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Formation and Reaction of Carbonyl Ylides. Production of 2:1-Cycloadducts of 2-Benzopyrylium-4-olates with Carbonyl Compounds

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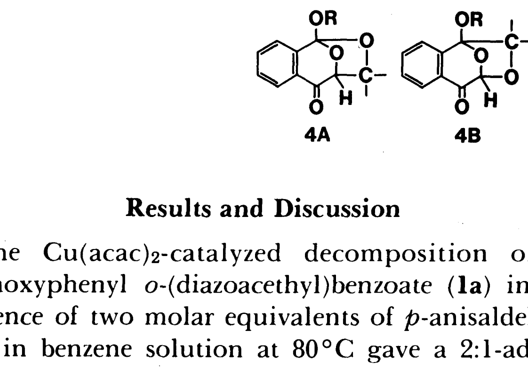
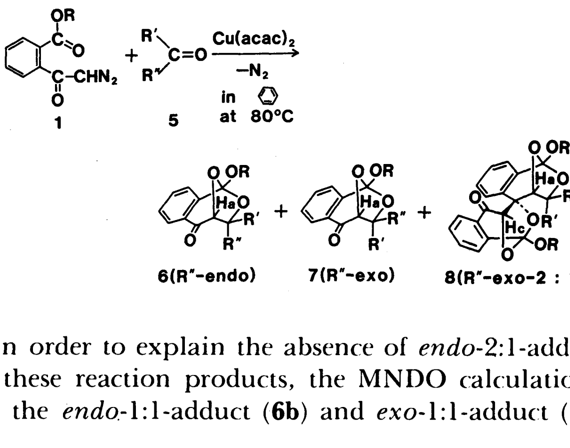
The Cu(acac)$_2$-catalyzed decomposition of *o*-(diazoacetyl)benzoates in the presence of carbonyl compounds such as benzaldehydes, acetophenones, acetone, fluorenone, and anthraquinone gave 2:1-adducts of the corresponding 2-benzopyrylium-4-olate (**3**) and the carbonyl compound, together with 1:1-adducts. The 2:1-adducts were confirmed to be produced by the cycloaddition of **3** toward the carbonyl group of the 1:1-adducts which have bulky aryl groups on exo-direction. The product ratios of the 2:1-adducts were explained according to the MNDO calculation.

In recent years the chemistry of carbonyl ylide has been studied extensively from the theoretical and synthetic interests.[1] The authors have developed the formation of carbonyl ylide through the carbene-carbonyl reaction[2,3] and reported the 1,3-dipolar cycloaddition with ethylenic,[3,4] and acetylenic compounds.[3,5] In the previous paper of this series, we have reported the Cu(acac)$_2$-catalyzed decomposition of *o*-(diazoacetyl)-benzoates (**1**) in the presence of carbonyl compounds to give not **4B** but **4A** type of cycloadducts of the carbonyl ylide intermediate, 1-(*p*-methoxyphenoxy)-2-benzopyrylium-4-olate (**3a**: R=*p*-$CH_3OC_6H_4$) and 1-methoxy-2-benzopyrylium-4-olate (**3b**: R=CH_3), with carbonyl compounds.[6] The reactions with carbonyl compounds of medium reactivity were found to yield 2:1-adducts containing two molecules of **3** and a molecule of carbonyl compound besides usual 1:1-adducts. In this paper the structure of the 2:1-adducts of **3** with various carbonyl compounds and the substituent effect on the yield of the 2:1-adducts in the reactions of substituted benzaldehydes and acetophenones were discussed.



