The Difference in Solvolytic Reactivity between Diastereomers in α-(*trans*-2-Arylcyclopropyl)arylmethyl 3,5-Dinitrobenzoates

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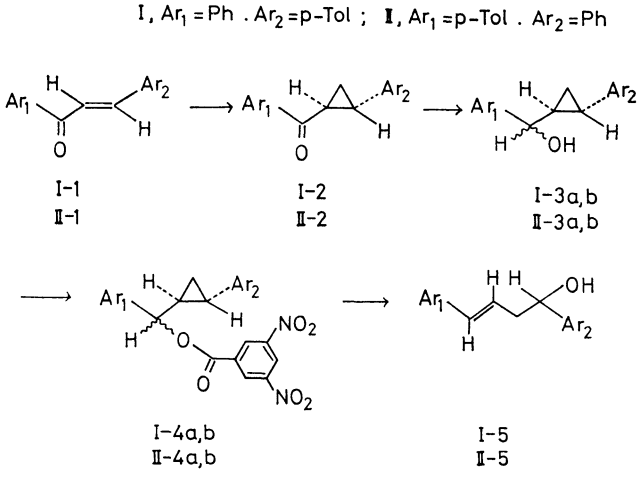
Each diastereoisomeric pair of α-(*trans*-2-*p*-tolylcyclopropyl)benzyl and α-(*trans*-2-phenylcyclopropyl)-*p*-tolylmethyl 3,5-dinitrobenzoates (**I-4a, b, II-4a, b**) has been synthesized. The relative solvolytic rates of **I-4b** to **I-4a** and of **II-4b** to **II-4a** in 80% aqueous acetone have been found to be 3.59 and 1.86 respectively at 25 °C. In the presence of 2,6-lutidine, the major products in the solvolysis were homoallylic alcohols.

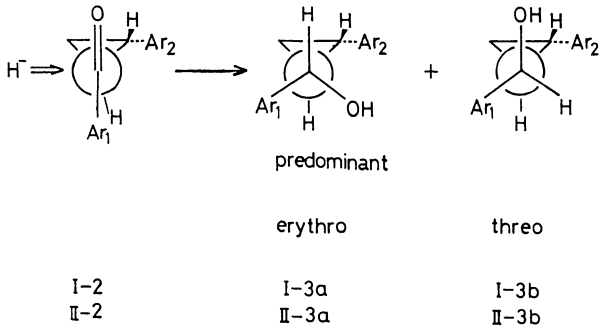
Although there have been many stereochemical studies in the rate comparisons of rigid cyclic compounds in the solvolysis of cyclopropylmethyl systems,[1-3] no investigations of the difference in reactivity between a diastereoisomeric pair of such systems in which a cyclopropyl group can freely rotate have been reported. One of the reasons for this may be the experimental difficulty in the separation of such diastereomers. It may be of importance, however, to study the conformational situation of a participating cyclopropyl group at the transition state when the free rotation of the group is permitted in the substrate molecule.[4] In connection with our previous researches,[5] we wish now to report such a reactivity difference between diastereoisomers of certain arylcyclopropylmethyl systems.

Each isomer of the titled esters (**I-4a, b** and **II-4a, b**) has been synthesized and successfully isolated by Scheme 1, shown below. The physical properties and spectral and analytical data are summarized in Table 1.



Scheme 1.

The parent alcohols (**I-3a, b** and **II-3a, b**) were mixtures of diastereoisomers, in which one of the diastereoisomers was preferentially produced in the hydride reduction of the ketones (**I-2, II-2**). The chemical shift of the carbinyl proton (a doublet) in the predominant alcohols (**I-3a** and **II-3a**) was slightly higher than that of the other (**I-3b** and **II-3b**). The hydride attack on the carbonyl group generally takes place from the less hindered side of the favorable conformer of the ketones, as is shown in Scheme 2. This reduction results in the preferential formation of



Scheme 2.

the erythro isomer (**I-3a, II-3a**) according to the above scheme. This interpretation accords with the previous result suggested for a similar system by Descotes *et al.*[6] and is consistent with Cram-Prelog rule.[7] If it is assumed that the two most bulky aromatic groups are situated in a *trans* relation in the stable, staggered conformation of the alcohol molecule, the carbinyl proton of *erythro*-isomer (**I-3a** and **II-3a**) may be more highly shielded by the effect of a cyclopropane ring.[8] Thus, the two diastereoisomers in a pair could be distinguished.

