Novel Transformations of Two Kinds of Chlorinated Photo [2+2] Cycloadducts of 2-Pyrone-5-carboxylate

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Novel reactions of 7,7-dichloro- and 7,7,8-trichloro-3-oxo-2-oxabicyclo[4.2.0]oct-4-ene-6-carboxylates **5** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in alcohol gave pyrano[4,3-*b*]pyran-2,5-diones **8** *via* (*Z*)-(2*H*-pyran-2-on-3-yl)butenoates **7**. On the other hand, the same treatment of 7,7,8-trichloro-2-oxo-3-oxabicyclo-[4.2.0]oct-4-ene-5-carboxylate **6b** afforded 2-oxo-3-oxabicyclo[4.2.0]oct-4,7-diene-5-carboxylate **14** *via* cyclobutene formation and S_N2' displacement by attack of the alkoxy anion.

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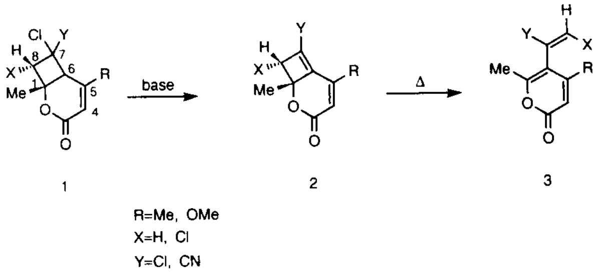
Cyclobutanes, which were easily obtained from photochemical cycloaddition reaction of heterocyclic ring system with halogenated olefins, often produce highly enhanced reactivity in the heterocyclic ring because of being cyclobutene equivalents as observed in the reaction of [2+2] cycloadducts derived from 2-pyridone and coumarin with chloroethylenes [1]. We demonstrated that photo [2+2] cycloadducts **1** between 2-pyrones and chloroethylenes provided a route to prepare ethenyl-2-pyrones **3** *via* ring-opening of cyclobutenes **2** bearing a double bond at C_6-C_7 position in **1** by using triethylamine (Scheme 1) [2]. Our interest in this subject had led us to extend the other photo [2+2] adducts of 2-pyrones which had some substituents at the 5-positions. They have possibility to give other cyclobutenes bearing a double bond at C_7-C_8 in a skeleton of **1** and other kinds of photoadducts.

Scheme 1



In this paper we report the novel transformation of two types of photo [2+2] cycloadducts between ethyl 4,6-dimethyl-2-pyrone-5-carboxylate (**4**) and chloroethylenes providing pyrano[4,3-*b*]pyran-2,5-diones and 3-oxabicyclo-[4.2.0]oct-4,7-dien-2-ones.

At first [2+2] cycloadducts, **5a**, **5b**, **6a** and **6b**, were prepared by photosensitized cycloaddition reactions of **4** with chloroethylenes in 20%, 13%, 25% and 5% yields, respectively. The structures of **5**, chlorinated ethyl 3-oxo-2-oxabicyclo[4.2.0]oct-4-ene-6-carboxylates, and **6**, chlorinated ethyl 2-oxo-3-oxabicyclo[4.2.0]oct-4-ene-5-carboxylates, were elucidated through spectral comparisons with previous data [2] (Scheme 2).

Scheme 2

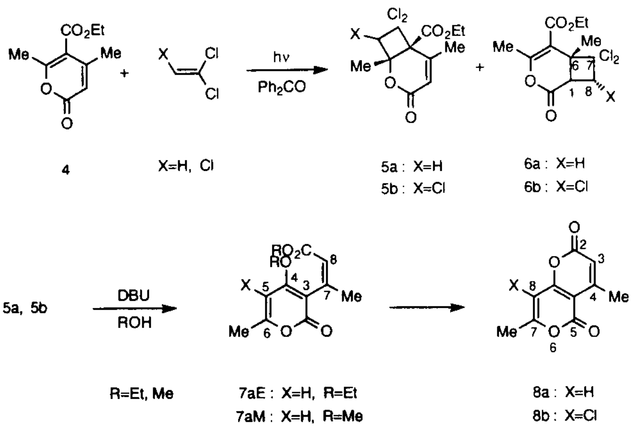


Table 1

Dehydrochlorination of **5a** and **5b** with DBU

[2+2] Cycloadduct	Base	Solvent	Temperature	Time/hours	Product (%)
5a	DBU	EtOH	rt	5	**7aE** (34)
	DBU	EtOH	rt	24	**8a** (54)
	DBU	MeOH	0°	1.2	**7aM** (50)
7aE [a]			70°	6	**8a** (quant)
7aM [a]			70°	20	**8a** (quant)
5b	DBU	MeOH	0°	1	**8b** (23)

