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THE BEHAVIOR OF (α-HYDROXY)-CYCLOPROPYLCARBINYL FREE RADICALS

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The unique ability of certain neighboring groups to facilitate carbonium ion formation has stimulated significant research effort and some controversy (1). In the formation of free radical intermediates, neighboring groups are much less effective. The only large neighboring group effects are observed for molecules possessing heavy atoms (2) and (3).

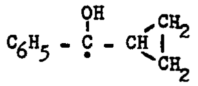
Of particular interest are those carbonium ions containing neighboring cyclopropyl groups. Roberts and coworkers have postulated, on the basis of kinetic and product isolation evidence, that the bicyclobutonium ion (I) is responsible for the increased stability of the cyclopropylcarbinyl system and that rearranged products result because of its intermediacy.

I

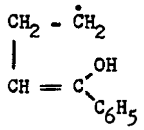
They predict by means of molecular orbital theory (4), that the same stability will not be imparted to developing cyclopropylcarbinyl free radicals or carbanions.

Some workers have observed neighboring group participation by an adjacent cyclopropyl moiety in free radical reactions. Neighboring group stabilization by cyclopropyl has been observed in both decomposition and addition reactions (5). Rearrangements of cyclopropylcarbinyl free radicals to the corresponding allylcarbinyl systems have been observed. The extent of rearrangement and the degree of rate acceleration appear to be a function of several variables.

It occurred to us that a unique cyclopropylcarbinyl free radical would be the (α-hydroxy)-cyclopropylcarbinyl free radical (II). Rearrangement of this free radical would lead to an enolate radical (III) which, upon chain transfer and tautomerization, would produce the corresponding open chain ketone. In addition, owing to the interesting stability of free radicals possessing α-hydroxy substituents (6) it was felt that an α-oxygen atom might magnify any contributions to the stability of the free radical intermediate by the cyclopropyl group.



(II)



(III)

As an approach to the problem, we have attempted to generate (α-hydroxy)-cyclopropylcarbinyl free radicals in solution by known methods. We have treated phenylcyclopropylcarbinol with di-*t*-butyl peroxide (DTBP) at 130° (7), and we have treated phenyl cyclopropyl ketone with 2-butanol and DTBP at 130° (8). In addition, we have attempted photoreduction of phenyl cyclopropyl ketone in alcoholic solvents (9).

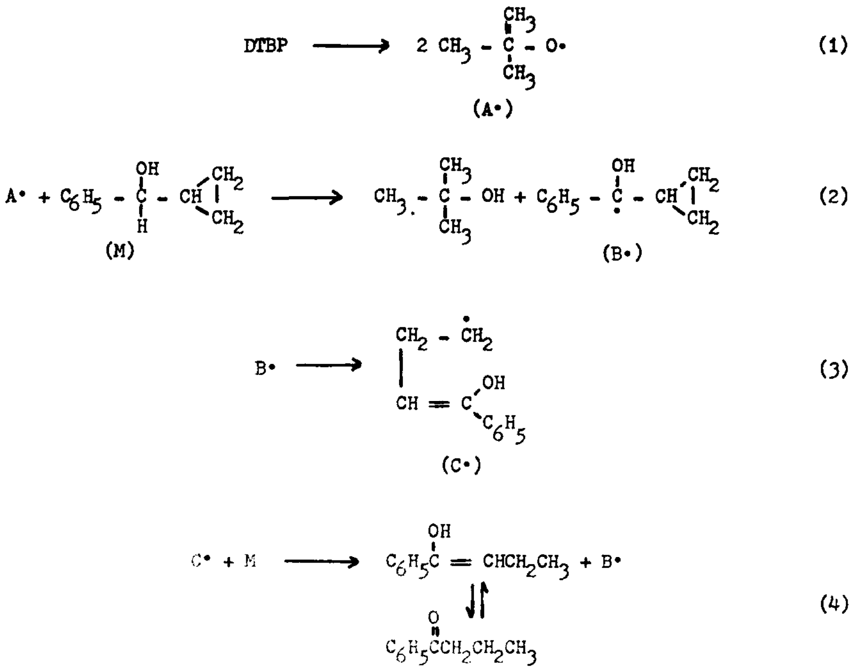
Treatment of phenylcyclopropylcarbinol with DTBP produced butyrophenone and phenyl cyclopropyl ketone. The results of a typical experiment as obtained by vapor phase chromatographic analysis by means of a column of 5% carbowax 4000 on firebrick at 125° and 40° are shown in Table I.