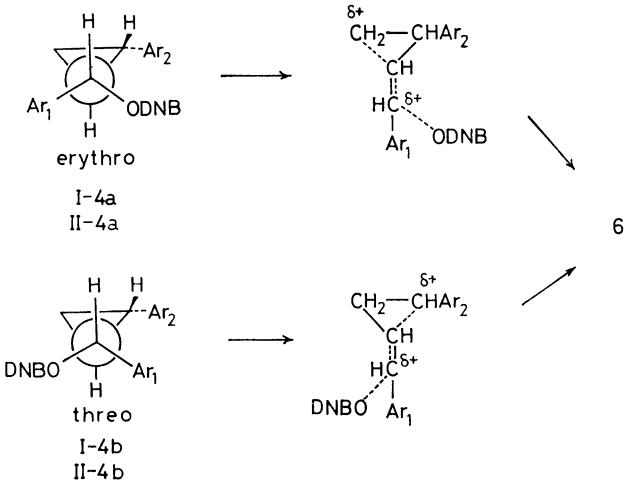
The diastereomerically mixed alcohols were converted into 3,5-dinitrobenzoates (**I-4a, b** and **II-4a, b**) by a usual procedure. Separation was made by the fractional recrystallization of the 3,5-dinitrobenzoates. As may be seen from Table 2, all these 3,5-dinitrobenzoates were solvolyzed smoothly in accordance with first-order kinetics. Thus, it was found that the *threo* isomer (**I-4b** or **II-4b**) was more reactive than the *erythro* isomer (**I-4a** or **II-4a**) in the solvolysis of both pairs in 80% aqueous acetone. The order of the difference in reactivity (3.59—1.86) is comparable with that for some rigid polycyclic systems.[3a,d]

When the reaction was interrupted during the course of solvolysis, each starting 3,5-dinitrobenzoate could be recovered in a good yield and neither the homoallylic nor the diastereomeric isomer of the reactant was detected for either series. Thus, it was experimentally confirmed that there was no interconversion between homoallylic and cyclopropylmethyl systems, or between the *erythro* and *threo* isomers, in the present solvolysis.

A product study was carried out in the presence of 2,6-lutidine under solvolytic conditions, since it was preliminarily found that the parent alcohols (**I-3a, b** and **II-3a, b**) and homoallylic alcohols (**I-5, II-5**) were stable under these conditions. The major solvolysis

products after 30 half-lives were homoallylic alcohols, as is shown in Table 3. These alcohols should be produced directly from the 3,5-dinitrobenzoates (**I-4a, b** and **II-4a, b**) under those reaction conditions, since rearranged homoallylic 3,5-dinitrobenzoates could not be solvolyzed under similar conditions.

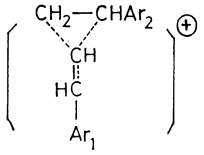
Starting from the diastereomerically different 3,5-dinitrobenzoates, the same *trans*-homoallylic alcohol was obtained as the sole product, so that it is reasonable to assume the intervention of the common carbocation in the reactions for both diastereomers. In contrast with this finding, a considerable rate difference has been found between *erythro* and *threo* isomers in kinetic studies of the two systems (I and II). Also, the rates are accelerated by the order of 10^4 in comparison with simple secondary arylmethyl systems. This may be attributed to participation by the α-substituted 2-arylcyclopropyl group. In order to attain a transition state which leads to a common carbocation in the present solvolysis, the C_1–C_2 bond of a cyclopropyl group is inevitably antiparallel to the leaving 3,5-dinitrobenzoate group in the *threo* isomers. Then, the aryl group on C_2 of a cyclopropyl group could accommodate the partial positive charge developed at the transition state. In the case of the *erythro* isomers, such



