Solvolysis of 2,3-Cyclopenteno-4*H*-homochromen-4-ol Acetate: Comparison with the Corresponding Carbocyclic System

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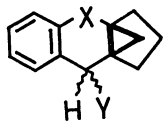
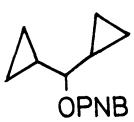
A novel secondary cyclopropylphenylmethyl acetate was prepared from a chromone skeleton *via* homochromone derivatives in order to study solvolytic behavior. Reduction of the cyclopropyl ketone (homochromone) with lithium aluminum hydride in ether to the corresponding secondary alcohol, was found to be highly stereospecific giving only one of the geometrical isomers. The alcohol was converted into its acetate and subjected to solvolysis in 80% acetone–water. The acetate was hydrolyzed at the rate of 3×10^{-5} s^{-1} (25 °C) undergoing alkyl-oxygen fission. This rate constant was as high as the most reactive secondary esters in solvolyses ever reported, and about 20 times as high as the corresponding carbocyclic ester by estimation of the same leaving group. Product studies were undertaken in the presence of sodium hydrogencarbonate, and seven-membered hemiacetal was obtained in good yield. The structural characteristics of the homochromenol ester in the solvolysis are discussed and benzohomopyrylium ion, an extremely delocalized homoaromatic species, is proposed as an intermediate carbocation.

A large number of studies have been made on solvolytic behavior in various cyclopropane derivatives since newer convenient synthetic routes for producing a cyclopropyl group have been reported. Thus, one of the attractive concepts from these studies may be homoconjugation or homoaromaticity in carbocations as the solvolytic intermediate.[1]

Here, a novel secondary cyclopropylphenyl methanol derivative (**1-OAc**) is presented, which is closely related to the corresponding carbocyclic system (**2-OPNB**).[2] The structural characteristics of these systems are: (i) the benzene ring and cyclopropane are connected to each other with both a carbon of the reaction center and an etherial oxygen (or methylene) group, and then a heterocyclic or a carbocyclic six-membered ring is formed, (ii) such a carbon skeleton enables two geometric isomers (*syn*, *anti*) between hydroxyl group and cyclopropane, and (iii) the cyclopropane ring is also fused with a trimethylene group (scissors effect).

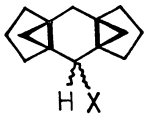


	X	Y
1-OH	O	OH
1-OAc	O	OAc
2-OH	CH_2	OH
2-OPNB	CH_2	OPNB
2-H	CH_2	H



3-OPNB

	X
4-OH	OH
4-OPNB	OPNB



	X
5-OH	OH
5-OPNB	OPNB
5-OAc	OAc

* *a* (*anti*) and *s* (*syn*) are referred between hydroxyl and cyclopropane

** -OPNB; paranitrobenzoate

In both systems, the phenyl and cyclopropyl groups are situated in the α-position to the carbon of the reactive center, where both groups can be effective for high reactivity in solvolysis.[3] It is one of the special interests in these substrates that the accelerative effects of each of these two groups seem to compete with each other in the solvolysis. Another interesting point is the difference between **1** and **2** due to the bridged oxygen or the bridged methylene.

Various carbocations may be predicted as solvolytic intermediates of **1-OAc**, and are shown in Fig. 1. From the available data in the literature, we may speculate upon the relative importance of these cations. In the case of a heterocyclic system (**1**), it is interesting that the cation (**e**) is taken for a fully-conjugated homopyrylium ion.[4]

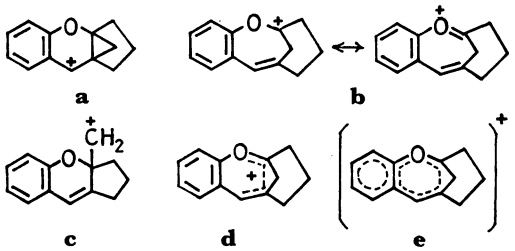


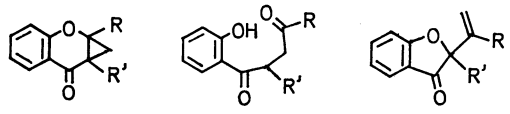
Fig. 1. Cabocations predicted as a solvolytic intermediate of **1-OAc**.

Both **1** and **2** have the cyclopropane fused with a trimethylene bridge which was suggested to be effective in contributing to the anchimeric assistance of the cyclopropane ring in solvolysis.[5] A similar effect of bridged methylene (forming a six-membered ring) in the biscyclopropylmethyl system was reported.[5,6] Regarding the first-order rate constants, the relative rate ratio of **3-OPNB** to **4s-OPNB** to **5s-OPNB** was $1:10^2:3\times10^3$, respectively. The reactivity of **1** is also interesting from another point of view, in which **1** is regarded as a 2-aryloxycyclopropyl methanol derivative. Julia *et al.* reported the isomerization of 2-alkoxy- and 2-aryloxycyclopropyl methanol into an β,γ-unsaturated carbonyl compound and an alcohol or a phenol with sulfuric acid.[7] The solvolytic study of **1-OAc** will be

referred to in the order: (1) synthetic procedure, (2) product study, and (3) kinetic results.

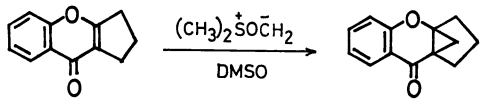
Results and Discussion

Syntheses. Preparation of the Homochromone: It was pointed out by Corey *et al.* that dimethyloxosulfonium methylide is convenient in preparing a cyclopropane ring from corresponding α,β-unsaturated ketones.[8] Chromones, regarded as unsaturated carbonyl compounds, were treated with the above reagent in dimethyl sulfoxide by Ollis *et al.* and three types of additional products were reported:[9] (**i**) 2,3-methanochroman-4-one (homochromone) derivatives, (**ii**) ketophenols obtained from further reaction (hydrolysis) of (**i**), and (**iii**) five-membered ketones including a non-conjugated double bond.