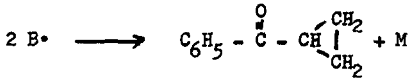
TABLE I

The Reaction of Phenylcyclopropylcarbinol with DTBP at 130°

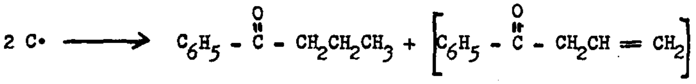
Reactants (amounts in mmoles)		Products	
Cyclopropylphenylcarbinol	6.94	t-Butyl Alcohol	.64
DTBP	.73	Acetone	.11
		Butyrophenone	.41
		Cyclopropyl Phenyl Ketone	.43
		Cyclopropylphenylcarbinol (Residual)	4.54

We propose the following mechanism for the reaction of phenylcyclopropylcarbinol with DTBP (1-7).

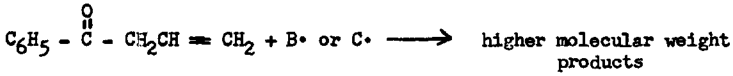




(5)



$$2\,C\cdot \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH_2CH_3+\left[C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH=CH_2\right] \tag{6}$$



$$C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH=CH_2+B\cdot \text{ or } C\cdot \longrightarrow \text{higher molecular weight products} \tag{7}$$

Table II lists the products, measured by vapor phase chromatographic analysis as before, obtained from cyclopropyl phenyl ketone, 2-butanol and DTBP.

TABLE II

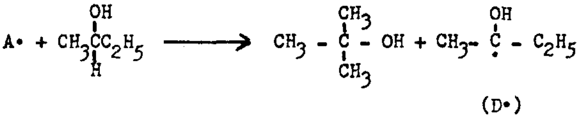
The Reaction of Cyclopropyl Phenyl Ketone with 2-Butanol and DTBP at 130°

Reactants (amounts in mmoles)	
Phenyl Cyclopropyl Ketone	1.69
DTBP	1.54
2-Butanol	31.36

Products	
Acetone	0.41
t-Butyl Alcohol	2.50
2-Butanone	1.89
Butyrophenone	0.60
Cyclopropylphenyl-carbinol	0.26
Phenyl Cyclopropyl Ketone (Residual)	0.35

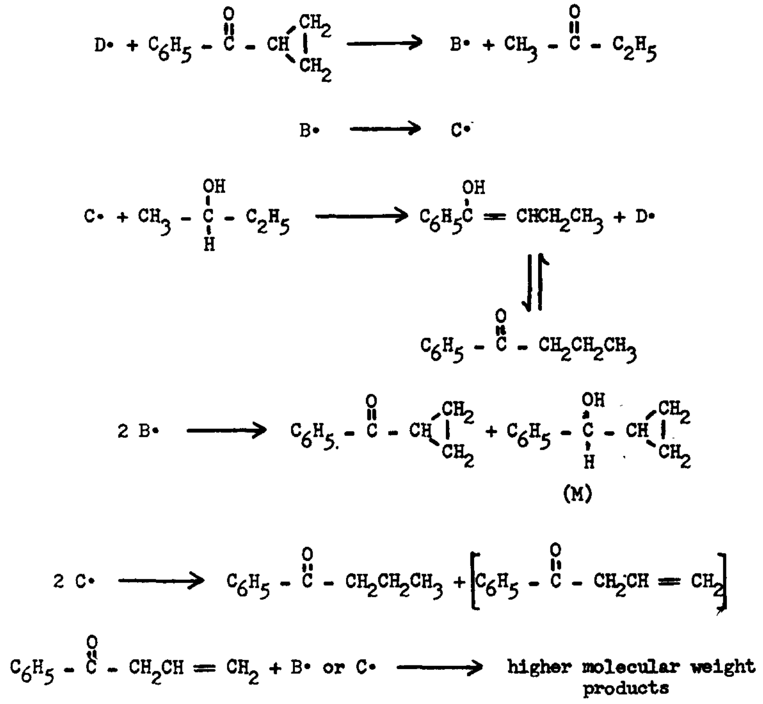
We propose the following mechanism for the reaction of cyclopropyl phenyl ketone with 2-butanol and DTBP (8-16).