Scheme 3.

concomitant participation from the most stable conformer may result in the formation of a different transition state in which the C_1–C_3 bond is antiparallel to the leaving group. Both transition states are illustrated in Scheme 3. These situations might cause the above rate difference between diastereomeric isomers, although the solvolysis products were the same. Thus, an unsymmetrical participation of a cyclopropyl group has been kinetically demonstrated in systems in which the cyclopropyl group can freely rotate. Regarding with the common intermediate that is a close precursor to the *trans*-homoallylic alcohol, there has been no direct experimental evidence in this study. However, the structure may be illustrated as a homoallylic cation, **6**, which might presumably be stabilized by homoconjugation.

In view of the facts that the secondary benzylic system



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is subject to almost no anchimeric assistance, and that the conformational requirement for the transition state in the solvolysis of compounds in which the free rotation of the α-substituted cyclopropyl group is permitted is not so strict as in a rigid polycyclic system, the present results seem to be rather interesting. A related investigation is now in progress.

Experimental

All the melting points are uncorrected. The IR spectra were obtained with a Hitachi 215 grating IR spectrophotometer. The NMR measurements were carried out on a Varian T-60 instrument, using tetramethylsilane as the internal reference. The physical properties of each compound are summarized in Tables 1 and 3.

Phenyl trans-*2*-p-*Tolylcyclopropyl Ketone (I-2) and* p-*Tolyl* trans-*2-Phenylcyclopropyl Ketone (II-2).* The cyclopropyl ketones (**I-2** and **II-2**) were prepared from benzylideneacetophenone derivatives[9] and trimethyloxosulfonium iodide by a previously reported method.[10]

*α-(*trans-*2*-p-*Tolylcyclopropyl)benzyl Alcohol (I-3a, b) and* α-*(*trans-*2-Phenylcyclopropyl)*-p-*tolylmethanol (II-3a, b).* To a stirred suspension of 2 g of $LiAlH_4$ in 200 ml of dry ether were added 13 g (55 mmol) of **I-2** dissolved in 100 ml of dry ether. The mixture was then stirred for 25 h before the excess hydride was carefully decomposed with a minimum amount of water. The mixture was filtered, and the precipitates were washed several times with ether. After the combined ether layer had then been dried, the removal of the solvent gave 10.5 g of **I-3a, b**, a colorless solid. It was found from the NMR spectrum that the solid consists of two diastereoisomers (**I-3a**: **I-3b**=3: 2). When the solid product was recrystallized from petroleum ether, a pure sample of **I-3a** (mp 52—53 °C) was obtained.

Found: C, 85.83; H, 7.59%. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61%.

Another pair of alcohols (**II-3a, b**) was prepared by a similar method in a 89% yield; the recrystallization of the crude product from petroleum ether gave rise to a pure sample of **II-3a** (mp 95—97 °C).

Found: C, 85.55; H, 7.73%. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61%.

*α-(*trans-*2*-p-*Tolylcyclopropyl)benzyl 3,5-Dinitrobenzoate (I-4a, b) and* α-*(*trans-*2-Phenylcyclopropyl)*-p-*tolylmethyl 3,5-Dinitrobenzoate (II-4a, b).* The 3,5-dinitrobenzoate (**I-4a, b**) was prepared by allowing 4.5 g (19 mmol) of **I-3a, b** to react with 5.2 g (22 mmol) of 3,5-dinitrobenzoyl chloride in 75 ml of dry pyridine at room temperature for 30 h. The product was extracted with ether, and the organic layer was successively washed with water, 1M-hydrochloric acid, 5% aqueous sodium hydrogencarbonate, and water. The ether layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. In the same ratio as the parent alcohols (**I-3a** and **3b**), 3,5-dinitrobenzoate (**I-4a, b**; 6.5 g) was obtained. Recrystallization from benzene and petroleum ether