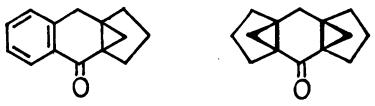
i **ii** **iii**

2,3-Cyclopentenochromone (**6**), an important precursor for producing homochromenol derivatives (**1**), was prepared according to the procedure reported by Boyd *et al.*[10] The reaction of **6** with dimethyloxosulfonium methylide gave homochromone (**7**) (type **i**) in good yield, which was purified using column chromatography on neutral alumina, but the other products (**ii** and **iii**) were not found in this experiment. Though chemical shifts of the protons belonging to the cyclopropane ring in **7** were not obvious owing to the duplication with the signals of a trimethylene group in its NMR spectrum, the wave number of maximum absorption ($\nu_{C=O}$) in the IR spectrum of **7** shifted to higher frequency (20 cm^{-1}) because of the change of the properties of the carbonyl function compared with the corresponding chromone (**6**).



6 **7**

Reduction of the Homochromone (7): Reduction of homochromone (**7**) with lithium aluminum hydride (LAH) in ether gave a secondary alcohol (**1-OH**) in *ca.* 70% yield, which was fairly unstable. Contrary to **7**, **1-OH** showed a typical AB quartet (J=6.5 Hz) due to cyclopropyl methylene protons (δ=1.15, 0.55 ppm) separated from other methylene protons (δ=2.5−1.5 ppm) in its NMR spectrum. Also **1-OH** showed a singlet at δ=4.65 ppm for α-hydrogen, while another singlet was observed at δ=4.92 ppm in the crude minor epimeric alcohol, which was obtained from the mother liquor after repeated recrystallization of the former. An attempt to obtain pure minor alcohol was not successful because of the high stereospecificity of the reduction. Moreover, facile decomposition often occurred (cleavage of the cyclopropane ring) during purification of the mixture of these epimers. Reduction of **7** with sodium borohydride (NBH) in 2-propanol was also stereospecific and gave only one isomer; the spectroscopic data agree well with those of the major product obtained by LAH reduction. The reduction of the closely related ketone (**8**) with both LAH and NBH was also stereospecific, giving only one stereoisomer.[2] It is interesting that the reaction of both **7** and **8** with LAH yielded single alcohols in contrast to **9**, which gave both epimeric alcohols in nearly equal amounts upon reduction with LAH.[5]



8 **9**

Stereochemistry of Homochromenol: It is generally accepted that α-proton *syn* to such a cyclopropane ring as in bicyclo[*m.* 1. 0]- or tricyclo[*m. n.* 1. 0]alkane-2-ol should be more shielded by the cyclopropane than the *anti* proton.[11] Also in the reduction of **7** and **8**, hydride addition with the carbonyl function should predominantly occur from less hindered *syn* to a cyclopropane ring in analogy with the reduction of the related ketone.

On the basis of these prospects, the structure of the main reduction product from **7** is assigned for the *anti* alcohol (between hydroxyl and cyclopropane) at this stage, though this assignment is tentative because of the following equivocal factors: (i) the difference between the carbocyclic and oxacyclic systems, and (ii) the existence of the benzene ring, which may play various roles affecting the magnetic properties of α-hydrogen of **7**.

Recently the stereochemistry of the reduction products from 1,3,5,7-tetramethyltricyclo[5.1.0.$0^{3,5}$]octan-2-one and its derivatives was discussed in another approach to interpreting the NMR spectrum.[12] According to Ref. 12, the reduction took place quite stereospecifically and gave only one isomer assigned to be *syn* alcohol. It is necessary to study from various viewpoints for the stereochemical problem of **1-OH**. This will be discussed by means of the NMR spectra of some substrates including a homochromenol skeleton in a forthcoming paper.

Preparation of the Ester: Attempts to prepare *p*-nitrobenzoate (**1-OPNB**) with *p*-nitrobenzoyl chloride in pyridine were unsuccessful owing to the production of a complex mixture. Then, **1-OH** was transformed into its acetate (**1-OAc**), a colorless liquid, with acetic anhydride in pyridine. The acetate was so unstable that a decomposition occurred in the course of the purification process in column chromatography over neutral alumina. The structure of the acetate was determined by spectroscopic analysis (*cf.* Experimental). This acetate was then subjected to a solvolytic study without further purification.

Product Study in Solvolysis. In the presence of sodium hydrogencarbonate as a suspension in 80% acetone–water at 25 °C for 4 days (*ca.* 10 half-lives), the major solvolysis product of **1-OAc** was a hemiacetal (**10**). Another alcohol (**11**) was contaminated with **10** though the **10**/**11** ratios were somewhat variable from the information of the NMR spectra. The structural determination of these products will now be discussed.

Structural Problem of **10**: On the basis of combustion

analysis, both **10** and **11** are structural isomers of the parent alcohol (**1-OH**). The major product showed a strong absorption at 1640 cm^{-1} in the IR spectrum, and a singlet at $\delta=5.87$ ppm (vinyl) and $\delta=3.55$ ppm (methylene) in the NMR spectrum. Two possible structures are expected from this data: (i) primary alcohol (**12**) produced by b-c bond cleavage of the cyclopropane ring, (ii) tertiary alcohol (hemiacetal) (**10**) produced by a-b bond cleavage of the cyclopropane ring. The signal at $\delta=3.55$ ppm may be assigned to the methylene proton of neopentyl group (i), and not to the allylic (bridged) methylene (ii), according to an estimation from the available data listed in Table 1.