Results and Discussion

The Cu(acac)$_2$-catalyzed decomposition of *p*-methoxyphenyl *o*-(diazoacethyl)benzoate (**1a**) in the presence of two molar equivalents of *p*-anisaldehyde (**5a**) in benzene solution at 80°C gave a 2:1-adduct of 1-(*p*-methoxyphenoxy)-2-benzopyrylium-4-olate (**3a**) and **5a** in 25% yield together with the corresponding *endo*- and *exo*-1:1-adducts. The 2:1-adduct (**8a**) has three methine proton signals at δ 4.04 (d, Ha), 4.65 (d, Hb=R′), and 5.25 (s, Hc) in which the two doublet signals are shown to couple each other. The similarity of the coupling pattern of two doublets of the 2:1-adduct (**8a**) with that of the *exo*-1:1-adduct (**7a**)[7] suggests that in **8a** and **7a** these methine protons (Ha and Hb) have the same configuration. That is, small coupling constants *J*ab, 1.5 Hz for **8a** and 1.3 Hz for **7a**, and their chemical shifts of Hb, δ 4.65 for **8a** and δ 4.63 for **7a** are quite similar. But the chemical shifts of Ha are separated by 0.5 ppm in **7a** and **8a**. This indicates that the magnetic environment of Ha are different in these two compounds. This suggests that the 2:1-adduct is produced by the second attack of **3a** on the carbonyl group of the *exo*-1:1-adduct (**7a**). The position of the second attack is inferred from the usual behavior of carbonyl compounds toward **3**.[6] In fact a similar 2:1-adduct (**9**) was observed in the reaction of **3b** (R=CH_3) with acenaphthylene.[8] In this case the second attack of **3b** has been confirmed to occur on the carbonyl group of a 1:1-adduct of **3b** and acenaphthylene, on the basis of the X-ray crystallography of **9**. Benzaldehyde was also found to give 2:1-adduct (**8b**) having an *exo*-phenyl group on bicyclic dioxolane ring system together with the corresponding 1:1-adducts (Table 1, Run b).



In order to explain the absence of *endo*-2:1-adduct in these reaction products, the MNDO calculation[9] for the *endo*-1:1-adduct (**6b**) and *exo*-1:1-adduct (**7b**)

Table 1. Yields of 1:1-Adduct and 2:1-Adduct between **3** and Carbonyl Compounds

Run	**1**	**5**		Yield of 1:1-Adduct/%		Yield of 2:1-Adduct/%	Total Yield/%	Ratio 2:1/1:1
	R	R′	R″	R″-endo **6**	R″-exo **7**	**8**		
a	p-$CH_3OC_6H_4$	H	p-$CH_3OC_6H_4$	35	21	25	81	0.45
b	p-$CH_3OC_6H_4$	H	C_6H_5	43	38	11	92	0.12
c	p-$CH_3OC_6H_4$	H	p-$NO_2C_6H_4$	60	36	0.6	97	0.006
d	p-$CH_3OC_6H_4$	CH_3	p-$CH_3OC_6H_4$	4	0	1	5[a)]	(0.25)
e	p-$CH_3OC_6H_4$	CH_3	C_6H_5	13	8	5	26[a)]	0.24
f	p-$CH_3OC_6H_4$	CH_3	p-$NO_2C_6H_4$	29	54	11	94	0.13
g	p-$CH_3OC_6H_4$	9-Fluorenone		53		37	90	0.41
h	CH_3	Anthraquinone		17		12	29[a)]	0.41
i	CH_3	CH_3	CH_3	75		12	87	0.16

a) Intractable tarry products were obtained.

Table 2. Spectroscopic Data of the 2:1-Adducts (**8**)

Adduct	IR/cm^{-1} C=O	^{1}H NMR/δ						
		OCH_3[a)]		CH			CH_3[a)]	Others[b)]
				Ha	Hb	Hc		
8a	1711	3.47	3.73	4.04 (d) J=1.5 Hz	4.65 (d)	5.25 (s)		6.27
8b	1710	3.47	3.76	4.09 (d) J=1.4 Hz	4.71 (d)	5.26 (s)		6.34
8c	1710	3.46	3.71	4.08 (s)	4.68 (s)	5.27 (s)		6.40
8d	1715	3.70 3.81	3.77	4.20 (s)	5.35 (s)		1.53	6.20
8e	1711	3.78	3.82	4.27 (s)	5.36 (s)		1.26	6.10
8f	1711	3.80	3.87	4.15 (s)	5.34 (s)		1.22	6.27
8g	1704	3.47	3.77	4.08 (s)	5.33 (s)			c)
8h	1710	3.30	4.00	4.45 (s)	5.10 (s)			5.80
8i	1714	3.63	3.71	4.38 (s)	5.26 (s)		1.26 1.57	6.22

a) Signals are all singlet. b) Only high field signals of aryl protons (Hd) are shown. c) Complex multiplets were observed together with other aromatic proton signals.