TABLE 1. PHYSICAL PROPERTIES AND SPECTRAL AND

Compound	Yield %	Mp °C	IR[a] $\tilde{\nu}$/cm^{-1}	NMR δ/ppm Ar$_1$	Ar$_2$	α-H
I-2	68	85—86.5 (lit, 85—87)[b]	1660 1240 810	8.1—7.9 (m, 2H), 7.6—7.5 (m, 3H)	7.07 (s, 4H)	
II-2	93	44.5—46	1680 1610 1240	7.95, 7.30 (ABq, J=8 Hz, 4H)	7.30 (s, 5H)	
I-3[c]	97	oil	3400 1460 1020		7.37(s), 7.00(s)	4.31 (d, J=7 Hz), 4.26 (d, J=7 Hz)
II-3[c]	86	solid	3370 1610 1030		7.4—6.9 (m)	4.38 (d, J=7 Hz), 4.30 (d, J=7 Hz)
I-4a	(80)[d]	114—116	1730 1550 1350	7.7—7.2 (m, 5H)	7.03, 6.87 (ABq, J=9Hz, 4H)	5.70 (d, J=8 Hz, 1H)
I-4b		124—125	1730 1550 1350	7.6—7.2 (m, 5H)	7.07, 6.93 (ABq, J=9 Hz, 4H)	5.80 (d, J=8 Hz, 1H)
II-4a	(95)[d]	96.5—98	1730 1550 1350	7.5—7.1 (m, 9H)		5.68 (d, J=8 Hz, 1H)
II-4b		124—125	1715 1550 1350	7.5—6.9 (m, 9H)		5.80 (d, J=8 Hz, 1H)

a) The infrared spectra of **I-3** was recorded in neat, and the others, in Nujol mulls. b) Ref. 10. c) The data of proton was observed at a higher field in the NMR spectrum was ascribed to the **a**-series, and the other one, to

TABLE 2. KINETIC DATA OF 3,5-DINITROBENZOATES (**I-4a, b** AND **II-4a, b**) IN 80% AQUEOUS ACETONE

Compound	Temp °C[a]	10^4k/s^{-1} [b]	$\Delta H^{\ddagger}$ kcal/mol[c]	$\Delta S^{\ddagger}$ eu[c]	k_{rel} at 25°C
I-4a	45.0	1.16±0.07			
	35.0	0.303±0.008			
	25.0	0.0766±0.0032	25.0	−2.62	1.00
I-4b	45.0	3.71±0.19			
	35.0	1.08±0.07			
	25.0	0.275±0.018	23.4	−5.44	3.59
II-4a	45.0	3.99±0.1			
	30.0	0.754±0.001			
	25.0	0.404±0.06	20.7	−13.7	1.00
II-4b	45.0	8.29±0.1			
	30.0	1.57±0.07			
	25.0	0.752±0.05	22.0	−8.14	1.86

a) ±0.03 °C. b) The kinetic plots were linear to a 75% conversion (2 half-lives). c) Calculated from $\Delta H^{\ddagger}=R\,(T_1T_2/T_2-T_1)\ln(T_1k_2/T_2k_1)$, $\Delta S^{\ddagger}=R\ln(k_ih/kT_i)+\Delta H^{\ddagger}/T_i$; T_i, absolute temperature; h, Planck's constant; k, Boltzmann's constant.

gave a pure sample, **I-4b** (mp 124—125 °C). A pure sample of **I-4a** was obtained in a 92% yield by esterification between a pure **I-3a** and 3,5-dinitrobenzoylchloride. By a similar method, another pair of esters (**II-4a, b**) was obtained.

Assignment of the Geometry in 3,5-Dinitrobenzoate. 1) The ratio of the composition of diastereomers for each series was not changed between before and after esterification.

