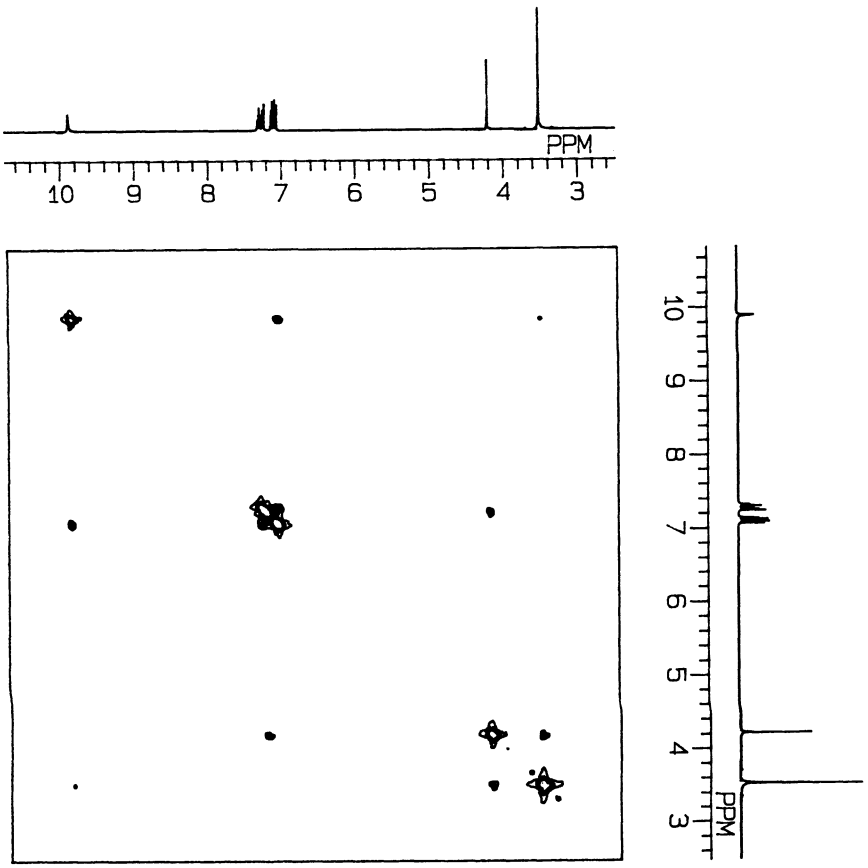

Fig. 1.
400 MHz proton NOESY NMR spectrum of **3a** at 27 °C. Data matrix was zero-filled to 2048 by 1024 points with a frequency range of 5000 Hz in both dimensions.

This result shows that in the first step of this reaction, dehydrochlorination causing cyclobutene formation took place, whereupon there are two possible routes in the second stage; the intermolecular S_N2' displacement by the attack of methoxy anion on the carbonyl α carbon in the cyclobutene intermediate (**2**) to produce a new cyclobutene compound (**3a**) and the [2+2] cycloreversion of **2** to yield trichloroethenyl-2-quinolone (**4**). The second

stage was strongly influenced by the base or nucleophile used (Runs 1-4, Table 1). As **2** should be very unstable, the following competitive nucleophilic substitution reaction and the cycloreversion of the cyclobutene should take place immediately when **2** is produced.

The exclusive formation of **4** was performed by the use of NaH or Et_3N as a base (Runs 6 and 7). The possible reaction route in this case is a [2+2] cycloreversion only, similar to the reaction of tetrachlorocyclobuta[c]chromen-3-one with a non-nucleophilic base.[1] Additionally, in the reaction of **1** with NaOH in aqueous acetone, **4** was formed quantitatively. The reactions of **1** are summarized in Table 1.

These results imply a highly enhanced tendency to dehydrochlorination of the cross adduct (**1**), which is attributed to the strain of the tetrachlorinated cyclobutane ring fused to a rigid 6-membered lactam ring. In the case of [4,6,6] lactone-fused ring system, the first stage of the reaction with nucleophiles was lactone-opening. However, lactam-opening of **1** never occurs under such mild conditions, since the lactam system has rather strong amide

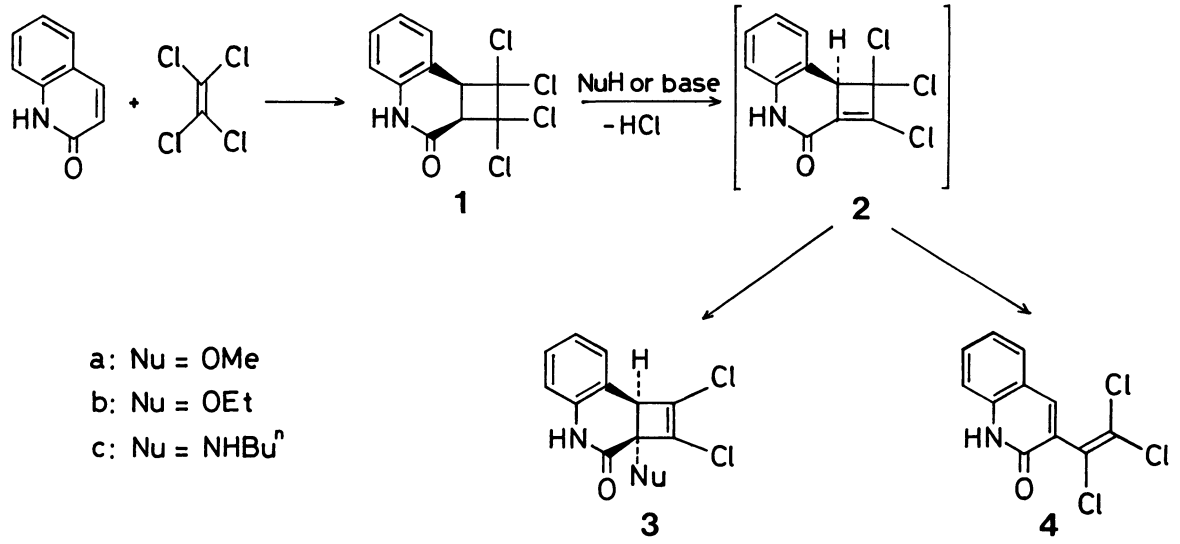

Table 1. Reaction of **1** with bases[5]