was undertaken. From the previous work, these cycloadditions were found to proceed through the interaction controlled by carbonyl ylide-HOMO and carbonyl compound-LUMO.[6b,10)] In this cycloaddition the interacting molecular orbitals of carbonyl compounds are C=O π^*. The energy levels and atomic orbital coefficients of the C=O π^* do not show significant difference for the *endo*- (**6b**) and *exo*-1:1-adduct (**7b**) as is seen in Fig. 1. Therefore, difference in the reactivity of two 1:1-adducts can not be explained in this aspect. The small reactivity of **6b** possibly be attributed to the steric factor. The *endo*-adduct (**6b**) has a phenyl group in the vicinity of the carbonyl group which is the reaction center of the second cycloaddition. The free rotation of the phenyl group of the *endo*-adduct (**6b**) hinders the developement of sp^3 orbital of C–O bond during the approach of the second **3a** to the C=O double bond, and presumably suppresses the reactivity of **6b**.

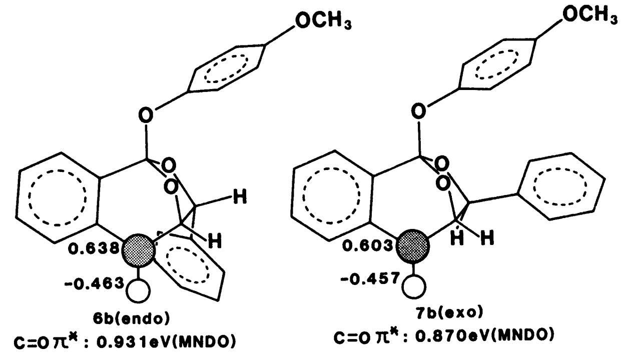


Fig. 1. The energy levels and atomic orbital coefficients of C=O π^* of **6b** and **7b**.

The substituted acetophenones also gave 2:1-adducts besides the corresponding two types of 1:1-adducts in the reactions with 2-benzopyrylium-4-olate (**3a**) (Table 1, Run d, e, f). For example, acetophenone gave *endo*-Ph-1:1-adduct (**6e**), *exo*-Ph-1:1-adduct (**7e**), and 2:1-adduct (**8e**) in 13, 8, and 5% yields, respectively. The structural determination of the bicyclic dioxolane ring system of **8e** was done as follows. The 2:1-adduct (**8e**) shows a singlet signal of CH_3(=R′) at δ 1.26 which is closer to the methyl signal of *exo*-Ph-1:1-adduct (**7e**) at δ 1.31 than to the signal of *endo*-Ph-1:1-adduct (**6e**) at δ 1.90. This indicates that the methyl group in the 2:1-adduct has *endo* configuration in the same manner as that of *exo*-Ph-1:1-adduct. In other words, phenyl group has *exo* configuration in **7e** and **8e**. These facts suggest that the 1:1-adducts (**6**) having bulky aryl groups in *endo*-direction exhibit no reactivity of cycloaddition toward **3a** depending upon the steric hindrance.

The reaction of **3a** with fluorenone also gave a 2:1-adduct in 37% yield together with a 1:1-adduct in 53% yield. In this case the CPK model shows that the fluorene ring of the 1:1-adduct does not deter the second approach of **3a** from the side of bridged oxygen of the 1:1-adduct, because the fluorene ring is fixed not to rotate like the phenyl group of **6b** described above. The reaction of 1-methoxy-2-benzopyrylium-4-olate (**3b**) with anthraquinone also gave a 2:1-adduct in 12% yield. However the structure of the 2:1-adduct is not determined yet because the 1:1-adduct have two carbonyl groups to be attacked by the second molecule of **3b** and the spectroscopic data do not characterize the structure. Acetone also gave a 1:1-adduct and a 2:1-adduct in the yields of 75 and 12%, respectively.