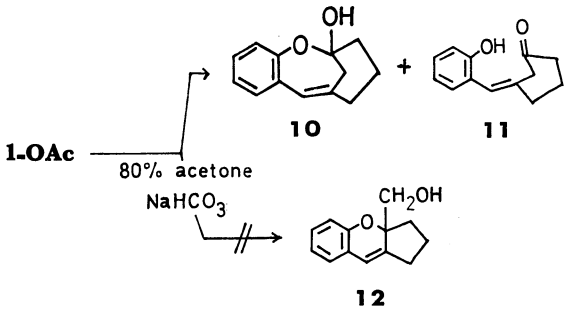
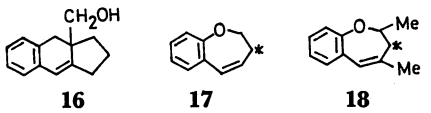


Table 1. Chemical shifts for dual type methylene signals (corresponding to **10** and **12**, respectively)

Substrate	Methylene (ppm)	Reference
>C-CH_2-O-	3.36—4.48	13[a,c]
H_3C-CH_2-OH	3.26	14[a,e]
F_3C-CH_2-OH	3.93	14[a,e]
16	3.28	2[a]
>C-CH_2-C=C<	1.86—2.12	13[b,d]
H_3C-CH_2-C=C<	2.02	14[b,e]
F_3C-CH_2-C=C<	2.69	14[b,e]
17	2.6	15[b]
18	2.43	22[b]
10	3.55	f

a) Examples for primary alcohol **12**. b) Examples for hemiacetal **10**. c) Summed for 42 substrates. d) Summed for 11 substrates. e) Calculated value by means of Shoolery's effective shielding constants. f) Observed chemical shift of the major solvolysis product obtained from **1-OAc**.



16 **17** **18**

Acetylation of the alcohol was performed with acetic anhydride in pyridine for the purpose of distinguishing between primary and tertiary alcohols. In contrast to the expectation based on the chemical shift, downfield shift of the signal at $\delta=3.55$ ppm was not observed at all, but a slight upfield shift (0.1 ppm) occurred. Thus, the alcohol was assigned preferably to be tertiary alcohol (ii) from these observations of the NMR spectra.

Europium dipivaloyl methanate, $Eu(dpm)_3$, was utilized in order to obtain further information about the structure. In general, a characteristic downfield shift is expected for methylene adjacent to a hydroxyl group if the substrate is a primary alcohol. On the other hand, such a phenomenon is not expected for tertiary alcohol (hemiacetal). The experimental results for the alcohol obtained in solvolysis are shown in Fig. 2. The extent of the induced downfield shift of both the methylene signal at $\delta=3.55$ ppm and the signals assigned as part of the trimethylene group at $\delta=1.7$—2.6 ppm may be worth noticing in comparison to those of other signals. According to the situation, the structure of this alcohol may be characterized as tertiary alcohol (**10**) rather than primary alcohol (**12**), on the basis of the result from acetylation. The major solvolysis product from **1-OAc** is concluded to be a hemiacetal (**10**). Though the chemical shift of the bridged methylene group of **10** appears at a fairly lower field value ($\delta=3.55$ ppm) than expected, this might be due to steric compression as has been mentioned for cage molecules.[16]

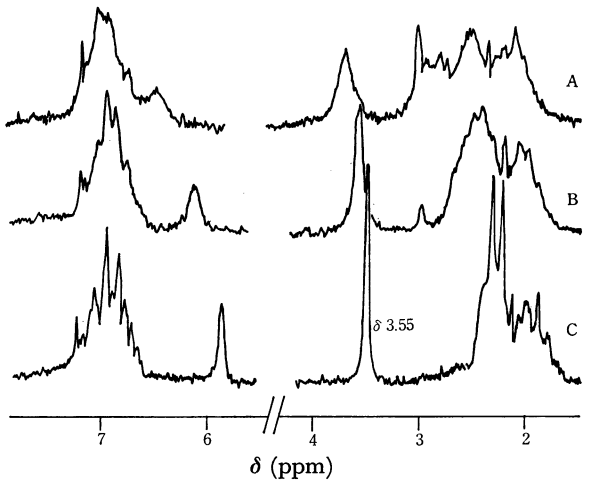


Fig. 2. The NMR spectra of **10** (spectrum C) in $CDCl_3$. After the addition of $Eu(dpm)_3$ into the solution, the spectrum B (10.0 mg) and the spectrum A (18.0 mg) were recorded. Signals for hydroxyl proton were not shown in both spectra A and B owing to enormous downfield shift.

Structural Problem of 11: Characteristics of the minor solvolysis product of **1-OAc** are: (i) positive for $FeCl_3$ in chloroform–phenolic material, (ii) typical IR and UV absorption bands for the aliphatic carbonyl group at 1720 cm^{-1}, and 315 nm ($\varepsilon=350$), respectively, and (iii) the presence of an allylic methylene group adjacent to a carbonyl function ($\delta=3.05$ ppm) based on the NMR spectra. From speculation based on these data, ketophenol (**11**) might be proposed as the structure of this material. Hemiacetal (**10**) was transformed into **11** in the presence of **11** in the medium, *e.g.*, in $CDCl_3$ prepared for the measurement of a NMR spectrum. It is probably due to the phenolic function of **11**. On the basis of this phenomenon, the uncertainty of the ratio **10/11** in the solvolysis may be explained satisfactorily.

When the NMR spectrum of **10** in trifluoroacetic acid (TFA) was observed at room temperature, a mixture of **10** and **11** was produced and the former was predominant under the condition. Similarly when the

spectrum of **11** was recorded in TFA, the same mixture as above was evidently produced. In both cases, the mixture could be isolated in good yield by quenching the solution. It is interesting that **10** and **11** are converted into each other in TFA. Such a mutual exchange suggests the validity of each structure, since **10** is an intramolecular hemiacetal of a ketophenol (**11**). It was, moreover, found that homochromenol (**1-OH**) was clearly converted into a mixture analogous to the above in TFA at room temperature. Isolation of the mixture was similarly achieved, thus

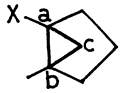
Parent alcohol $\xrightarrow{\text{in TFA}}$ Hemiacetal $\underset{\text{in TFA}}{\overset{\text{in TFA or 11}}{\rightleftharpoons}}$ Ketophenol

(**1-OH**) (**10**) (**11**)

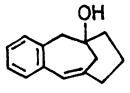
Solvolysis in Another Condition: The hemiacetal (**10**) was also obtained in solvolysis of **1-OAc** in the presence of either pyridine or 2,6-lutidine instead of in the presence of sodium hydrogencarbonate as described above. However, a complex mixture was obtained if any acid was used in order to remove the alkali during a work-up process. It is suggested that the hemiacetal (**10**) may be highly sensitive to acidic substances.

