Reversible Cyclopropyl Ring Opening of 1-Aroyl-2-phenylcyclopropane Radical Anions. Determination of the Ring Opening and Closure Rates of the Intermediate Ketyls

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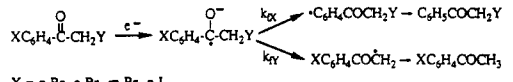
Abstract: The phenylcyclopropylketyl ring opening has been used as a mechanistic probe for the detection of radical intermediates. The reaction is of limited use since the ring-opening reaction is reversible. 1-Benzoyl-2-phenylcyclopropane (II) was considered to be a better probe since the ring opening of its radical anion was believed to be irreversible. In this study, the ring opening of $II^{\bullet-}$ is also found to be reversible since the radical-initiated reduction of (+)-*trans*-1-benzoyl-2-phenylcyclopropane ((+)-*trans*-II) with 1,3-dimethyl-2-phenylbenzimidazoline (DMBI) leads to racemized and isomerized products ((±)-*trans*-II and (±)-*cis*-II). The rate constants (k_o) for the ring opening of both *trans*- and *cis*-II ketyls have been estimated from the intramolecular competitive reduction of both *trans*- and *cis*-1-(*p*-chlorobenzoyl)-2-phenylcyclopropane with DMBI ($k_{o,trans} = (2.8 \pm 0.1) \times 10^5$ s^{-1}, $k_{o,cis} = (1.6 \pm 0.2) \times 10^6$ s^{-1}, 22 °C). The rate constants for the ring closure (k_c) of the opened radical to give the trans and cis ketyls were estimated from the DMBI reduction of *trans*-II using dicyclohexylphosphine as a hydrogen atom donor ($k_{c,trans} = 4 \times 10^2$ s^{-1}, $k_{c,cis} = 23 \pm 9$ s^{-1}, 61 °C).

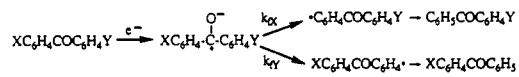
Introduction

The cyclopropylcarbinyl–allylcarbinyl radical rearrangement ($k = 1.0 \times 10^8$ s^{-1}, 25 °C; 3.4×10^8 s^{-1}, 60 °C)[3] has been used as a mechanistic probe for the detection of radical intermediates and for the estimation of the rates of competing radical processes.[4] Similarly, aryl cyclopropyl ketones have been employed as chemical probes to investigate the intermediacy of ketyls formed during the reactions of ketones with nucleophilic reagents.[5] Recently intramolecular competitive fragmentation reactions of disubstituted acetophenone and benzophenone radical anions have been used to estimate the cleavage rate constants of a series of monosubstituted acetophenone and benzophenone ketyls.[6] Since the electrochemically measured cleavage rate constants of a number of ring-halogenated acetophenone and benzophenone ketyls have previously been reported[7,8] and since it is established that these cleavage rates are little affected by substitution at the α-position of the ring-halogenated acetophenones or at the other phenyl ring of the ring-halogenated benzophenones (eqs 1 and 2),[6] the product ratios of the competitive fragmentations allowed the determination of the fragmentation rates of the α-substituents.



(1)

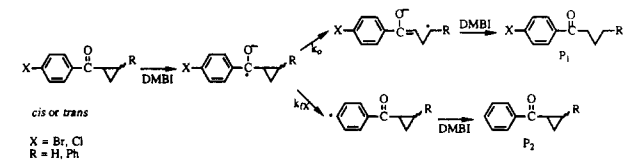
X = *p*-Br, *o*-Br, *m*-Br, *p*-I
Y = Br, Cl, F, OCOR, OPh, SO_2Tol-*p*, SPh



(2)

X; Y = Br, Cl, I

The intramolecular competitive ketyl cleavage reaction has now been used to estimate the rate constants for the arylcyclopropylketyl rearrangement. Several *p*-halophenyl cyclopropyl ketones were reduced using 1,3-dimethyl-2-phenylbenzimidazoline (DMBI)[6] (see eq 3).



(3)

A determination of the ratio of the products resulting from the competitive cyclopropylketyl ring opening and its dehalogenation was anticipated to give a direct measurement of the ring-opening rate constant (k_o), since the dehalogenation rate constant (k_{fX}) can be estimated from previously reported electrochemical measurements.[7,8]

Results and Discussion

The radical anions of *p*-halophenyl cyclopropyl ketones undergo competitive dehalogenation and cyclopropyl ring opening (see eq 3). Hydrogen abstraction by the two intermediate radicals formed gives the corresponding reduction products, P_1 and P_2. The electron-transfer hydrogen atom abstraction chain reduction of the *p*-halophenyl cyclopropyl ketones allows the measurement of the ketyl cleavage rate ratio, k_o/k_{fX}. The absolute value for k_o can be determined since k_{fX} is known.

The cyclopropyl group has been shown to have no significant stabilizing conjugative effect on the carbinyl radical[9] nor on the carbinyl carbanion.[10] Since the fragmentation rate constant of the ring halogen in the ring-halogenated α-substituted acetophenone ketyl is the same as the fragmentation rate of the corresponding ring-halogenated acetophenone ketyl,[6] it can also reasonably be assumed that the cleavage rates of the halide ion from the (*p*-halophenyl)cyclopropylketyls are the same as those measured for the corresponding *p*-haloacetophenone ketyls (k_{fX} (23 °C): Br, 3.2×10^7 s^{-1}, AN,[6] DMF;[8] Cl, 3×10^3 s^{-1}, AN[7a]).