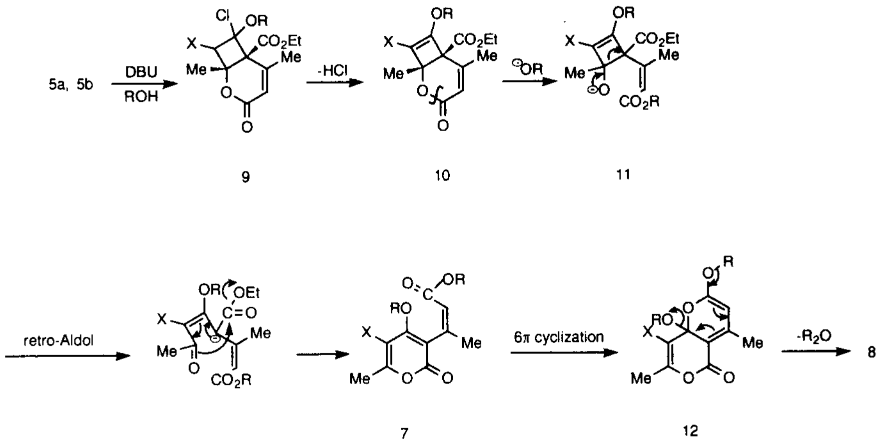
[a] Heated without solvent.

Transformation of the [2 + 2] cycloadducts **5** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in alcohol at room temperature or 0° afforded pyrano[4,3-*b*]pyran-2,5-diones **8**. In the short time reaction of **5a** in ethanol and methanol, (*Z*)-(2*H*-pyran-2-on-3-yl)butenoates, **7aE** and **7aM**, being an intermediate of **8** were isolated, respectively (Scheme 2). These reactions did not occur by using triethylamine.

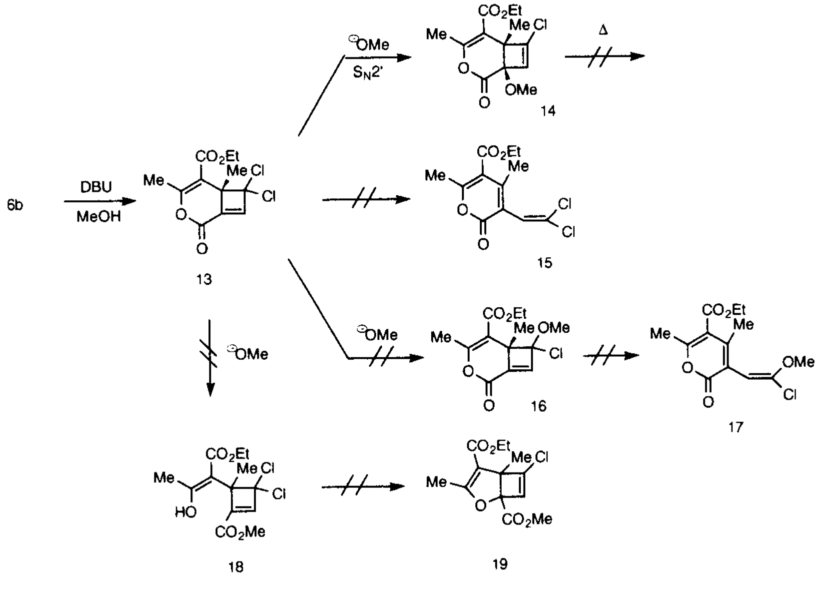
Treatment of dichloro-substituted adduct **5a** with DBU in ethanol at room temperature afforded a product **7aE** or **8a** depending upon the reaction conditions, while trichloro-substituted adduct **5b** gave **8b** in methanol at 0° (Table 1). The reaction of **5a** in methanol at 0° afforded **7aM**, and the products, **7aE** and **7aM**, were converted into **8a** quantitatively at 70°.