In the absence of any alkali, solvolysis of **1-OAc** gives a yellowish oil whose NMR spectrum suggested the production of complex mixtures, and **10** was not observed at all. Thus, the presence of an alkali is obviously essential to the production of **10** in such reaction conditions.

A Comparison of the Solvolysis Products of 1-OAc with Those from the Corresponding Carbocyclic Ester: According to the product study of a closely related ester (**2-OPNB**), the mixture of **2a-OH**, **2s-OH** and a tertiary alcohol (**13**) was obtained in the ratio of 1.0: 3.3: 3.5 in 80% acetone–water at 25 °C in the presence of the alkali.[2] This is somewhat different from the result for **1-OAc**. A parent alcohol (**2a-OH**) was isomerized into the thermodynamically more stable isomer **13** in the presence of *p*-nitrobenzoic acid, but both parent alcohols (**2a-OH**) and (**2s-OH**) were stable in the presence of the alkali under solvolytic conditions. The alcohol (**13**) is produced in a mode similar to the cleavage of the cyclopropane ring (a-b cleavage), as in the case of hemiacetal (**10**). It is noteworthy that considerably strained bridgehead alcohols, **10** and **13**, were thermodynamically the most stable products in both cases, although a partial ketonization sometimes occurred for **10**. Together with the kinetic results discussed later, these facts might support possible intervention of the homoallylically conjugated or homoaromatically conjugated carbocation in these solvolyses.



Modes of the cleavage of cyclopropane



13

Alkyl-oxygen Fission of Homochromenol Acetate (1-OAc) during Solvolysis: The parent alcohol (**1-OH**) was found to be stable in the presence of sodium hydrogencarbonate under the solvolytic condition. So alkyl-oxygen fission may occur during the solvolysis of **1-OAc** based on the fact that rearranged alcohols **10** and **11** were isolated as solvolysis products of **1-OAc**.

The mode of fission may be confirmed by means of solvolysis in anhydrous methanol (methanolysis). If the solvolysis of **1-OAc** proceeds with an acyl-oxygen fission, the products should be alcohol(s) and methyl acetate. But methyl ether and acetic acid should be obtained in the case of an alkyl-oxygen fission. The reaction scheme is as follows:

$$\mathrm{RO{-}\overset{\overset{\mathrm{O}}{\|}}{C}CH_3} \xrightarrow{\text{SO-H}} \mathrm{RO{-}H} + \mathrm{SO{-}\overset{\overset{\mathrm{O}}{\|}}{C}CH_3}$$

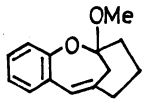
acyl-oxygen fission

$$\mathrm{R{-}O\overset{\overset{\mathrm{O}}{\|}}{C}CH_3} \xrightarrow{\text{SO-H}} \mathrm{R{-}OS} + \mathrm{H{-}O\overset{\overset{\mathrm{O}}{\|}}{C}CH_3}$$

alkyl-oxygen fission

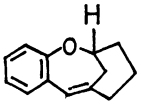
SO- = MeO-, HO-

Methanolysis of **1-OAc** was carried out in the presence of pyridine at 25 °C for 4 days, the methyl ether (**14**) of **10** was obtained as the sole product, and the ether was determined from its spectra. Thus, alkyl-oxygen fission of **1-OAc** during solvolysis may be more plausible.

1-OAc $\xrightarrow{\text{methanol}}$ 

14

Trapping a Reactive Carbocation with a Hydride Reagent: A high solvolytic reactivity of appropriate esters provides an effective route to the parent (or isomerized) hydrocarbon, which is called *trapping* an intermediate carbocation.[17] The acetate (**1-OAc**), could be converted to a seven-membered unsaturated ether (**15**), as the sole product in 50% aqueous diglyme containing excess NBH. From these product studies in various reactions for **1-OAc** it has been shown that a nucleophile attacks specifically at the bridgehead carbon adjacent to etherial oxygen in the intermediate cation. This is contrary to the fact that the *p*-nitrobenzoate (**2-OPNB**) was converted to a mixture of isomeric alcohols (**2a-OH**, **2s-OH** and **13**) upon solvolysis or to the *parent* hydrocarbon (**2-H**) by the hydride reagent. The difference between the products from the two systems (**1-OAc** and **2-OPNB**) may correspond to the properties of the intermediate carbocation in the reactions, although the leaving groups are different.

1-OAc $\xrightarrow[\text{50\% diglyme}]{\text{NaBH}_4}$ 

15

Kinetic Study of the Solvolysis. The rates of the solvolysis of **1-OAc** were determined in 80% acetone–water solution at 25—40 °C by tracing the increment of the acetic acid produced with 18 aliquots at regular intervals. Each aliquot was quenched by acetone, followed by means of the usual alkaline titration using bromothymol blue as an indicator. All runs showed

Table 2. Solvolysis rates of **1-OAc** and **2-OPNB** in 80% acetone–water[a]

Substrate	Temperature[b] °C	k s^{-1}	$\Delta H^{\neq}$ kcal/mol	$\Delta S^{\neq}$ e.u.	Relative rate[c]	Reference
1-OAc	25	$3.2_4\times10^{-5}$	21.2	−5.8	1.0	This work
	35	$9.5_1\times10^{-5}$				
	40	$1.9_0\times10^{-4}$				
2a-OPNB	25	$8.6_0\times10^{-5}$	20.6	−8.0	0.052	2
2s-OPNB	25	$1.7_3\times10^{-4}$			0.10	2

a) The rate constants (k) are first-order, and the mean values obtained from several runs are shown. b) Accuracy was ±0.03 °C. c) Estimation was based on available data in Ref. 5 as the same leaving group.