1,3-Dimethyl-2-phenylbenzimidazoline (DMBI) was used as the reducing agent for the reduction of the cyclopropyl ketones, since its reactions with α-halo ketones[11] and ring-halogenated acetophenones[6] have been shown to proceed via an ET hydrogen abstraction chain process (see Scheme I). All of the reactions were carried out in acetonitrile (AN) either at 61 or at 22 °C.

(1) Killam predoctoral fellow, 1987–1990.
(2) (a) NSERC Summer Undergraduate fellowship, 1990. (b) NSERC Summer Undergraduate fellowship, 1991.
(3) Beckwith, A. L. J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1989**, *54*, 2681.
(4) (a) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (b) Kruisic, P. J.; Fagan, P. J.; San Filippo, J., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 250. (c) Kinney, R. J.; Jones, W. D.; Bergman, R. G. *Ibid.* **1978**, *100*, 7902.
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(9) (a) McMillen, M. H.; Golden, D. M.; Benson, S. W. *Int. J. Chem. Kinet.* **1971**, *3*, 359. (b) Baghal-Vayjovee, M. H.; Benson, S. W. *J. Am. Chem. Soc.* **1979**, *101*, 2338. (c) Newcomb, M.; Glenn, A. G. *Ibid.* **1989**, *111*, 275.
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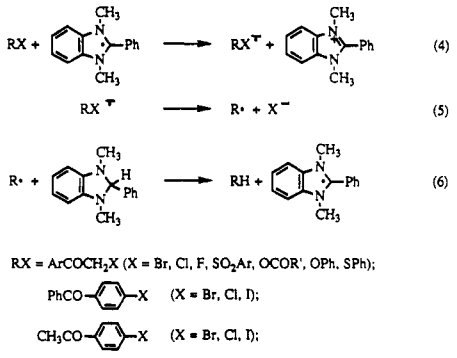
Table I. DMBI Reduction of (+)-*trans*-1-Benzoyl-2-phenylcyclopropane in Acetonitrile

reaction	conditions	reactant		product (%)					[III]/
		[(+)-*trans*-II]^0	[DMBI]	(+)-*trans*-II[a]	(±)-*trans*-II[b]	(±)-*cis*-II	III	$k_{c,trans}{}^c/k_{c,cis}$	[(±)-*cis*-II]
1	6% DBPO, 22 °C, 22 h	0.021	0.0132	25.3	70.5	1.83	*d*	37.5 ± 2.7 (3)[e]	
2	3% AIBN, 61 °C, 18 h	0.021	0.0132	64.2	33.6	1.8	*d*	24 (1)	
3	3% AIBN, 61 °C, 45 h	0.021	0.0132	39.0	58.8	2.8	*d*	24 (1)	
4	3% AIBN, 61 °C, 44 h	0.041	0.0271	31.1	61.2	2.2	*d*	28 (1) av 25 ± 1.6	
5	11% AIBN, 61 °C, 52 h[f]	0.044	0.103		97.2	2.1	0.28		0.13
6	4% AIBN, DCPH (0.041 M), 61 °C, 85 h[g]	0.043	0.0332		95	2.6	2.4		0.92
7	4% AIBN, DCPH (0.041 M), 61 °C, 85 h[g]	0.043	0.0332		94	2.5	5.0		2.00

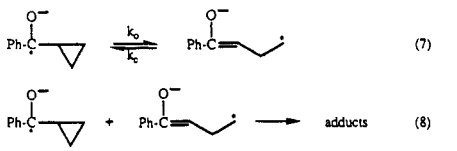
[a] (+)-*trans*-II% = $[\alpha]^D/[\alpha]_0^D \times 97.8\%$ (or 99.5%), where $[\alpha]^D$ and $[\alpha]_0^D$ were the observed rotations of the reaction mixture before the reaction and after the reaction, respectively. [b] (±)-*trans*-II% = 97.8 (or 99.5%) − (+)-*trans*-II%. [c] $k_{c,trans}/k_{c,cis}$ = (±)-*trans*-II%/(±)-*cis*-II%. [d] Not observed. [e] The number in parentheses are the number of independent experiments. [f] 0.0435 M (±)-*trans*-II was used instead. [g] 0.043 M (±)-*trans*-II was used instead.

Scheme I



AIBN (61 °C) or di-*tert*-butyl peroxyoxalate (DBPO, 22 °C) was used to initiate the radical chain reductions. Under the same reaction conditions, no reaction occurred in the absence of the radical initiators.