Run	Base	equiv.	Solvent	Time / h	Conv.(Yield)/% **3**	**4**
1	NaOH	10	MeOH	16	89(70)	11(7)
2	$NaHCO_3$	23	MeOH	23	40(32)	60(50)
3	NaOH	10	EtOH	7	40(35)	60(51)
4	NaOMe	900	MeOH	14	86(70)	14(5)
5	NaOH	1900	Acetone	16	0	100(85)
6	NaH	15	Benzene	5	0	100(90)
7	NEt_3	45	Benzene	7	0	100(92)
8	$BuNH_2$	10	Acetone	7	100(97)	0

linkage. Then the first stage should be dehydrochlorination to yield unstable intermediate **2**. Further, the absence of the intramolecular attack to the cyclobutene carbon should raise the opportunity of [2+2] cycloreversion, resulting in the formation of **4** in every cases.

More detailed descriptions about 2D NMR analysis will be presented in a subsequent paper.

The authors would like to thank Mr. Tokiji Kawamura for his technical assistance in obtaining 2D NMR spectra. The present work was partially supported by a Grant-in-Aid for Scientific Research No. 61750815 from the Ministry of Education, Science and Culture.

References

1) N. Yonezawa, S. Nonoyama, K. Saigo, and M. Hasegawa, J. Org. Chem., 50, 3026 (1985); S. Nonoyama, N. Yonezawa, K. Saigo, Y. Iitaka, and M. Hasegawa, Bull. Chem. Soc. Jpn., 60, 349 (1987).

2) Typical reviews for tricyclic compounds having hetero atoms: D. C. Neckers and A. H. A. Tinnemans, "Synthetic Organic Photochemistry," ed by W. M. Horspool, Plenum Press, New York (1984), p. 285; C. Kaneko, Kagaku Sousetsu, 47, 107 (1985).

3) G. R. Evanega and D. L. Fabiny, J. Org. Chem., 35, 1757 (1970).

4) W. Braun, C. Bösch, L. R. Brown, N. Go, and K. Wüthrich, Biochim. Biophys. Acta, 667, 377 (1981).

5) **3a:** Mp 183 °C (decomp); IR (KBr) 1680, 1640, 1100, and 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.51 (3H, s, methoxy protons), 4.21 (1H, s, cyclobutene ring proton), 7.00-7.14 (2H, m, aromatic protons), 7.23-7.32 (2H, m, aromatic protons), and 9.51 (1H, s, NH proton); ^{13}C NMR ($CDCl_3$) δ = 53.2 (d), 54.3 (q), 80.7 (s), 116.6 (d), 118.3 (s), 123.9 (d), 126.2 (s), 128.5 (d), 129.3 (d), 131.9 (s), 135.3 (s), and 166.0 (s); Found: C, 53.24; H, 3.39; N, 5.18%. Calcd for $C_{12}H_9Cl_2NO_2$: C, 53.36; H, 3.36; N, 5.19%.
3b: Mp 190 °C (decomp); ^1H NMR ($CDCl_3$) δ = 1.30 (3H, t, ethoxy methyl protons), 3.70 (2H, q, ethoxy methylene protons), 4.01 (1H, s, cyclobutene ring proton), 6.80-7.30 (4H, m, aromatic protons), and 9.72 (1H, s, NH proton); ^{13}C NMR ($CDCl_3$) δ = 15.3 (q) 54.2 (d), 63.0 (t), 80.0 (s), 116.8 (d) 118.4(s), 123.8 (d), 126.5 (s), 128.4 (d), 129.2 (d), 131.6 (s), 135.4(s), and 166.7 (s).
3c: Glass; ^1H NMR ($CDCl_3$) δ = 0.90 (3H, t, J = 7.5 Hz, $CH_2CH_2CH_2\underline{CH}_3$), 1.32-1.43 (2H, m, $CH_2CH_2\underline{CH}_2CH_3$), 1.49-1.57 (2H, m, $CH_2\underline{CH}_2CH_2CH_3$), 2.58-2.66 (2H, m, $\underline{CH}_2CH_2CH_2CH_3$), 4.20 (1H, s, cyclobutene ring proton), 6.68 (1H, br s, amine proton) 6.89-7.18 (2H, m, aromatic protons), 7.20-7.29 (2H, m, aromatic protons), and 9.12 (1H, s, amide proton).
4: Mp 276-278 °C; IR (KBr) 1660, 1570, and 1430 cm^{-1}; ^1H NMR(d_6-DMSO) δ = 7.21-7.37 (2H, m, aromatic protons), 7.55-7.76 (2H, m, aromatic protons), and 8.27 (1H, s, olefinic proton); Found: C, 47.92; H, 2.20; N, 5.09%. Calcd for $C_{11}H_6Cl_3NO$: C, 48.13; H, 2.20; N, 5.10%.

(Received December 9, 1986)