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Migrations of Cyclopropylmethyl Groups in Thermal and Acid Catalyzed Reactions of Cyclohexadienones[1]

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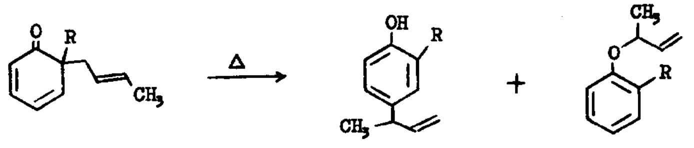
Thermal migrations of allyl groups in linearly-conjugated cyclohexadienones (e.g., eq. 1)



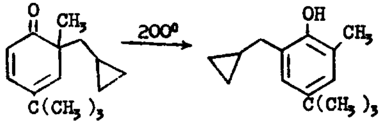
(1)

proceed readily at temperatures as low as 100°.[2] The same reactions, as well as a disconcerting variety of other rearrangements, occur at room temperature in the presence of very dilute acid catalysts.[3]

Analogs of Cope or Claisen rearrangements in which cyclopropylmethyl groups have replaced allyl groups have never been observed.[4] The very mild conditions necessary for thermal migrations of allyl groups in cyclohexadienones suggest that similar migrations of cyclopropylmethyl groups might occur at not unreasonable temperatures. The ease of formation of the cyclopropylmethyl carbonium ion[5] suggests that acid-catalyzed migrations of cyclopropylmethyl groups should similarly occur under very mild conditions. In view of the pronounced tendency for internal rearrangement of the cyclopropylmethyl carbonium ion,[5] simultaneous rearrangements of the cyclopropyl methyl group and the cyclohexadienone ring might be anticipated.

We have previously reported the syntheses of cyclohexadienones bearing cyclopropylmethyl groups at the quaternary carbons.[6] In this communication, we report the rearrangements of these molecules on heating or in acid solutions.

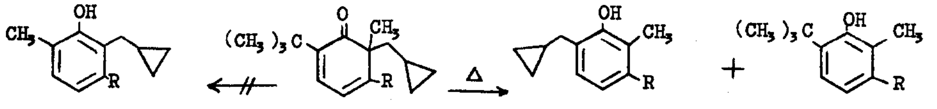
Dienone 1 was unchanged after prolonged heating at 100-150°. After several days at 200° in diglyme (diethylene glycol dimethyl ether), however, 1 rearranged completely to give a quantitative yield of 2. No evidence could be observed for formation of any other reaction product.



1 2

Similar rearrangements proceeded readily even when the migration terminus was already substituted. Rearrangement of dienone 3 in diglyme at 200° gave 4 as the only rearrangement product, accompanied by 10% of the cleavage product 5.

Rearrangement of dienone 6 similarly gave 7 as the only detectable rearrangement product.



9, R = CH_3

3, R = H
6, R = CH_3

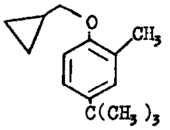
4, R = H
7, R = CH_3

5, R = H
8, R = CH_3

(Rearrangement was again accompanied by cleavage to phenol 8). Phenol 9 was synthesized for comparison, and shown by vpc to constitute less than 0.1% of the reaction product. Thus, rearrangement proceeds by migration of the cyclopropylmethyl group, which migrates at least 10^3 times as fast as a methyl group.

The presence of a t-butyl group at C-2 has surprisingly little effect on the rate of rearrangement. Dienone 1 rearranges only four times as rapidly as 3 (k_1 for 1 = $1.01 \times 10^{-5} sec^{-1}$, k_1 for 3 = $0.25 \times 10^{-5} sec^{-1}$), even though the cyclopropylmethyl group migrates to a "neopentyl" position.[7]

The rearrangements of 1 and 6 proceed with clean first order kinetics, ruling out bimolecular rearrangement mechanisms. Dissociation of the dienones to cyclopropylmethyl and phenoxy radicals (or ions), followed by recombination, should produce ethers as major products, or, when the para-position is unsubstituted, the products of substitution at that position. Since none of these products were observed, such mechanisms have been rejected. No evidence suggesting that



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these rearrangements proceed by free radical chains has been observed. Such chains would also be expected to give products of attack at oxygen or C-4, particularly when C-6 is already substituted with a t-butyl group.[8] The possibility that the cyclopropylmethyl group first migrates to the oxygen atom and then to the ortho-carbon was excluded when it was found that ether 10 was stable under conditions in which 1 rearranges readily to 2

Two feasible, symmetry allowed, rearrangements which are consistent with the data presented above are: 1) a direct [1,5] sigmatropic shift of the cyclopropylmethyl group from C-6 to C-2; and 2) migration with cleavage and reformation of the cyclopropyl ring (a [$\pi 2_s + \pi 2_s + \sigma 2_s + \sigma 2_a$] reaction) as shown in figure A.