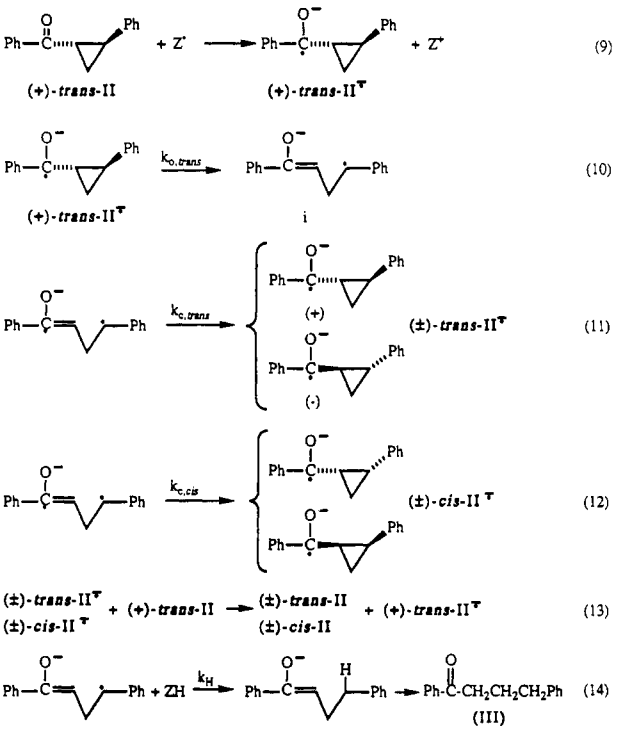
Reduction of *p*-Halophenyl Cyclopropyl Ketones (Ia,b). The AIBN-initiated (3–5%) DMBI reductions (61 °C, 53–60 h) of *p*-chlorophenyl cyclopropyl ketone (Ia) and *p*-bromophenyl cyclopropyl ketone (Ib) gave only the dehalogenated product, phenyl cyclopropyl ketone, in 24.6% and 78.7% yields. No ring-opened products (<0.1%, GC and GC/IR), *p*-halophenyl *n*-propyl ketones, were observed. From these results an upper limit of $<1.2 \times 10^1$ s^{-1} might have been placed on the rearrangement rate constant of the phenylcyclopropylketyl (k_o). Using cyclic voltammetry, House estimated the half-life of the phenylcyclopropylketyl in DMF to be 5 s ($k_o = 1.4 \times 10^{-1}$ s^{-1}).[5b] However, an electrochemical investigation of the ketyl rearrangement recently demonstrated that the ring opening of the phenylcyclopropylketyl is reversible and that the ketyl decays by the rate-limiting coupling of the ketyl radical ion with the ring-opened radical (eqs 7 and 8).[12] Since the ring-closure rate constant (k_c) was not determined,



it was not possible to calculate the ring-opening rate (k_o) from the reduction products obtained from the competitive reactions of the ketyl formed from Ia,b.

The ring opening of a closely related α-cyclopropylbenzyl radical was also recently reported to be reversible ($k_o = 1.3 \times 10^6$ s^{-1}, $k_c = 1.2 \times 10^7$ s^{-1}, 42 °C).[13] The reversibility of the ring opening is attributed to the conjugative stabilization of the α-cyclopropylbenzyl radical, which does not require further stabilization by ring opening. It is anticipated that the replacement of one hydrogen on the cyclopropyl ring by a phenyl group will increase

Scheme II



the ring-opening rate[14] since the overall rate of ketyl decay is faster for *trans*-1-benzoyl-2-phenylcyclopropane (*trans*-II) than for phenyl cyclopropyl ketone.[12] It is implied that the extra stabilization of the ring-opened benzylic radical (i) makes ring opening irreversible.[12]

Substitution also generates a racemic pair of diastereoisomers. The electron-transfer reduction of one of the enantiomers of the cis or trans diastereomer allows the observation of reversible ring opening, since closure generates a racemic intermediate. Scheme II shows a mechanism for the racemization and isomerization of (+)-*trans*-1-benzoyl-2-phenylcyclopropane ((+)-*trans*-II). The ring opening of (+)-*trans*-II$^{\bullet-}$ yields an achiral benzylic radical (eq 10), which can cyclize to produce racemic trans or cis ketyls (eqs 11 and 12). The electron transfer between (±)-*trans*-II$^{\bullet-}$ or (±)-*cis*-II$^{\bullet-}$ and starting (+)-*trans*-II produces (±)-*trans*-II or (±)-*cis*-II (eq 13). The ring-opened benzylic radicals (i) can also undergo hydrogen abstraction to form the ring-opened ketone, 1,4-diphenyl-1-butanone (III) (see eq 14).

DMBI Reduction of (+)-*trans*-1-Benzoyl-2-phenylcyclopropane. The reduction of (+)-*trans*-II ($[\alpha]^{22}_D = 398.1$, $CHCl_3$; reported[15,16]

(11) Tanner, D. D.; Chen, J. J. *J. Org. Chem.* **1989**, *54*, 3842.
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(14) Most recently the ring opening of the *trans*-(2-phenylcyclopropyl)-carbinyl radical ($k_o = 1.8 \times 10^{11}$ s^{-1}, 20 °C)[14a] was reported to be about 1000 times faster than that of the parent cyclopropylcarbinyl radical. (a) Newcomb, M.; Manek, M. B. *J. Am. Chem. Soc.* **1990**, *112*, 9662.

Table II. Competitive DMBI Reduction of *trans*- and *cis*-1-(*p*-Halobenzoyl)-2-phenylcyclopropanes (IVa,b) in AN

reaction	substrate IVa,b, trans/cis	reaction conditions	product[b] (%) *trans*-II	*cis*-II	*trans*-IVa,b	*cis*-IVa,b	k_0 (s^{-1})[c]
7	IVa, 18.9/81.1	22 °C, 6% DBPO, 15 h	0.7	0.12	56.2[d]	23.9	$(1.6 \pm 0.2) \times 10^6$[e]
8	IVa, 6.5/93.5	61 °C, 4% AIBN, 2 h	0.9	0.1	6.0[f]	86.5	4.2×10^6[e]
9		61 °C, 4% AIBN, 5.5 h	1.0	1.0	66.1[f]	25.8	4.7×10^6[e]
10		61 °C, 4% AIBN, 15 h	4.4	1.2	79.5[f]	6.2	4.9×10^6
11		61 °C, 4% AIBN, 34 h	12.0	1.4	74.9[f]	4.8	4.4×10^6[e]
							av $(4.6 \pm 0.2) \times 10^6$[e]
12	IVa, >99.9/1	22 °C, 3% DBPO, 23 h	0.28		99.0	0.78	$(2.8 \pm 0.1) \times 10^5$[g]
13		61 °C, 4% AIBN, 48 h	2.4		97.8	3.2	$(9.4 \pm 6.2) \times 10^5$[g]
14	IVb, >99.9/1	61 °C, 8% AIBN, 45 h	70.1		31.4		not calcd
15	IVb, 76.2/23.8	61 °C, 11% AIBN, 50 h	39.8	5.8	45.9	20.0	not calcd