The spectral data indicated that the products, **7aE** and **7aM**, and **8a** and **8b**, have similar structures with each other. For instance, **7aE**, (*Z*)-ethyl (4-ethoxy-6-methyl-2*H*-pyran-2-on-3-yl)butenoate, showed strong carbonyl absorptions at 1720 (sh), 1715 cm^{-1} and C = C bond absorptions at 1640, 1545 cm^{-1} in the ir spectrum for a 2-pyrone ring and conjugated ester group. The ^{1}H nmr spectrum showed two olefinic protons, δ 5.89, 5.22, assigned to 5-H and 8-H, respectively, in addition with two kinds of ethoxy groups. The position of the substituents in the 2-pyrone ring was supported from the conversion of **7aE** to **8a** which was identified from the literature [3]. The *Z* configuration of **7** was also suggested from the high-field shifts of methylene proton (OCH$_2$CH$_3$, δ 3.59) at 4-position of **7aE** and that of methyl proton (OCH$_3$, δ 3.32) of **7aM** by considering the shielding effect of the carbonyl group at the 8-position.

Scheme 3

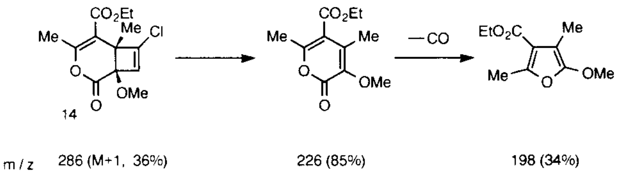


Scheme 4

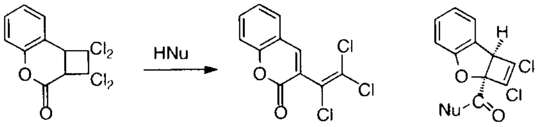


On the basis of these results as shown in Scheme 2, the formation of **8** is inferred to occur as shown in Scheme 3. Thus, **5a** and **5b** undergo nucleophilic replacement with base, followed by dehydrochlorination, retro-Aldol reaction and lactonization to give **7**. Finally **8** are obtained *via* elimination of ether from **7** in order to stabilize by the aromatization.

Scheme 5



Scheme 6



Treatment of **6b** with DBU in methanol gave **14** in 58% yield, whose structure was assigned as ethyl 7-chloro-1-methoxy-4,6-dimethyl-2-oxo-3-oxabicyclo[4.2.0]oct-4,7-diene-5-carboxylate, on the basis of spectral data (Scheme 4). Thus, the ir spectrum of **14** showed γ,δ-unsaturated lactone carbonyl absorption and new C=C absorption at 1760 and 1583 cm^{-1}, respectively. The ^{1}H nmr spectrum showed olefinic proton at δ 5.95, with the disappearance of 1-H in **6b**, and methoxy proton at δ 3.82 whose low-field shift was estimated from the deshield effect by the carbonyl group of lactone. Product **14** was stable on heating at 200°. The fragmentation pattern of **14** revealed the existence of 2-pyrone ring and its decarbonylated fragment ion (Scheme 5). Other possible structures of **14**, such as **15-19**, which were predicted from the similar dehydrochlorination of coumarin photo cycloadducts (Scheme 6) [1b], were excluded from the fact that **15**, **17-19** had no γ,δ-unsaturated lactone. Thermal stability of the product **14** precluded **16** which was estimated to be labile.

The formation of **14** is considered to proceed through dehydrochlorination of **6b**, giving intermediate **13**, followed by intramolecular S$_N$2′ displacement by the attack of the methoxy anion on the sp^2 carbon in the cyclobutene ring. Similar mechanism was reported by Nonoyama and co-workers [4] in the dehydrochlorination of quinolone photo cycloadducts.

EXPERIMENTAL

All the melting points were measured on a Yanagimoto Meltemp apparatus and are uncorrected. The ir, uv and mass spectra were recorded on JASCO A-3, Hitachi EPS-3 and JEOL JMSO-ISG spectrometers. The ^{1}H and ^{13}C nmr spectra were measured on JEOL JMN-MH-100 (100 MHz) and JEOL FX-100 (25 MHz) spectrometers using TMS as the internal reference. All the reactions were monitored by tlc on silica-gel plates.

Ethyl 4,6-dimethyl-2-pyrone-5-carboxylate (**4**) was prepared according to the method previously described in the literature [5].