Table 3. Relative rates of solvolysis for related secondary esters on the basis of **1-OAc**

Substrate	 **4-sOPNB**	 **5-OAc**	 **19-OAc**	 **20-OPNB**	 **21-OPNB**	 **22-OPNB**
Relative rate[a]	0.15	a : 2.4 s : 4.6	0.39	6.1	$\times10^{-4}$	$\times10^{-8}$
Solvolysis product	b	b	c	d	b	b
References	5, 6	5	19	20	18	18

a) Calculated as the same leaving group, solvent (80% acetone–water), and temperature (25 °C, or 30 °C if necessary). b) Parent alcohol (in aqueous acetone). c) Anthracene. d) Tetralin.

strictly first-order kinetics up to almost two half-lives (Fig. 3.), despite the fact that the purification of **1-OAc** was difficult. The observed kinetic data are shown in Table 2, and the relative rates of solvolysis for related systems in Table 3.

Thus, **1-OAc** was solvolyzed accompanying alkyl-oxygen fission in 80% acetone–water at the rate of $3.2_4\times10^{-5}$ s^{-1} (25 °C), which is as high as those of the most reactive secondary esters (**5a-OAc**, **5s-OAc**, **19-OAc**, and **20-OPNB**) that have ever been measured in solvolysis.[5,19,20] The acetate (**1-OAc**) was about 20 times as reactive as the corresponding carbocyclic system (**2a-OPNB**), by estimation of the same leaving group as shown in Table 2, and was solvolyzed *ca.* 10^4 times faster than the secondary cyclopropylphenylmethyl

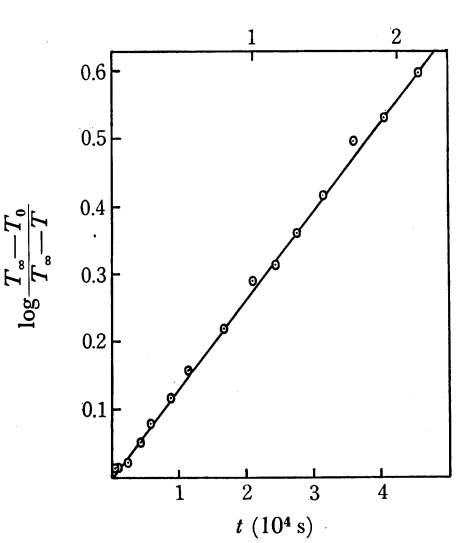


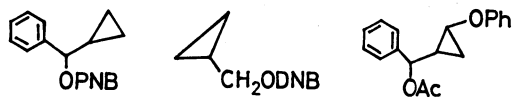
Fig. 3. Plots of the first-order function *vs.* reaction time (or half-lives) for **1-OAc** at 25 °C in 80% acetone–water.

p-nitrobenzoate (**21-OPNB**).[18] In the following discussion, **21-OPNB** may be chosen as the standard substrate.

Since the benzene ring and the cyclopropane are connected to each other by the bridged oxygen in **1-OAc**, dual types of contributions may be expected for such a high reactivity due to the etherial oxygen: (i) the effect of an *ortho*-alkoxy group on the benzene ring, and (ii) a contribution as β-phenoxy substitution of the cyclopropane. Now the role of the bridged oxygen in the solvolysis will be discussed from such viewpoints.

Substituent Effect of the Benzene Ring: According to the study of Shono *et al.* for the *para* substituent effect of the benzene ring (–OMe, –Me, –H, and –Cl) on **21-OPNB**, the *para*-methoxy ester was 780 times more reactive than the corresponding parent ester (**21-OPNB**): $\rho=-3.61$ *vs.* σ^+.[18] From these results, an *ortho*-alkoxy substitution in the benzene ring seems to be one of the important factors for the high reactivity of **1-OAc**, though the accelerative effect of the *ortho*-alkoxy group may be usually smaller than that of the *para*-alkoxy group according to available data.[21]

Effects of Substitution on the Cyclopropane: Rate enhancement due to the substitution was reported for *primary* cyclopropylmethyl 3,5-dinitrobenzoate (**23-ODNB**) such that every methyl substitution at the β-position increased the rate about 10 times that of the corresponding ester, and the substitution of a *trans* β-ethoxy group caused a great acceleration (nearly 10^3 times).[23] But the substituent effect of the cyclopropane ring for **21-OPNB** has not been reported to date. Therefore, *trans* 2-phenoxycyclopropylphenylmethyl acetate (**24-OAc**) was adopted as an acyclic model system corresponding to its cyclic acetate (**1-OAc**). If a clear rate enhancement in comparison with **21-OPNB** should be observed, the β-aryloxy substitution may be an important cause of the high reactivity of **1-OAc**.

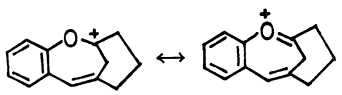


21-OPNB **23-ODNB** **24-OAc**

* -ODNB; 3,5-dinitrobenzoate

In our preliminary experiments, **24-OAc** was not hydrolyzed appreciably under similar solvolytic conditions for **1-OAc.**[22] The effect of the β-aryloxy substitution, therefore, should be explained by means of another contribution, probably due to a *cis* substitution which constitutes a six-membered heterocycle, **1-OAc**. Since it has been pointed out that both the phenyl group and the cyclopropyl group are effective in increasing the reactivity in **21-OPNB,**[18] these are perturbations of such relatively highly reactive systems. The ester (**1-OAc**) involves many complex factors which cause difficulty in determining the origins of the increase in reactivity compared with the standard substrate (**21-OPNB**). Consequently, it appears risky to interpret the observed kinetic data on the basis of the simple additional summation of the effects of *ortho*-alkoxy group of the benzene ring and of the substitution of the cyclopropane in such a sophisticated system as **1-OAc**. The structural characteristics of **1-OAc** may play an important role in solvolysis, since a homochromenol ester is, in general, suitable for creating high reactivity.