[a] All of the reductions were carried out in the dark except where specified in the table. [IVa,b] = 0.03–0.06 M; [DMBI] = 0.02–0.05 M. [b] Yields of products of a typical run. Determined by GC and GC/IR. [c] Calculated from eqs 26 and 27 and $k_{fCl} = 3 \times 10^3$ s^{-1} (23 °C), 7.0×10^4 s^{-1} (61 °C). [d] Corrected for the *trans*-IVa originally present in the starting substrate (18.9%). [e] $k_{o,cis}$. [f] Corrected for the *trans*-IVa originally present in the starting substrate (6.5%). [g] $k_{o,trans}$.

for (−)-*trans*-II, $[\alpha]^{24}_D = -407$) was carried out in AN in the presence of DBPO (22 °C) or AIBN (61 °C). The results are listed in Table I. The yield of racemized product was determined polarimetrically. The racemic mixture (GC) contained (±)-*trans*-II and (±)-*cis*-II. The ring-opened product, III, was not detected under the reaction conditions ([(+)-*trans*-II] = 0.0208 M, [DMBI] = 0.0132 M). In the absence of AIBN or DBPO, no racemization or isomerization occurred. Trace initiation established that the DMBI reduction of (+)-*trans*-II proceeds via a free radical chain process (see Scheme II).

Since the racemization and isomerization proceed through a common ring-opened intermediate, i, the ratio of products formed, (±)-*trans*-II/(±)-*cis*-II, is determined by the ratio of the rate constants for ring closure to both the trans and cis ketyls, $k_{c,trans}/k_{c,cis}$ (eqs 11 and 12, Scheme II). A steady-state treatment of the reactions in Scheme II, with the assumption that at low conversion spin exchange between the ketyl and the neutral ketone (eq 13) is rapid,[17] allows the calculation of the relative ring-closure rate constants, $k_{c,trans}/k_{c,cis}$. The product yields, [(±)-*trans*-II] and [(±)-*cis*-II], and the relative rate ratios for ring closure of i to the racemized products, $k_{c,trans}/k_{c,cis}$, are listed in Table I. Ring closure to the trans ketyl (eq 11) is favored compared to closure to give cis ketyl and, as expected for an irreversible competitive process,[18] the ratio of closure rates is lower at higher temperatures ($k_{c,trans}/k_{c,cis} = 25 \pm 1.6$, 61 °C; 37 ± 3 at 22 °C).

When the reduction of *trans*-II is carried out with higher concentrations of the transfer agent (DMBI, >0.1 M), it is possible to observe the formation of the ring-opened product, since III is formed by biomolecular hydrogen transfer of the ring-opened radical, i, with DMBI (see eq 14, Scheme II). The initiated DMBI (0.103 M) reduction of *trans*-II (0.0435 M, 61 °C, 52 h) gave two products, III and *cis*-II, in a ratio of 0.13/1 (see Table I). Since the reduction was carried out to low conversion (<2.5%), it is reasonable to assume that the concentration of DMBI remains unchanged during the reduction. A steady-state treatment of the reactions shown in Scheme II allows the calculation of the ratio of rates of ring closure to give the cis ketyl (eq 11) to the rate of hydrogen abstraction from DMBI (see eq 15).

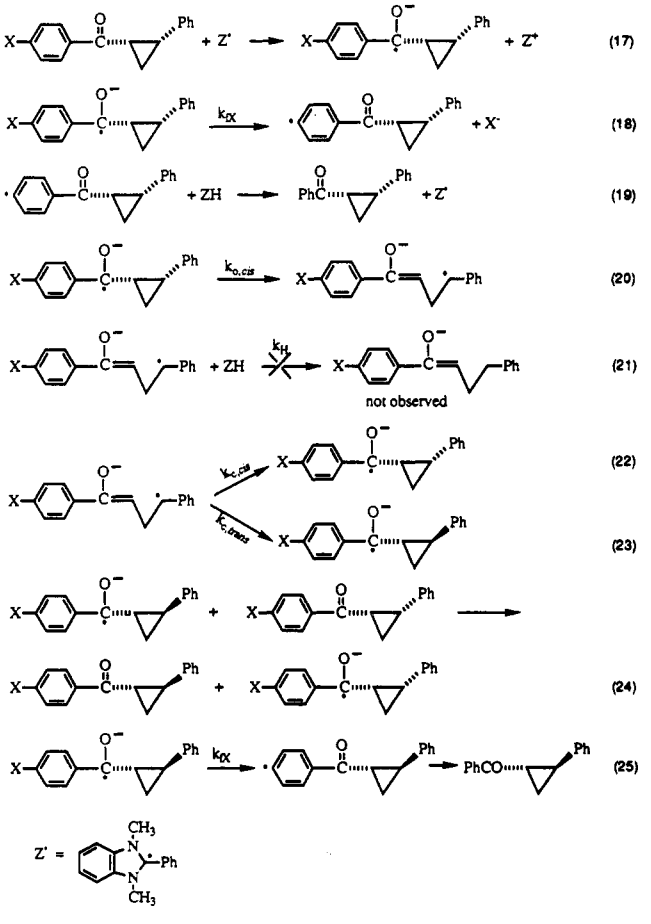
$$\frac{k_{H,DMBI}}{k_{c,cis}} = \frac{[III]}{[cis\text{-II}][DMBI]} = 1.3\ M^{-1} \qquad (15)$$