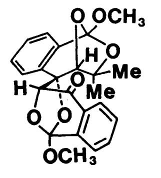
Stereochemistry of the Second Cycloaddition of 3. The stereochemistry of the second cycloaddition of the 2-benzopyrylium-4-olate (**3**) to the *exo*-1:1-adduct (**7**) is the next question. From the results of the previous works of this series, the regiochemistry of the second cycloaddition may be concluded to proceed in the same manner as the first cycloaddition.6) That is, the C_1 of the benzopyryliumolate bound to the carbonyl oxygen of the 1:1-adduct. Concerning the stereochemistry of the second cycloaddition, there are four possible structures **8iA**(**RRR**), **8iB**(**RRS**), **8iC**(**RSR**), and **8iD**(**RSS**) and their mirror image structures in the 2:1-adduct (**8i**) of **3b** and acetone. The CPK model inspection of these isomers reveals that the **8iB**(**RRS**) structure is free from the steric repulsion in the molecule. This indicates that the **8iB** is sterically the most stable one and then the most probable structure of the four possible ones.

The coupling constant $^3J(^{13}C, H)$ has been reported to be useful for the determination of configuration of rigid cyclic system,11) and to be calculated using the dihedral angle according to the equation (Eq. 1).12) The calculation of torsion angles of C_9–C_4–C_5–Ha and C_5–C_4–C_9–Hc, using the observed coupling constants $^3J(^{13}C_9\text{–Ha})=2.35$ and $^3J(^{13}C_5\text{–Hc})=3.18$ Hz of **8f** are 56 and 48°, respectively. These values are con-

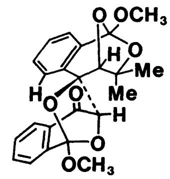
$$^3J(^{13}C, H) = 4.26 - 1.00\cos\theta + 3.56\cos 2\theta \qquad (1)$$

sistent with the values of torsion angles, 50° and 30°, estimated by the Dreiding model inspection for **RRS** structure in the possible four structures cited above.

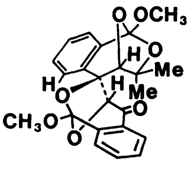
It also supports the above conclusion that the 2:1-adduct of **3b** and acenaphthylene has the same **RRS** structure.8) The 2:1-adduct (**8iB**) of acetone shows a doublet signal of an aromatic proton at δ 6.19 which is at higher field by 1 ppm than the usual ones. This high field shift can not be expected from the other three structures than **8iB**. In the structure **8iB**(**RRS**) Hd attached to benzene ring A locates above the benzene ring B. The ring current anisotropy effect may shift the signal of Hd at higher field than usual.8) A similar high field shift has been observed in the 2:1-adduct (**9**) of acenaphthylene and **3b** which has the same **RRS** structure.8) This also supports the above assignment. Other 2:1-adducts of benzaldehydes and acetophenones also have similar aromatic proton signals at higher field (Table 2). From these results the stereochemistry at the C_5, C_4, and C_9 of the 2:1-adducts was confirmed to have **RRS** structure.



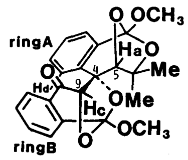
8iA(RRR)



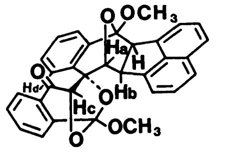
8iC(RSR)



8iD(RSS)



8iB(RRS)



9 (RRS)