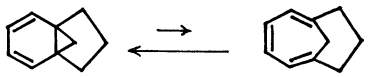
Intermediate Carbocation in the Solvolysis. As shown in the product studies of **1-OAc**, each nucleophile attacks at the carbon adjacent to the etherial oxygen quite specifically in spite of different reaction conditions. According to these product studies, the cation (**b**) appears at first sight to be suitable as a solvolytic intermediate of **1-OAc**.



b

The difficulty in the production of the bridgehead cation is well known, in general. Owing to the assistance of the oxygen adjacent to the carbon of the cationic center, the bridgehead cation (**b**) might be an exception to the above general rule though such a phenomenon has not yet been reported.

Otherwise, the presence of the double bond on the opposite bridge ead carbon diminishes the possibility of **b**. Recently, the relative stability between the norcaradiene form (**f**) and the cycloheptatriene form (**g**) using the NMR spectra was discussed by Vogel *et al.*[24] According to their report, the former (**f**) is much more stable than the latter (**g**) in case of the presence of a trimethylene group. The cation (**b**) is *isoelectronic* to the cycloheptatriene form (**g**), so that **b** may be invalid as a solvolytic intermediate for **1-OAc**.



f **g**

Norcaradiene form Cycloheptatriene form

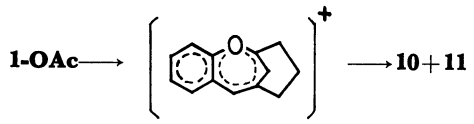
Aromatization sometimes occurs in the solvolysis of highly reactive systems, as shown in Table 3, where the intermediate carbocation may be somewhat stabilized by means of its aromaticity, *e.g.*,

19-OAc ⟶ anthracene[19]

and

20-OPNB ⟶ tetralin[20]

From these prospects, the benzohomopyrylium ion (**e**) might be proposed as the cationic intermediate in the solvolysis of **1-OAc**, and the formation of such extremely delocalized homoaromatic species might greatly contribute to decreasing the activation energy for solvolysis.[1]



e

Benzohomopyrylium ion

Experimental

General. All melting points are uncorrected. The IR spectra were measured using a Hitachi 215 spectrometer, the UV spectra on a Yanaco spectrometer, the mass spectra on a Hitachi RMS-4 spectrometer, and the NMR spectra on a Hitachi R-20 spectrometer. The chemical shifts of the NMR spectra are given in δ, with tetramethylsilane as an internal standard.

Materials. The preparation of 2,3-cyclopentenochromone (**6**) was carried out according to the procedure reported by Boyd *et al.*[10] Mp 127—128 °C (lit,[10] 122—123 °C) (60% yield, colorless prisms, from cyclohexane).

2,3-Cyclopentenohomochromone (2,3-trimethylene-2,3-methanochroman-4-one) (7): To mineral oil-free sodium hydride (NaH), prepared from commercial NaH (3.4 g, 0.071 mol; mineral oil dispersion) by means of triple decantation with light petroleum, was added trimethyloxosulfonium iodide[8] (12.1 g, 0.055 mol) in one portion followed by the addition of anhydrous dimethyl sulfoxide (DMSO) (50 ml) with stirring over a period of 20 min, at first carefully at 20 °C. After the cessation of the violent evolution of hydrogen, the milky-white solution was kept in a nitrogen atmosphere. To the dimethyloxosulfonium methylide produced in DMSO, was added a saturated solution of **6** (9.3 g, 0.05 mol) in DMSO (100 ml) with stirring over a period of 40 min at a temperature of 17—20 °C. The solution turned to grayish green, and then to reddish violet. The mixture was then allowed to stand at room temperature for 2.5 h under nitrogen, warmed to 40° C, maintained for 5 min then cooled in an ice-bath, and anhydrous ether (100 ml) was then added to the solution. The mixture was poured into ice-water, separated, and the aqueous layer was extracted thoroughly with ether. The combined extract was satisfactorily washed with water, and dried on anhydrous sodium sulfate. During the work-up process, separation was sometimes difficult probably due to the poor solubility of unreacted **6**, when the reaction was not complete. The ether was evaporated *in vacuo*, and a yellowish viscous syrup (7.6 g) was obtained, chromatographed on neutral alumina (30 g, activity III, short column) using petroleum ether (boiling range below 40 °C) as an eluent, and the solvent was removed *in vacuo* to give a colorless syrup (7.4 g), which crystallized slowly in a refrigerator. Mp 60—61 °C (6.9 g, 70% yield, colorless prisms, from petroleum ether). IR

(Nujol): 1660, 1610, 1235, 1065 cm^{-1}. NMR (CCl_4): 7.9—6.7 (4H, m, aromatic), 2.6—1.3 (8H, m, trimethylene and cyclopropane). Found: C, 78.15; H, 6.04%. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%.

*2,3-Cyclopenteno-4H-homochromen-4-ol (Homochromenol) (**1-OH**)*: *(a) Reduction of **7** with $LiAlH_4$ in ether.* A solution of **7** (2.00 g) in ether (30 ml) was added portionwise to the well-stirred suspension of lithium aluminum hydride (0.40 g, excess) in ether (10 ml) with ice-cooling. Then the mixture was allowed to sit at room temperature, stirred overnight, and quenched by adding 5 ml of water carefully over 30 min with ice-cooling. The resulting clear solution was decanted and the residue was washed twice with ether. The combined organic solutions were dried over anhydrous potassium carbonate, evaporated *in vacuo* without externel heating to give a colorless oil (2.00 g, quantitative yield), which crystallized in a refrigerator. This material was recrystallized from petroleum ether to yield pure **1-OH** (1.15 g, 57% yield), mp 101—102 °C. IR (nujol): 3350, 1605, 1230, 1070 cm^{-1}. NMR (CCl_4): 7.6—6.5 (4H, m, aromatic), 4.65 (1H, s, α-proton, 2.5—1.5 (7H, m. trimethylene and hydroxyl), 1.15, 0.55 (2H, AB quartet, J=6.5 Hz, cyclopropane). Found: C, 76.95; H, 7.10%. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%.