When an equivalent amount of a more reactive chain-transfer agent, dicyclohexylphosphine (DCPH),[19] was added to the reaction mixture and the reaction was carried out to low conversion, the small amount of ring-opened product was greatly increased. From the concentration of DMBI used, 0.033 M, the ratio of [III]/[*cis*-II] arising from transfer with DMBI, [III]/[*cis*-II] = 0.04, is negligible compared to the ratio obtained in the reaction with added DCPH, 0.92 (see Table I). Since the absolute rate constant for transfer of hydrogen from a dialkylphosphine (bis(2-cyanoethyl)phosphine) to a secondary benzyl radical (a polystyryl radical) has been determined ($k_H = 7.26 \times 10^2$ M^{-1} s^{-1}, 60 °C),[20] the assumption is made that the rate of transfer of i with DCPH can be approximated by the transfer rate determined from styrene polymerization. Using k_H, the absolute rate of ring closure to the cis product, $k_{c,cis}$, can be estimated (Table I, reactions 5 and 6; see eq 16).

$$k_{c,cis} = k_{H,DCPH}\frac{[cis\text{-II}][DCPH]}{[III]} = 23 \pm 9\ s^{-1} \qquad (16)$$

When the kinetic eqs 15 and 16 were combined, $k_{H,DCPH}$/

Scheme III



(15) Walborsky, H. M.; Plonsker, L. *J. Am. Chem. Soc.* **1961**, *83*, 2138.
(16) Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *Ibid.* **1976**, *98*, 122.
(17) The rate constant for the spin exchange between a neutral molecule and its radical anion has been measured for acetone,[17a] benzophenone,[17b] and benzoquinones[17c] and is usually $\geq 10^7$ M^{-1} s^{-1}. (a) Meisel, D. *Chem. Phys. Lett.* **1975**, *34*, 263. (b) Adam, F. C.; Weissman, S. I. *J. Am. Chem. Soc.* **1958**, *80*, 1518. (c) Layloff, T.; Miller, T.; Adams, R. N.; Fäh, H.; Horsfield, A.; Proctor, W. *Nature* **1965**, *205*, 382.
(18) The observed temperature dependence supports the assumption that ring closure is irreversible since spin exchange is rapid.

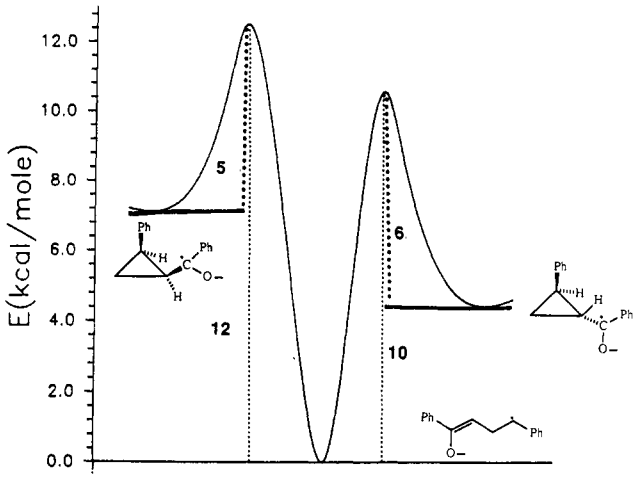


Figure 1. Activation energies for the reversible ring opening of the 1-benzoyl-2-phenylcyclopropane radical anion.

$k_{H,DMBI} = 25$ was obtained. The rate constant for transfer of the open radical, i, with DMBI is $k_{H,DMBI} = 29\ M^{-1}\ s^{-1}$ at 61 °C. Using the value obtained for $k_{c,cis}$ and the ratio of $k_{c,trans}/k_{c,cis}$ listed in Table I, the rate of ring closure for the open ketyl, i, to reform the trans ketyl is calculated as $k_{c,trans} = 4 \times 10^2\ s^{-1}$ at 61 °C.

DMBI Reduction of 1-(*p*-Chlorobenzoyl)-2-phenylcyclopropane (IVa). The DBPO- or AIBN-initiated reductions of *cis*-1-(*p*-chlorobenzoyl)-2-phenylcyclopropane (*cis*-IVa) gave two products, the dechlorinated ketone, *cis*-II, and the isomerized chlorinated ketone, *trans*-IVa. Similarly, the DBPO- or AIBN-initiated reductions of *trans*-IVa yielded *trans*-II and *cis*-IVa. The ring-opened product, 1-(*p*-chlorophenyl)-4-phenyl-1-butanone (V), was not detected (<0.2%) in either of the mixtures of the reduction products. The results of these reductions are listed in Table II.