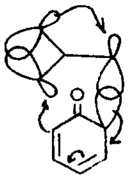
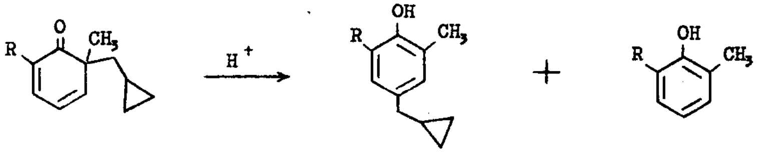


Fig. A Rearrangement via Mechanism 2

Rearrangement of 3-d_2[6], containing 1.7 $\pm$ 0.05 atoms of deuterium at the methylene group bearing the three membered ring, gave 4 bearing 1.7 $\pm$ 0.05 atoms of deuterium at the benzylic methylene group. This is clearly inconsistent with mechanism 2. Migrations of the cyclopropylmethyl groups in these reactions, therefore, appear to be among the rare [1,5] sigmatropic carbon shifts which are not also 1,2 migrations.[9,10]

Reaction of 1 or of 6-cyclopropylmethyl-6-methylcyclohexa-2,4-dien-1-one[6] with 0.1 to 2N HCl in methanol resulted solely in cleavage to 4-*t*-butyl-2-methylphenol and *o*-cresol, respectively. Reaction of dienone 3 with 1.0 to 2.0 NHCl in methanol, or of 11 with 0.1N HCl in methanol, also resulted largely in cleavage, but gave approximately 10% of the rearrangement products 12 and 13. Rearrangement of 3-d_2 bearing 1.8 $\pm$ 0.1 atoms of deuterium at the exocyclic methylene group[6] gave 7 containing 0.8 $\pm$ 0.1 atoms of deuterium at the benzylic methylene group. When the reaction was interrupted after one half-life, it was found that the deuterium distribution in the recovered 6-d_2 was unchanged. When 12-d_2 bearing 1.8 $\pm$ 0.1 atoms of deuterium at the benzylic methylene group[6] was kept in 1N methanolic HCl for long periods, no change in the deuterium distribution could be detected. The appreciable equilibration of the deuterium label had therefore taken place during the rearrangement process.



3, R = t-Bu
11, R = CH_3

12, R = t-Bu
13, R = CH_3

R = t-Bu, CH_3

Formation of 12 and 13 can most readily be explained as occurring by cleavage of the dienones to phenols and cyclopropylmethyl carbonium ions, which then realkylate the concurrently formed phenols at the *para*-positions. The large degree of equilibration of the methylene carbons of the cyclopropylmethyl group is consistent with many previous observations in such systems[5], but the absence of cyclobutyl substituted phenols is surprising.

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References

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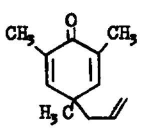
2) D.Y. Curtin and R.J. Crawford, J. Am. Chem. Soc., 79, 3156 (1957); B. Miller, ibid., 87, 5115 (1965); B. Miller, J. Org. Chem., 35, 4262 (1970).
3) B. Miller, J. Am. Chem. Soc., 92, 6246 (1970)
4) Replacement of a double bond by a cyclopropane ring in another common thermal process, the Diels-Alder reaction, has been reported, [S. Sarel and E. Breuer, ibid., 81, 6522 (1959)].
5) R. Breslow in "Molecular Rearrangements", P. de Mayo, ed., Interscience Publishers, New York, 1963, pp. 254-276.
6) B. Miller and K.-H. Lai, Chem. Comm., 334 (1971)

7) In contrast, we have observed that dienone i rearranges readily to allyl 2,4,6-trimethylphenyl ether at 120°, while dienone ii is unchanged after 5 hours at 225°.



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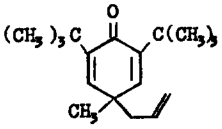

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8) We have previously found that the cyclopropylmethyl radical opened entirely to the allylcarbinyl radical when it acted as a chain carrier in a radical chain reaction [B. Miller, and K.-H. Lai, *Journal of the Amer. Chem. Soc.*, in press.

9) a) Alkyl groups in internal positions in dihydropyrenes undergo facile [1,5] shifts. These may also be classified as [1,9] or [1,13] shifts. [V. Boekelheide and E. Sturm, *J. Am. Chem. Soc.*, 91, 902 (1969); V. Boekelheide and T.A. Hylton, *ibid.*, 92, 3669 (1970)].

9) b) Methyl groups undergo [1,5] shifts, along with other reactions, in cyclohexadienes at *ca.* 400° [C.W. Spangler and D.L. Boles, Abstr. of the 161st Meeting of the ACS, Los Angeles, 1971, 161.]

10) Rearrangement by a series of 1,2 shifts, as shown below, is not excluded by the evidence. Such shifts should be sterically reasible only if they proceed by forbidden $[\sigma 2_s + \pi 2_s + \pi 2_a + \pi 2_a]$ processes, however.