Ethyl 7,7-Dichloro-1,5-dimethyl-3-oxo-2-oxabicyclo[4.2.0]oct-4-ene-6-carboxylate (**5a**) and Ethyl 7,7-Dichloro-4,6-dimethyl-2-oxo-3-oxabicyclo[4.2.0]oct-4-ene-5-carboxylate (**6a**).

A solution of **4** (10.0 g, 51 mmoles), 1,1-dichloroethylene (41 ml, 510 mmoles) and benzophenone (3.0 g, 16.5 mmoles) in acetonitrile (500 ml) was irradiated under nitrogen with a 400W high-pressure mercury lamp through a Pyrex jacket for 5 hours at room temperature. The solvent was then removed under reduced pressure and the residue was chromatographed using benzene-acetone 10:1 v/v mixture to give **5a** (3.0 g, 20%) and **6a** (3.7 g, 25%).

Compound **5a** was obtained as an oil; ir (neat) 1740, 1730, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.32, 4.31 (CO$_2$Et), 1.89, 2.16 (each s, 3H, Me), 3.13, 3.24 (each d, 1H, 8-CH$_2$, J = 14.0 Hz), 6.16 (s, 1H, 4-H); ms: m/z (relative intensity) 293 (M+1, 28), 196 (100).

Anal. Calcd. for C$_{12}$H$_{14}$Cl$_2$O$_4$: C, 49.17; H, 4.81. Found: C, 49.17; H, 4.92.

Compound **6a** was obtained as an oil; ir (neat) 1782, 1720, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.34, 4.28 (CO$_2$Et), 1.89, 2.23 (each s, 3H, Me), 3.10 (dd, 1H, 1-H, $J_{1,8}$ = 10.0, $J_{1,8'}$ = 4.0 Hz), 3.28, 3.36 (each dd, 1H, 8-CH$_2$, $J_{8,8'}$ = 15.0, $J_{8,1}$ = 10.0, $J_{8',1}$ = 4.0 Hz); ms: m/z (relative intensity) 293 (M+1, 1), 168 (100).

Anal. Calcd. for C$_{12}$H$_{14}$Cl$_2$O$_4$: C, 49.17; H, 4.81. Found: C, 49.25; H, 5.07.

Ethyl 7,7,8-Trichloro-1,5-dimethyl-3-oxo-2-oxabicyclo[4.2.0]oct-4-ene-6-carboxylate (**5b**) and Ethyl 7,7,8-Trichloro-4,6-dimethyl-2-oxo-3-oxabicyclo[4.2.0]oct-4-ene-5-carboxylate (**6b**).

A solution of **4** (5.1 g, 26 mmoles), trichloroethylene (9.4 ml, 104 mmoles) and benzophenone (1.0 g, 5.5 mmoles) in acetonitrile (200 ml) was irradiated for 16 hours. The same workup mentioned above gave **5b** (1.1 g, 13%) and **6b** (0.43 g, 5%).

Compound **5b** was obtained as an oil; ir (neat): 1745, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.36, 4.31 (CO$_2$Et), 1.70, 2.08 (each s, 3H, Me), 4.92 (s, 1H, 8-H), 6.09 (bs, 1H, 4-H); ms: m/z (relative intensity) 327 (M+1, 68), 168 (100).

Anal. Calcd. for C$_{12}$H$_{13}$Cl$_3$O$_4$: C, 44.00; H, 4.00. Found: C, 43.82; H, 4.04.

Compound **6b** had mp 126-127°; ir (potassium bromide): 1780, 1720, 1660 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.32, 4.28 (CO$_2$Et), 1.69, 2.28 (each s, 3H, Me), 3.32 (d, 1H, 1-H, $J_{1,8}$ = 10.0 Hz), 5.14 (d, 1H, 8-H, $J_{1,8}$ = 10.0 Hz); ms: m/z (relative intensity) 327 (M+1, 4), 168 (100).

Anal. Calcd. for C$_{12}$H$_{13}$Cl$_3$O$_4$: C, 44.00; H, 4.00. Found: C, 43.96; H, 3.96.