Scheme III details the reaction mechanism leading to both isomerized and dehalogenated ketones. A steady-state treatment of the reactions listed, including rapid spin exchange (eq 24), yields equations which define the rate constants of ketyl ring opening from both *cis*-IVa (eq 26) and *trans*-IVa (eq 27).

$$k_{o,cis} = k_{fX}\left(\frac{k_{c,cis}}{k_{c,trans}} + 1\right)\left(\frac{[trans\text{-IVa}]}{[cis\text{-II}]}\right) \quad (26)$$

$$k_{o,trans} = k_{fX}\left(\frac{k_{c,trans}}{k_{c,cis}} + 1\right)\left(\frac{[cis\text{-IVa}]}{[trans\text{-II}]}\right) \quad (27)$$

The $k_{c,trans}/k_{c,cis}$ values (37, 22 °C; 25, 61 °C) obtained from the reduction of (+)-*trans*-II were used since it can be reasonably assumed that halogen substitution on the benzoyl moiety would not significantly affect the relative ring-closure rates. It is further assumed that the dehalogenation rate constants of *trans*-IVa and *cis*-IVa ketyls are the same as that of corresponding *p*-haloacetophenone ketyls (vide supra). The k_{fCl} value is available at 23 °C ($k_{fCl} = 3 \times 10^3\ s^{-1}$, 23 °C),[7a] and the value at 61 °C ($k_{fCl} = 7.0 \times 10^4\ s^{-1}$, 61 °C) was calculated using the preexponential factor reported for the cleavage reaction of *p*-chlorobenzophenone.[7b]

The values for $k_{o,cis}$ and $k_{o,trans}$ are calculated using eqs 26 and 27 and are included in Table II. At higher conversions the reduction of *cis*-IVa also yielded *trans*-II, which is formed through the further reduction of *trans*-IVa since the rate of isomerization is 2 powers of 10 times faster than dehalogenation. This conclusion is supported by the observation that the same $k_{o,cis}$ values are obtained at different conversions when the yield of *trans*-II is added to that of *trans*-IVa during the calculation of the value of $k_{o,cis}$ using eq 26.

Table III. Summary of the Relative Rate Constants and the Estimated Individual Rate Constants Obtained for the Reactions of the 2-Phenylcyclopropylketyls

reaction rates	estimated and determined values
$k_{o,trans}$	$3 \times 10^5\ s^{-1}$, 22 °C; $9 \times 10^5\ s^{-1}$, 61 °C
$k_{c,trans}$	$4 \times 10^2\ s^{-1}$, 61 °C
$k_{o,cis}$	$2 \times 10^6\ s^{-1}$, 22 °C; $5 \times 10^6\ s^{-1}$, 61 °C
$k_{c,cis}$	$23 \pm 9\ s^{-1}$, 61 °C
$k_{c,trans}/k_{c,cis}$	25 ± 1.6, 61 °C; 37 ± 3, 22 °C
$k_{H,DMBI}/k_{c,cis}$	$1.3\ M^{-1}$, 61 °C
$k_{H,DCPH}/k_{H,DMBI}$	25

Ring opening of the cis ketyl should be favored over that of the trans ketyl since the rate of cis ring opening will be accelerated by a relief of the eclipsed interactions in the transition state. As expected, the *cis*-IVa ketyl undergoes ring opening faster than the *trans*-IVa ketyl ($k_{o,cis}/k_{o,trans}$ = 5.5, 22 °C; 4.6, 61 °C) (see Table II).

DMBI Reduction of 1-(*p*-Bromobenzoyl)-2-phenylcyclopropane (IVb). In contrast to the DMBI reduction of *trans*-IVa, the reduction of *trans*-IVb gave only the corresponding debrominated ketone, *trans*-II (see Table II). The reduction of a mixture of *trans*- and *cis*-IVb yielded *trans*- and *cis*-II. The products and the starting substrates did not undergo isomerization since the ratio, (*cis*-IVb + *cis*-II)/(*trans*-IVb + *trans*-II), was the same as the ratio of *cis*-IVb/*trans*-IVb in the starting mixture (see Table II). The results indicate that the debromination of *cis*-IVb or *trans*-IVb ketyl is faster than the ring opening of either ketyl. If the ketyl ring opening were competitive with debromination, the *cis*-IVb would be converted to *trans*-IVb by the same ET chain process as in the reduction of *cis*-IVa. The rate of bromide cleavage ($k_{fBr} = 3.2 \times 10^7\ s^{-1}$, 23 °C, vide supra) is, as expected, faster than the rate of the ring opening ($k_{o,cis} = 1.6 \times 10^6\ s^{-1}$, 22 °C).

A combination of all of the relative rate constants which were determined and the individual rate constants which can be estimated (see Table III) allows a clear and consistent understanding of the energetics associated with the reaction of the (2-phenylcyclopropyl)ketyls.

The activation energies for the ring opening of *trans*- and *cis*-(2-phenylcyclopropyl) phenylketyls were calculated from the rate constants of the ring-opening reactions at 22 and at 61 °C using the Arrhenius equation. Since the rate constants for the ring closure to give cis and trans ketyls were determined at only one temperature (61 °C), the activation energies for the ring-closure reactions were estimated using the log *A* value of 9.5 reported for the cyclization of the 5-hexenyl radical.[21] The numerical values obtained are graphically displayed in Figure 1.

Experimental Section

Instrumentation. Instruments used for ^1H NMR, GC/MS, GC/IR, and GC measurements have been described previously.[6] Optical rotations were measured using a Perkin-Elmer 241 polarimeter. All observed rotations were read to 0.001° and were the average values measured on the same sample five times or more.