$$\text{DTBP} \longrightarrow 2\,A\cdot \tag{8}$$



$$A\cdot + CH_3\underset{H}{\overset{OH}{C}}C_2H_5 \longrightarrow CH_3-\underset{CH_3}{\overset{CH_3}{C}}-OH + CH_3-\underset{\cdot}{\overset{OH}{C}}-C_2H_5 \tag{9}$$

(D•)



$$\mathrm{D\cdot + C_6H_5-\overset{O}{\overset{\|}{C}}-CH\!\begin{smallmatrix}\diagup CH_2\\ |\\ \diagdown CH_2\end{smallmatrix} \longrightarrow B\cdot + CH_3-\overset{O}{\overset{\|}{C}}-C_2H_5} \tag{10}$$

$$\mathrm{B\cdot \longrightarrow C\cdot} \tag{11}$$

$$\mathrm{C\cdot + CH_3-\underset{H}{\overset{OH}{C}}-C_2H_5 \longrightarrow C_6H_5\overset{OH}{C}=CHCH_2CH_3 + D\cdot} \tag{12}$$

$$\rightleftharpoons$$

$$\mathrm{C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH_2CH_3} \tag{13}$$

$$\mathrm{2\,B\cdot \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-CH\!\begin{smallmatrix}\diagup CH_2\\ |\\ \diagdown CH_2\end{smallmatrix} + C_6H_5-\underset{H}{\overset{OH}{C}}-CH\!\begin{smallmatrix}\diagup CH_2\\ |\\ \diagdown CH_2\end{smallmatrix}} \tag{14}$$

(M)

$$\mathrm{2\,C\cdot \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH_2CH_3 + \left[C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH=CH_2\right]} \tag{15}$$

$$\mathrm{C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2CH=CH_2 + B\cdot\ or\ C\cdot \longrightarrow}\ \text{higher molecular weight products} \tag{16}$$

Attempts to photoreduce cyclopropyl phenyl ketone in alcohol solutions were frustrated by an extremely low quantum yield of photoreduction. This observation parallels a similar finding by Brown and Coyle (10). Work is being continued on this aspect of the problem.

Hydrogen atom addition to the carbonyl group oxygen provides a method for determining the relative stabilities of transition states in which aryl alkyl carbinol radicals are being produced. Listed in Table III are the relative reactivities for addition of a hydrogen atom to the carbonyl oxygen of a series of aryl alkyl ketones.

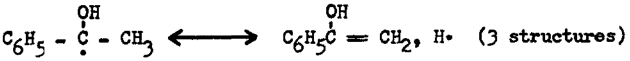
TABLE III [a]

Relative Reactivities of Aryl Alkyl Ketones Towards Hydrogen Atom Addition

Ketone	k Aryl Alkyl Ketone / k Isobutyrophenone
Acetophenone	7.60 + .80
Propiophenone	3.33 + .20
Isobutyrophenone	1.00
Cyclopropyl Phenyl Ketone	36.00 + 1.00

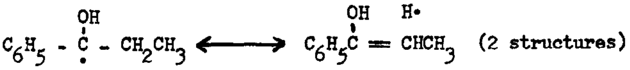
[a] Determined by the method of Huyser and Neckers (8).