2) The esterification of a pure alcohol (**I-3a**) gave rise

TABLE 3. PHYSICAL PROPERTIES AND SPECTRAL DATA OF

Compound	Mp °C	IR in Nujol mulls $\tilde{\nu}$/cm^{-1}	NMR δ/ppm Aromatic	Vinylic
I-5	78.5—80.0	3350 960	7.4—7.0 (m, 9H)	6.53 (d, J=16 Hz, 1H), 6.12 (dt, J=16, 6 Hz, 2H)
II-5	70—71	3330 960	7.37 (s, 5H), 7.2—7.0 (m, 4H)	6.50 (d, J=16 Hz, 1H), 6.07 (dt, J=16, 6 Hz, 2H)

ANALYTICAL DATA OF I-2, 3, 4a, b AND II-2, 3, 4a, b

in $CDCl_3$			Found (Calcd)		
Cyclopropyl	Others	(Calcd for)	C, %	H, %	N, %
3.0—2.5 (m, 2H), 2.0—1.3 (m, 2H)	2.30 (s, 3H); Methyl				
3.0—2.5 (m, 2H), 2.0—1.4 (m, 2H)	2.41 (s, 3H); Methyl	($C_{17}H_{16}O$)	86.35 (86.41)	6.90 (6.82)	
2.2—0.8 (m)	2.27 (s); Methyl, 2.00 (s); OH				
2.2—0.8 (m)	2.35 (s); Methyl, 1.95 (s); OH				
2.5—2.1 (m, 1H), 2.1—1.6 (m, 1H), 1.19 (t, J=8 Hz, 2H)	9.15 (s, 4H); Ester, 2.28 (s, 3H); Methyl	($C_{23}H_{21}NO_4$)	66.58 (66.66)	4.68 (4.60)	6.27 (6.48)
2.3—1.6 (m, 2H), 1.3—1.0 (m, 2H)	9.16 (s, 4H); Ester, 2.30 (s, 3H); Methyl	($C_{23}H_{21}NO_4$)	66.10 (66.66)	4.60 (4.60)	6.30 (6.48)
2.6—2.2 (m, 1H), 2.2—1.8 (m, 1H), 1.4—1.1 (m, 2H)	9.16 (s, 4H); Ester, 2.37 (s, 3H); Methyl	($C_{23}H_{21}NO_4$)	66.39 (66.66)	4.65 (4.60)	6.49 (6.48)
2.3—1.6 (m, 2H), 1.6—1.0 (m, 2H)	9.16 (s, 4H); Ester, 2.37 (s, 3H); Methyl	($C_{23}H_{21}NO_4$)	66.65 (66.66)	4.80 (4.60)	6.42 (6.48)

I-3 and II-3 were obtained with a mixture of two diastereoisomers. The alcohol in which the doublet of the α-
the b-series. d) Yield from a mixture of two diatereoisomers of alcohol.

to a pure 3,5-dinitrobenzoate (**I-4a**; 92% yield). The geometry of this 3,5-dinitrobenzoate (**I-4a**) should eventually correspond to that of the *erythro* isomer of its parent alcohol (**I-3a**).

3) The chemical shift of the carbinyl proton in **I-4b** is about 0.1 ppm lower than that in **I-4a**. An analogous relation is observed between parent alcohols (**I-3a** and **b**), as has been described before.

Treatment of I-3a, b and II-3a, b with Perchloric Acid. A solution of **I-3a, b** (1.0 g) and 0.2 ml of 70% perchloric acid dissolved in 50 ml of 80% aqueous acetone was stirred at 25 °C for 24 h. After a work-up, 950 mg of a colorless solid were obtained in a 95% yield. Recrystallization from petroleum ether gave rise to a pure sample, *trans*-1-phenyl-4-*p*-tolyl-3-buten-1-ol (**I-5**). Another homoallylic alcohol (II-5) was obtained by a similar method in a 92% yield and was recrystallized from petroleum ether. The spectral data of **I-5** and **II-5** are shown in Table 3.