Materials. The purification and preparation of acetonitrile, 1,3-dimethyl-2-phenylbenzimidazoline, AIBN, DBPO, and di-*tert*-butylbenzene have been previously described.[22] Phenyl cyclopropyl ketone (Aldrich), *p*-chlorophenyl cyclopropyl ketone (Aldrich), and dicyclohexylphosphine (Aldrich) were used as supplied. Their purities (>95%) were determined by GC.

***p*-Bromophenyl cyclopropyl ketone (Ib)** was prepared by the method of Close:[23] bp 202–204 °C (10 mmHg) [lit.[24] mp 108–109 °C (1.2 mmHg)]; ^1H NMR δ 1.12 (m, 2 H), 1.3 (m, 2 H), 2.7 (m, 1 H), 7.5 (m, 2 H), 7.85 (m, 2 H), 7.85 (m, 2 H); λ_{max} (GC/IR) 1692, 1588, 1401, 1216, 1071, 994 cm^{-1}.

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p-Chloro- and p-bromobutyrophenone were prepared by a Friedel-Crafts reaction of the halobenzene and *n*-butyric anhydride in the presence of $AlCl_3$.[25-27] The products were recrystallized from petroleum ether at 0 °C. *p*-Chlorobutyrophenone: mp 35–36 °C (lit.[26] mp 36 °C); ^{1}H NMR δ 1.05 (t, 3 H), 1.8 (m, 2 H), 2.95 (t, 2 H), 7.45 (d, 2 H), 7.9 (d, 2 H); λ_{max} (GC/IR) 1704, 1593, 1211, 1097, 994, 821 cm^{-1}. *p*-Bromobutyrophenone: mp 36–37 °C (lit.[27] mp 38–39 °C); ^{1}H NMR δ 1.05 (t, 3 H), 1.88 (m, 2 H), 3.0 (t, 2 H), 7.7 (d, 2 H), 7.9 (d, 2 H); λ_{max} (GC/IR) 1704, 1588, 1209, 1074, 994, 817 cm^{-1}.

***trans*-1-Benzoyl-2-phenylcyclopropane (*trans*-II), *trans*-1-(*p*-chlorobenzoyl)-2-phenylcyclopropane (*trans*-IVa), and *trans*-1-(*p*-bromobenzoyl)-2-phenylcyclopropane (*trans*-IVb)** were synthesized from the corresponding chalcones and trimethyloxosulfonium iodide according to the literature procedure.[28] *p'*-Bromochalcone (p-BrC_6H_4COCH=$CHPh$)[29] and *p'*-chlorochalcone (p-ClC_6H_4COCH=$CHPh$)[29] were prepared according to the literature procedure. The resulting cyclopropanes were isolated and purified by alumina column chromatography (eluant: ethyl acetate/hexane, 3/55, v/v).

***trans*-II**: mp 41–42 °C (lit.[30] mp 42–43.5 °C); ^{1}H NMR δ 1.6–1.72 (m, 1 H), 1.92–2.1 (m, 1 H), 2.7–2.9 (m, 1 H), 2.9–3.1 (m, 1 H), 7.2–7.7 (m, 8 H), 8.0–8.2 (m, 2 H); λ_{max} (GC/IR) 1690, 1398, 1337, 1217, 988, 698 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O$: C, 86.49; H, 6.31. Found: C, 86.37; H, 6.22.

***trans*-IVa**: mp 44–45 °C; ^{1}H NMR δ 1.6 (m, 1 H), 1.95 (m, 1 H), 2.65–2.9 (m, 2 H), 7.2–7.5 (m, 7 H), 7.85–8.0 (m, 2 H); λ_{max} (GC/IR) 1690, 1594, 1405, 1336, 1215, 1095, 989, 750 cm^{-1}. Anal. Calcd for $C_{16}H_{13}OCl$: C, 74.85; H, 5.07. Found: C, 74.89; H, 5.11.

***trans*-IVb**: mp 56–58 °C; ^{1}H NMR δ 1.7 (m, 1 H), 2.05 (m, 1 H), 2.7–3.0 (m, 2 H), 7.2–7.5 (m, 5 H), 7.7–7.8 (m, 2 H), 7.9–8.1 (m, 2 H); λ_{max} 1690, 1588, 1405, 1337, 1213, 1072, 988, 749 cm^{-1}. Anal. Calcd for $C_{16}H_{13}OBr$: C, 63.81; H, 4.35. Found: C, 64.05; H, 4.31.

***cis*-II and *cis*-IVa,b** were prepared by the irradiation (GE, 275-W sunlamp) through a Pyrex filter of a benzene solution of the corresponding trans ketones.[31] The cis ketones were characterized by their GC/MS spectra (identical to the corresponding trans ketones) and their GC/IR spectra: *cis*-II λ_{max} 1691, 13380, 1216, 995, 695 cm^{-1}; *cis*-IVa λ_{max} 1691, 1593, 1378, 1212, 1094, 990, 782, 896 cm^{-1}; *cis*-IVb λ_{max} 1692, 1588, 1400, 1210, 1072, 995, 780, 696 cm^{-1}. The strong absorption near 1000 cm^{-1} is characteristic of the cyclopropyl structures.[32] In agreement with the assignment of the structure of the cis ketones, a mixture of either of the trans and cis ketones (II and IVa) undergoes isomerization to yield the corresponding trans ketone as the major product during their DMBI-initiated reductions (see Table II). *cis*-IVa and *trans*-IVa were separated using column chromatography on alumina (eluant: ethyl acetate/hexanes, 4/60, v/v). The *cis*-IVa used in the reductions contained 6.5% of *trans*-IVa. A mixture of *cis*-IVa and *trans*-IVa (76.2/23.8) was also used as a reduction mixture (see Table II).