The relative reactivities of acetophenone, propiophenone and isobutyrophenone toward hydrogen atom addition can be explained by the hyperconjugative (or inductive) contributions of the α-hydrogen atoms to the free radical IV, V and VI .



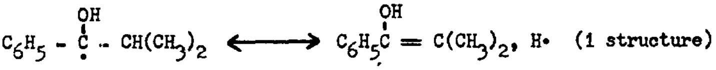
$$C_6H_5 - \underset{\bullet}{\overset{OH}{C}} - CH_3 \longleftrightarrow C_6H_5\overset{OH}{C} = CH_2,\ H\cdot \quad \text{(3 structures)}$$

(IV)



$$C_6H_5 - \underset{\bullet}{\overset{OH}{C}} - CH_2CH_3 \longleftrightarrow C_6H_5\overset{OH}{C} = \overset{H\cdot}{CHCH_3} \quad \text{(2 structures)}$$

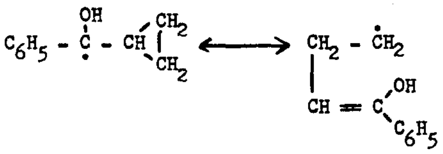
(V)



$$C_6H_5 - \underset{\bullet}{\overset{OH}{C}} - CH(CH_3)_2 \longleftrightarrow C_6H_5\overset{OH}{C} = C(CH_3)_2,\ H\cdot \quad \text{(1 structure)}$$

(VI)

On this basis, one would expect cyclopropyl phenyl ketone to be about as reactive as isobutyrophenone. However, cyclopropyl phenyl ketone is some 36 times more reactive toward hydrogen atom addition. Since products are isolated which point to a cyclopropylcarbinyl - allylcarbinyl radical rearrangement, stabilization of the free radical through contributions by both the allylcarbinyl and the cyclopropylcarbinyl systems to the hybrid may be indicated. The highly electronegative oxygen atom located on the carbon at which the free radical is developing (VII) causes the radical carbon to have more electropositive character.



(VII)

Experiments with similar systems, including these containing cyclobutyl groups, are in progress.

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REFERENCES

1. See, for example, a. H. C. Brown, "The Transition State", Special Publication #16, The Chemical Society, London, 1962; b. S. Winstein and R. Baker, *J. Am. Chem. Soc.*, **86**, 2071 (1964).

2. See, for example, a. J. C. Martin and T. W. Koenig, *J. Am. Chem. Soc.*, **86** 1771 (1964); b. J. E. Leffler, D. D. Faulkner and C. Petropoulos, *J. Am. Chem. Soc.*, **80**, 5435 (1958).

3. R. H. Mazur, W. N. White, D. A. Semenov, C. D. Lee, M. S. Silver and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959).

4. J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 3542 (1951).

5. a. H. Hart and R. A. Cipriani, *J. Am. Chem. Soc.*, **84**, 3697 (1962); H. Hart and D. P. Wyman, *ibid.*, **81**, 4891 (1959); b. C. G. Overberger and A. Lebovits, *ibid.*, **76**, 2722 (1954); c. E. S. Huyser and J. D. Taliaferro, *J. Org. Chem.*, **28**, 3442 (1963); d. H. C. Brown and M. Borkowski, *J. Am. Chem. Soc.*, **74**, 1894 (1952); e. J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 2509 (1951).

6. C. Walling and M. J. Gibian, J. Am. Chem. Soc., 86, 3902 (1964).

7. E. S. Huyser and C. J. Bredeweg, J. Am. Chem. Soc., 86, 2401 (1964).

8. E. S. Huyser and D. C. Neckers, J. Am. Chem. Soc., 85, 3641 (1963).

9. W. M. Moore, G. S. Hammond and R. P. Foss, J. Am. Chem. Soc., 83, 2789 (1961).

10. W. G. Brown and D. J. Coyle, U. S. Dept. of Commerce Office Tech. Serv. PB Rept. 171, 156 (1960). Chem. Absts., 57, 4219 (1962).