*(b) Reduction of **7** with $NaBH_4$ in aqueous 2-propanol.* A solution of sodium borohydride (90 mg) in 2-propanol–water (60 ml; 2: 1, by volume) was added to a stirred solution of **7** (1.00 g, 5 mmol) in 2-propanol (40 ml). After being stirred for 2 days at room temperature, 2-propanol was evaporated slowly *in vacuo* without heating and the residue was extracted twice with ether (20 ml). The extracts were combined, washed with water, and dried over anhydrous potassium carbonate. The extract was condensed *in vacuo* to give a colorless oil, whose spectroscopic data agreed well with those of **1-OH** prepared by the above procedure. Pure material (mp 98—100 °C) (0.40 g, 40% yield) was obtained by recrystallization from cyclohexane.

*2,3-Cyclopenteno-4H-homochromen-4-ol Acetate (Homochromenol Acetate) (**1-OAc**)*: To a magnetically-stirred solution of **1-OH** (0.30 g) in pyridine (8 ml), was added a solution of acetic anhydride (0.3 ml) in pyridine (2 ml) over a period of 5 min in an ice–salt bath. After being stirred overnight at room temperature, dry ether (20 ml) was added to the solution, and the mixture was worked up by pouring into ice–water (300 ml). The organic layer was separated, and the aqueous layer was extracted twice with ether (50 ml). The extract was combined, washed with cold water, with ice-cold dilute hydrochloric acid, with water, with 5% sodium hydrogencarbonate and finally with water, and then dried over anhydrous sodium sulfate. The extract was concentrated *in vacuo* without heating to give a colorless oil (0.33 g, 85%). IR (neat): 1730, 1580, 1235, 745 cm^{-1}. MS: (*m/e*) 244 (M^+). NMR (CCl_4): 7.3—6.7 (4H, m, aromatic), 6.05 (1H, s, α-proton), 2.10(3H, s, acetoxy), 2.4—1.2(6H, m, trimethylene), 1.15, 0.75 (2H, AB quartet, J=6.5 Hz, cyclopropane).

For the purpose of purification, the oil was chromatographed on a neutral alumina column. Elution with benzene–petroleum ether (1: 1) produced decomposed substances. When heated for 30 min at 130 °C in a neat condition in a capillary, the oil decomposed.

*Product Studies. Homochromenol Acetate (**1-OAc**) in 80% Acetone–Water*: A solution of the acetate (750 mg) in 80% acetone–water (250 ml) containing sodium hydrogencarbonate (250 mg) was allowed to sit at 25 °C (in a thermostatic bath) for 4 days (*ca.* 12 half-lives). Most of the acetone was evaporated *in vacuo* without heating, and the remaining suspension was extracted with three 50-ml portions of ether. The ether extract was washed with water. After drying over anhydrous sodium sulfate, the ether was removed and the residual partially-crystallized material (602.4 mg, 97% yield) was recrystallyzed from cyclohexane to give pure **10** (310.0 mg, 50% yield). Mp 126—128 °C. IR (Nujol): 3140, 1640, 1270, 1250, 755 cm^{-1}. MS (*m/e*): 202 (M^+). UV λ_{max} (ε) (ethanol): 235 (14000), 277 (2900) nm. NMR ($CDCl_3$): 7.4—6.7 (4H, m, aromatic), 5.87 (1H, s, vinyl), 3.55 (2H, s, allylic bridged methylene), 2.7—1.7 (7H, m, trimethylene and hydroxyl) *cf.* Fig. 2. Found: C, 77.39; H, 6.88%. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Acetylation of **10** in a similar manner as described above (from **1-OH** to **1-OAc**) was accomplished to give a colorless oil. IR ($CHCl_3$): 2960, 1770, 1750, 1660 cm^{-1}. NMR ($CDCl_3$): 7.4—6.9 (4H, m, aromatic), 5.87 (1H, s, vinyl), 3.45 (2H, s, allylic bridged methylene), 2.23 (s, acetoxy), 2.6—1.7 (m, others). The above crude product from **1-OAc** in such a solvolytic condition was dissolved in $CDCl_3$, and the NMR measurement was carried out immediately, at which time **10** was found to be almost the sole product, though small amounts of **11** and traces of unidentified materials were present.

When the solvolysis of **1-OAc** was carried out in 80% acetone–water in the presence of pyridine or 2,6-lutidine (a slightly excess amount of the ester), **10** was obtained as a major product. But using any acidic material for removing the alkali during the work-up process, a complex mixture was obtained as a solvolysis product and **10** was not found at all. Similarly, solvolysis of **1-OAc** in 80% acetone–water in the absence of alkali gave a complex mixture. Particular attention should be paid to the treatment of hemiacetal (**10**), since it is highly sensitive to acidic materials.

In addition, parent alcohol (**1-OH**) was stable under the solvolytic condition (in 80% acetone–water at 25 °C for 4 days in the presence of sodium hydrogencarbonate).

*Methanolysis of **1-OAc***: The ester (**1-OAc**) (100 mg) was dissolved in absolute methanol (100 ml) containing pyridine (0.5 ml), and the mixture was allowed to sit at 25 °C for 4 days. After removing the methanol *in vacuo* without heating, CCl_4 (40 ml) was added to the residue and the solvent was removed azeotropically. The residue was dissolved in CCl_4, filtered, and the filtrate was analyzed by NMR spectroscopy. The solvent was removed, ether (50 ml) was added to the residue, the mixture was poured into ice-cold 1M-HCl (70 ml), extracted twice with ether (50 ml), washed with water (50 ml), with 5% sodium hydrogencarbonate (50 ml), and finally with water (50 ml), and then dried over anhydrous sodium sulfate. The colorless oil (96.3 mg) obtained by evaporation of the extract was difficult to crystallize, and produced the same NMR spectrum as the pre-measured NMR spectra made during the work-up process. IR (CCl_4); 3380, 2940, 1480, 1240, 1110, 1050 cm^{-1}. MS (*m/e*): 216 (M^+). NMR (CCl_4); 7.3—6.65 (4H, m, aromatic), 6.08 (1H, s, vinyl), 3.12 (3H, s, methoxy; *cf.* 3.37 for MeO–H), 2.5—1.15 (*ca.* 8H, m, others).