(*Z*)-Ethyl (4-Ethoxy-6-methyl-2*H*-pyran-2-on-3-yl)butenoate (**7aE**), (*Z*)-Methyl (4-Methoxy-6-methyl-2*H*-pyran-2-on-3-yl)butenoate

(**7aM**), 4,7-Dimethylpyrano[4,3-*b*]pyran-2,5-dione (**8a**) and 8-Chloro-4,7-dimethylpyrano[4,3-*b*]pyran-2,5-dione (**8b**).

A solution of **5a** (1.0 g, 3.4 mmoles) and DBU (1.98 g, 13.6 mmoles) in ethanol (20 ml) was stirred at room temperature for 5 hours. The solvent was then removed under reduced pressure and the residue was chromatographed by using benzene-acetone 30:1 v/v mixture to afford **7aE** (0.31 g, 34%). Similar treatment of **5a** (0.20 g, 0.68 mmole) for 24 hours and the same workup gave **8a** (0.07 g, 54%). A solution of **5a** (0.51 g, 1.76 mmoles) and DBU (1.07 g, 7.04 mmoles) in methanol (10 ml) was stirred at 0° for 1.2 hours. The same workup gave **7aM** (0.21 g, 50%). Both **7aE** and **7aM** were found to be labile and convert to **8a** quantitatively at 70° for 6-20 hours by using nmr measurement.

Compound **7aE** had mp 68-73° dec; ir (potassium bromide): 1720 (sh), 1715, 1655, 1640, 1545 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.17, 3.59 (CO_2Et), 2.20, 2.28 (each s, 3H, Me), 5.22 (s, 1H, 8-H), 5.89 (s, 1H, 5-H); uv (acetonitrile): 242 (ϵ 10900), 324 nm (10600); ms: m/z (relative intensity) 266 (M$^+$, 15), 43 (100).

Compound **7aM** had mp 75-78° dec; ir (potassium bromide): 1725, 1654, 1640, 1550 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 2.21, 2.33 (each s, 3H, Me), 3.32 (s, 6H, OMe, CO_2Me), 5.18 (s, 1H, 8-H), 5.89 (s, 1H, 5-H); ms: m/z (relative intensity) 192 (M-Me_2O, 96), 164 (100).

Compound **8a** had mp 217-219° (lit [3], mp 217°); ir (potassium bromide): 1748, 1640, 1602 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 2.30, 2.52 (each s, 3H, Me), 6.01, 6.13 (each s, 1H, 3-H, 8-H); ^{13}C nmr (deuteriochloroform): δ = 20.4, 22.2, 99.5, 101.9, 112.7, 156.0, 158.5, 159.8, 165.8, 166.8; uv (acetonitrile): 277 (ϵ 9800), 338 nm (10600); ms: m/z (relative intensity) 192 (M$^+$, 62), 164 (M-CO, 100).

Anal. Calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.44; H, 4.16.

A solution of **5b** (0.20 g, 0.61 mmole) and DBU (0.37 g, 2.44 mmoles) in methanol (20 ml) was stirred at 0° for 1 hour and the same workup gave **8b** (0.03 g, 23%).

Compound **8b** had mp 123-124°; ir (potassium bromide): 1745 (sh), 1730, 1635, 1600, 1540, 675 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 2.48, 2.56 (each s, 3H, Me), 6.12 (s, 1H, 3-H); ms: m/z (relative intensity) 226 (M$^+$, 85), 198 (M-CO, 100). High-resolution ms Calcd. for $C_{10}H_7ClO_4$: 226.0032. Found: 226.0036.

Ethyl 7-Chloro-1-methoxy-4,6-dimethyl-2-oxo-3-oxabicyclo[4.2.0]oct-4,7-diene-5-carboxylate (**14**).

A solution of **6b** (0.20 g, 0.61 mmole) and DBU (0.37 g, 2.44 mmoles) in methanol (20 ml) was stirred at room temperature for 10 minutes and the same workup afforded **14** (0.10 g, 58%).

Compound **14** was obtained as an oil; ir (neat): 1760, 1705, 1630, 1583 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 1.30, 4.20 (CO_2Et), 1.38, 2.27, 3.82 (each s, 3H, Me), 5.95 (s, 1H, 8-H); uv (methanol): 249 nm (7470); ms: m/z (relative intensity) 286 (M$^+$, 38%), 227 (100).

Anal. Calcd. for $C_{13}H_{15}ClO_5$: C, 54.46; H, 5.27. Found: C, 54.70; H, 5.43.

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