Reactivity of the Substituted Benzaldehydes and Acetophenones. In the reactions of **3a** with benzaldehydes, electron-attracting group like *p*-NO_2 decreases the yields of the 2:1-adducts. For example, the ratios of the yield of 2:1-adduct/1:1-adduct decreased from 0.45 (*p*-CH_3O), to 0.12 (H), and 0.006 (*p*-NO_2). On the other hand, *p*-anisaldehyde is concluded less reactive than benzaldehyde or *p*-nitrobenzaldehyde from the results of competitive reactions.13) Similar result is also observed in the reactions of acetophenones. The reactivity of acetophenones is lower than that of benzaldehydes having the same substituent. For example, *p*-methoxyacetophenone and acetophenone gave 1:1- and 2:1-adducts in small total yields (5 and 26%) accompanying a lot of intractable tarry products. The product ratio seems to be explained by the competitive reaction between initially formed *exo*-Ar-1:1-adduct (**7**) and starting carbonyl compounds (**5**). Once a small amount of **7** is produced in the reaction system, **3** reacts with **7** or **5** competitively. The substituent effect on the reactivity of the 1:1-adducts is smaller than the effect on the reactivity of benzaldehydes and acetophenones. When electron-attracting *p*-NO_2 group is attached, benzaldehyde and acetophenone have larger reactivity than the corresponding 1:1-adduct, and then the ratios

Table 3. Melting Points and Results of Elemental Analysis of the 2:1-Adducts

Adduct	Mp	Found(%)			Calcd(%)			Molecular formula
	θ_m/°C	C	H	N	C	H	N	
8a	246—247	71.85	4.88		71.42	4.79		$C_{40}H_{32}O_{10}$
8b	241—243	73.06	4.92		72.89	4.70		$C_{39}H_{30}O_9$
8d	248—250	70.76	5.17		71.71	4.99		$C_{41}H_{34}O_{10}$
8e	214—216	72.74	4.84		73.16	4.91		$C_{40}H_{32}O_9$
8f	253—255	68.61	4.48	2.08	68.47	4.45	2.00	$C_{40}H_{31}O_{11}N$
8g	265—267	73.41	4.38		75.41	4.50		$C_{45}H_{32}O_9$
8h	>300	73.07	4.45		72.85	4.32		$C_{34}H_{24}O_8$
8i	184—185	67.71	5.47		67.31	5.40		$C_{23}H_{22}O_7$

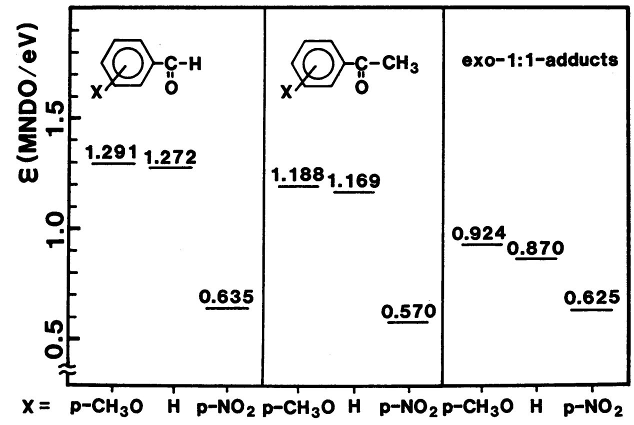


Fig. 2. The ε values of substituted benzaldehydes, acetophenones, and *exo*-1:1-adducts (**7a**—**c**).

of 2:1-adduct/1:1-adduct come to small. On the other hand, electron-releasing *p*-CH_3O group lowers the reactivity of the starting carbonyl compounds, and then the reactivity of anisaldehyde and the 1:1-adduct becomes comparable to give large 2:1/1:1 ratio.

The MNDO Calculation on the Energy Levels of Carbonyl Compounds. The results of MNDO calculation[9)] supports the above assumption. As described previously,[6b)] these cycloadditions proceed through the concerted process controlled by the carbonyl ylide-HOMO and carbonyl compound-LUMO (C=O π^*). Therefore, we can conclude that the carbonyl compound of the lower C=O π^* level have higher reactivity by decreasing the values of E(C=O π^*)$-$$E$(**3**-HOMO).[6b,10)]