(+)-*trans*-1-Benzoyl-2-phenylcyclopropane was prepared from (+)-*trans*-2-phenylcyclopropanecarboxylic acid according to the literature procedure:[15,16] mp 67–69 °C (lit.[15] mp 74–75 °C); $[\alpha]^{22}_D$ +398.1 ($CHCl_3$), (lit.[33] $[\alpha]_D$ +407 °C); 97.8 or 99.5% optically pure.[33] The (+)-trans acid was resolved by successive recrystallization of its quinine salt.[16] The ^{1}H NMR and IR (GC/IR) spectra of (+)-*trans*-II and the (+)-trans acid were identical with those of the corresponding racemic mixtures.

1,4-Diphenyl-1-butanone was prepared according to the literature procedure:[34] mp 53–54 °C (lit.[34] mp 55–56.5 °C); ^{1}H NMR δ 2.1 (m, 2 H), 2.7 (t, 3 H), 3.0 (t, 2 H), 7.2–7.6 (m, 8 H), 7.95 (m, 2 H); λ_{max} (GC/IR) 1701, 1450, 1224, 696 cm^{-1}.

1-(*p*-Chlorophenyl)-4-phenyl-1-butanone (V) was synthesized through the Grignard reaction of (3-phenylpropyl)magnesium bromide and *p*-chlorobenzonitrile.[35] The product was isolated and purified by column chromatography on alumina (eluant: ethyl acetate/hexanes, 3/50, v/v) and recrystallization from hexanes: mp 51.5–52 °C; ^{1}H NMR δ 2.1–2.3 (m, 2 H), 2.75–2.85 (t, 2 H), 2.95–3.1 (t, 3 H), 7.2–7.55 (m, 7 H), 7.9–8.0 (d, 2 H); λ_{max} 1703, 1593, 1224, 1096, 992, 823, 702 cm^{-1}. Anal. Calcd for $C_{16}H_{15}OCl$: C, 74.27; H, 5.84. Found: C, 74.15; H, 5.95.

General Procedure for the DMBI Reductions. An aliquot of a mixture of the substrate (0.03–0.05 M), DMBI (0.010–0.08 M), internal standard (di-*tert*-butylbenzene, 0.02 M), and the additive (AIBN, DBPO, 3–10 molar % of the substrate) in AN was placed in a Pyrex ampule. The ampule was degassed three times, sealed, and thermostated at the desired temperature for the time specified (see Tables I and II). The ampule was opened and analyzed by GC using either an SE-30 or OV-101 column.[6] For each new reaction the products were further identified by a comparison of their GC/IR and GC/MS spectra with those of authentic samples.[6]

The reductions initiated by DBPO were modified to avoid possible reactions during degassing. A solution (1 mL) of the substrate, internal standard, and the additives and a solution (1 mL) of DMBI were each put in the separate arms of an H-form ampule. After being degassed, sealed, and thermostated at room temperature (22 ± 0.5 °C), the solutions in the two arms were mixed and kept at room temperature in the dark for the specified time.

The product yields were determined from both GC and GC/IR measurements. The average values obtained are reported in Tables I and II. The quantitative calculation of yields from GC/IR experiments used the relative intensities of the IR spectra and the relative areas obtained from the FID detector connected to the GC/IR. A standard solution was run to obtain the response factors for each compound. Known concentrations of several standard solutions were analyzed by GC/IR to obtain the limit of detection for each compound (see the text).

For the reduction of (+)-*trans*-II, the optical rotation of the reaction mixture was taken before and after the reaction. The percentage of (+)-*trans*-II left after the reduction was calculated according to the following equation:

$$(+)\text{-}trans\text{-II}(\%) = \frac{[\alpha]^D}{[\alpha]^D_0} \times 97.8\%$$

where $[\alpha]^D$ and $[\alpha]^D_0$ are the observed rotations of the reaction mixture after and before the reduction. The yield of (±)-*trans*-II formed during the reduction was obtained from the equation

$$(\pm)\text{-}trans\text{-II}(\%) = 97.8 - [(+)\text{-}trans\text{-II} + (\pm)\text{-}cis\text{-II}]\%$$

The yield of (±)-*cis*-II was determined from GC and GC/IR measurements. The results of these reductions are listed in Table I.

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Registry No. Ia, 6640-25-1; Ib, 6952-89-2; *cis*-II, 1145-91-1; *cis*-II$^{\bullet-}$, 137693-41-5; (±)-*cis*-II, 58641-90-0; *trans*-II, 1145-92-2; *trans*-II$^{\bullet-}$, 127909-64-2; (+)-*trans*-II, 21019-54-5; (±)-*trans*-II, 137693-42-6; III, 5407-91-0; *cis*-IVa, 137595-86-9; *trans*-IVa, 63016-92-2; *cis*-IVb, 137595-87-0; *trans*-IVb, 137595-88-1; V, 126314-18-9; i, 137595-89-2; DMBI, 3652-92-4; *p*-chlorobutyrophenone, 4981-63-9; *p*-bromobutyrophenone, 4981-64-0.

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