Trapping a Reactive Carbocation with Hydride Reagent: A solution of sodium borohydride (2.0 g) in 50% aqueous diglyme (30 ml) including sodium hydroxide (80 mg) was added to the homochromenol ester (**1-OAc**) (183.2 mg). After being stirred overnight at room temperature, *n*-pentane (50 ml) and water (50 ml) were added to the reaction mixture, separated, and the aqueous layer was extracted twice with *n*-pentane (30 ml). The combined organic layers were washed with water (30 ml), and dried over anhydrous sodium sulfate. The colorless oil (250.4 mg) obtained by evaporation of the extract *in vacuo*, included the remaining diglyme. After distillation, **15** was obtained; bp *ca.* 130 °C/2 mmHg (bath temp) (40 mg). No isomerization (or decomposition) occurred during the distillation as verified by IR, NMR, and GC data. IR (neat): 2900, 1470, 1440, 1180, 1110 cm^{-1}. MS (*m/e*): 186 (M^+). UV (ethanol) λ_{max} 254.5 nm. NMR (CCl_4): 7.4—6.5 (4H,

m, aromatic), 6.10 (1H, s, vinyl), 5.03 (1H, m, bridgehead methine), 3.0—1.7 (8H, m, others).

Kinetic Studies. The rates of solvolysis of homochromenol acetate (**1-OAc**) in 80% acetone–water were determined using solutions in about 0.004 mol concentration and titrating the liberated acetic acid with 0.01 M NaOH in methanol to a bromothymol blue end-point. The base was frequently restandardized against oxalic acid during the course of the work.

Solutions of the acetate in 80% acetone–water (by volume) were prepared in the following manner. The weighed **1-OAc** was dissolved in anhydrous acetone (40 ml). Then, a 75% acetone–water (by volume, 160 ml) solution was prepared, and both solutions were set in a thermostatic bath and maintained at 25 °C (±0.03 °C). About 10 min later, the latter solution poured into the former, and the mixture (**1-OAc** in 80% acetone–water) was well shaken, then dipped in the thermostatic bath. The first aliquot (10 ml) was pipetted after 5—10 min and taken as the zero point. Periodically, each aliquot was taken, quenched by anhydrous acetone (20 ml) and then subjected to titration. Infinity titrations were determined after 10 or more half-lives, and in those cases the liberated acetic acid reached 95—98% of the theoretical amount. Rate constants were calculated to the first-order, and mean values from several runs are shown in Table 2. Typical first-order plots are shown in Fig. 3.

Isomerization of the Parent Alcohol and Interconversion between Hemiacetal and Ketophenol in Trifluoroacetic Acid. A wine red solution of the parent alcohol (**1-OH**) (0.20 g) in trifluoroacetic acid (TFA) (1 ml) was analyzed by NMR spectroscopy. NMR (TFA) 7.5—6.7 (>4H, m, aromatic), 6.0 (<1H, s, vinyl), 3.72, 3.10 (2H, s, s, allylic methylene), 3.1—1.8 (7H, m, others). The ratio **10/11** in TFA was *ca.* 3: 1 in comparison with the characteristic signals of the NMR spectra. The ratio was variable though **10** always predominates in TFA at room temperature even after 3 days. The solution was poured into an ice-cold aqueous sodium hydrogencarbonate solution, extracted three times with ether, next the combined organic layer was washed with cold aqueous sodium hydrogencarbonate and with water, and then dried over anhydrous potassium carbonate. A pale yellow syrup (181.3 mg, 90%) obtained by evaporation of the ether, was pumping *in vacuo* to give **11** (mp 76—78 °C) as the sole product of the NMR spectrum in $CDCl_3$, which was dissolved in benzene and passed through a short column of alumina (activity III). Concentration of the filtrate produced pure **11**, mp 78—80 °C, IR (Nujol): 2950, 1720, 1580, 1240, 750 cm^{-1}. MS (*m/e*): 202 (M^+). UV λ_{max} (ε) (ethanol): 279 (2900), 315 (350) nm. NMR ($CDCl_3$): 7.5—6.6 (5H, m, aromatic and vinyl), 3.05 (2H, s, allylic methylene), 3.0—1.7 (7H, m, trimethylene and hydroxyl). Positive for the $FeCl_3$ test in $CDCl_3$. Found: C, 76.78; H, 6.86%. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%.

When dry ether was added to the above TFA solution before the work-up process, a mixture of **10** and **11** was isolated after similar treatment, and the former was found to be predominant (*ca.* 2: 1) in the NMR spectra in $CDCl_3$. Heating the contents of the $CDCl_3$ solution at 50 °C for 30 min, **11** was obtained as the sole product.

When **11** (40 mg) was dissolved in TFA (0.3 ml) the ratio of **10/11** was *ca.* 9: 4 from the NMR spectrum. NMR (TFA): 7.5, 6.7 (>4H, m, aromatic), 6.02 (<1H, s, vinyl), 3.76, 3.14 (2H, s, s, methylene), 3.0—1.8 (*ca.* 7H, m, others). Ether was added to the solution, then the mixture was treated in the same manner as described above. The yellowish oil (35.8 mg, 90%) obtained was dissolved in $CDCl_3$ for measuring both the IR and NMR spectra. The IR spectrum of this oil was found to be consist of duplicates of **10** and **11**, and the former was at first predominant depending on the relative intensity of each characteristic absorption band (especially 1640 cm^{-1} for **10**, and 1720 cm^{-1} for **11**). However, after several hours the relative intensities were clearly reversed, and the information from NMR spectroscopy agreed well with these results. Similarly, a mixture of **10** and **11** was obtained from **10** in TFA. According to the NMR study, the ratios of **10/11** derivated from **1-OH**, **10**, or **11** in TFA appear to depend on the temperature.

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