The C=O π^* energy levels (ε, eV) of 1,3-dipolarophiles, such as benzaldehydes, acetophenones, and *exo*-1:1-adducts (**7**), are shown in Fig. 2. The C=O π^* energy levels (ε) of benzaldehydes and acetophenones are stabilized largely by the substitution of electron-attracting *p*-NO_2 group, and are destabilized by electron-releasing *p*-CH_3O group (Fig. 2). On the other hand, the *exo*-1:1-adducts (**7a**—**c**) receive similar but much smaller substituent effect than benzaldehydes and acetophenones. When we compare the ε values of **7a**—**c** and benzaldehydes (**5a**—**c**), compounds (**7c** and **5c**) with *p*-NO_2 group have almost same ε values. However, the values for unsubstituted and *p*-CH_3O-substituted compounds are much smaller for **7** than for aldehydes. When we assume that the energy difference between carbonyl compound-LUMO (C=O π^*) and **3**-HOMO is the most effective factor on the reaction rate, *p*-nitrobenzaldehyde and *p*-NO_2-1:1-adduct (**7c**) should have comparable rate. However, the reaction of *p*-nitrobenzaldehyde with **3a** actually gave only 0.6% of expected 2:1-adduct (**8c**). This indicates that *p*-nitrobenzaldehyde is much more reactive than **7c**.

Other possible factors to affect the reactivity of **5c** and **7c** are as follows: (1) The atomic coefficient values of C=O π^* of **7c** and **5c**; (2) the extent of dipole–dipole interaction between **3a** and dipolarophiles, **7c** or **5c**;[10)] (3) steric depression on the rate of the reaction of **7c**. In this case the factors (1) and (2) seem to be less effective than (3). The CPK model inspection reveals the large crowdedness around carbonyl group of the 1:1-adduct. Therefore, the steric depression is thought to be the most effective one. In the case of unsubstituted or *p*-CH_3O-substituted compounds, *exo*-1:1-adduct have smaller ε values than aldehydes by 0.40 eV for unsubstituted and 0.37 eV for *p*-CH_3O. The reactivity of **7a** or **7b** becomes comparable to **5a** or **5b**, under consideration of deactivation on **7** according to steric effect. Hence **3a** reacts competitively with **5** or **7** to give large values of 2:1-adduct/1:1-adduct.

Substituent effect on ε values of acetophenones is quite similar to benzaldehydes. However the small reactivities of acetophenones in comparison with those of benzaldehydes are probably caused by the steric hindrance on acetophenones, which lowers the total yields of the adducts except the case of *p*-nitroacetophenone.

Experimental

All melting points were measured on a Yanagimoto Melting Piont Apparatus and recorded without correction. The IR spectra were taken on a Perkin Elmer, model 983 in KBr pellet. The ^1H NMR spectra were recorded on a Varian Spectrometer, model EM390 in a $CDCl_3$ solution using TMS as an internal standard. The ^{13}C NMR spectra were measured on a Brucker NMR spectrometer, model AM360 in $CDCl_3$.

Materials. *p*-Methoxyphenyl *o*-(diazoacetyl)benzoate (**1a**) and methyl *o*-(diazoacetyl)benzoate (**1b**) were prepared by the procedure described in the previous paper.[6b)] Benzaldehydes, acetophenones, fluorenone, and anthraquinone were purified just before use by vacuum distillation or recrystallization of the commercial reagents. Benzene was purified by distillation over lithium aluminum hydride.

General Procedure of the Reaction of 3 and Carbonyl Compounds. The Cu(acac)$_2$-catalyzed decomposition of **1** was carried out according to the method described in the previous paper[6b)]: A benzene solution of **1** was added drop by drop into a magnetically stirred benzene solution of 2 molar equivalents of carbonyl compound and catalytic amount (1/10 equivalent) of Cu(acac)$_2$ under reflux of benzene at 80°C in N$_2$ atmosphere. The reaction mixture was heated until no more N$_2$ was evolved (about one hour) and then the reaction products were separated by silica-gel column chromatography using benzene as an eluent. The reaction with acetone was carried out using large excess acetone because of its high volatility.

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7) ^{1}H NMR (CDCl$_3$) of **7a**: δ3.69 (s, OCH$_3$), 3.79 (s, OCH$_3$), 4.70 (d, Ha, J=1.3 Hz), 4.63 (d, Hb, J=1.3 Hz) and multiplet signals of aromatic protons.

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13) Details on the competitive reactions will be published elsewhere.