Preparative Solvolysis of 3,5-Dinitrobenzoate (I-4a, b and II-4a, b). A solution of 388 mg (1 mmol) of **I-4a** and 0.5 ml (*ca.* 4.6 mmol) of 2,6-lutidine in 200 ml of 80% aqueous acetone was heated at 45 °C for 30 half-lives. After the solution had then been concentrated under reduced pressure, 100 ml of water was added and the resulting suspension was extracted with ether. The combined ether extracts were washed with water and dried over anhydrous K_2CO_3. The removal of the solvent under reduced pressure gave 171 mg (71%) of a yellow solid. The other esters (**I-4b** and **II-4a, b**) were solvolyzed in the presence of 2,6-lutidine by a similar method. Each product in solvolysis was identified on the basis of a comparison of its NMR spectra with those of an authentic sample. The product distributions were determined from the ratio of the NMR integral intensities of the α-hydrogen signal for cyclopropyl methanol and the vinylhydrogen signal for homoallyl alcohol. The major products were homoallylic alcohols (**I-5, II-5**), accompanied by a trace of the parent alcohols (**I-3, II-3**).

A mixture containing 110 mg (0.46 mmol) of **I-3a**, 0.3 ml of 2,6-lutidine and 98 mg (0.46 mmol) of 3,5-dinitrobenzoic acid in 100 ml of 80% aqueous acetone was heated at 45 °C for 8 h (*ca.* 5 half-lives). After a usual work-up, 95 mg of a colorless solid were obtained. A comparison of the NMR spectrum before and after heating showed that **I-3a** was stable under these reaction conditions. Also, **II-3b** was not changed into **II-5** under these conditions.

Kinetic Procedures. The acetone was purified by distillation from potassium permanganate, followed by drying (K_2CO_3) and distillation. The water used in the kinetic studies was demineralized and distilled. 80% aqueous acetone (v/v) was prepared at 25 °C by mixing 4 volumes (accurately pipetted) of purified acetone with 1 volume of purified water.

THE HOMOALLYLIC ALCOHOLS (I-5 and II-5)

in $CDCl_3$				Found (Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61%)
α	Allylic	Hydroxylic	Methyl	
4.75 (t, J=6 Hz,1H)	2.62 (t, J=6 Hz, 2H)	2.13 (s, 1H)	2.33 (s, 3H)	C, 85.96; H, 7.62%
4.77 (t, J=6 Hz, 1H)	2.63 (t, J=6 Hz, 2H)	1.97 (s, 1H)	2.33 (s, 3H)	C, 85.44; H, 7.65%

For each run, approximately 100 mg (*ca.* 0.25 mmol) of 3,5-dinitrobenzoate (**I-4a, b** or **II-4a, b**) was weighed into a 100 ml volumetric flask and dissolved in 80% aqueous acetone (*ca.* 2×10^{-3} M). Aliquots of the solution (*ca.* 6 ml) were transferred as quickly as possible into glass ampoules, which were in turn sealed and immersed simultaneously into a constant-temperature bath. After approximately 5 min, one ampoule was removed and immediately plunged into an ice–water bath. The rate at each temperature was measured by quenching 5.00 ml aliquots in 25 ml of dry acetone and then immediately titrating with a standard aqueous sodium hydroxide solution (8.357×10^{-3} M), using a Hitachi-Horiba automatic titrator with a glass electrode. The infinite titer was measured after *ca.* 10 half-lives, and 95—103% of 3,5-dinitrobenzoic acid was removed. The rate constants obtained by such procedures were consistent with that obtained by the indicator method using Bromothymol Blue.

A solution of 240 mg of **I-4b** in 200 ml of 80% aqueous acetone was kept in a flask at 35 °C for 1.5 h (*ca.* 1/2 half life). The solution was then poured into a mixture of ether (300 ml) and water (500 ml). The ether layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed at reduced pressure, the solid residue weighed 230 mg. A comparison of the NMR spectra before and after the reaction indicated that **I-4b** was not isomerized into **I-4a** under the solvolysis conditions. Also, **I-4a** was not converted into the isomeric 3,5-dinitrobenzoate (**I-4b**) under the reaction conditions.

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