

CYCLOPENTENONE AND CYCLOHEXENONE ANNULATIONS VIA ACID-CATALYZED
 1,2- AND 1,3-ACYL MIGRATION OF 2-VINYLCYCLOBUTANONES. REARRANGEMENT ROUTE TO
 SPIRO- AND ANGULARLY SUBSTITUTED FUSED-CYCLOPENTENONES.

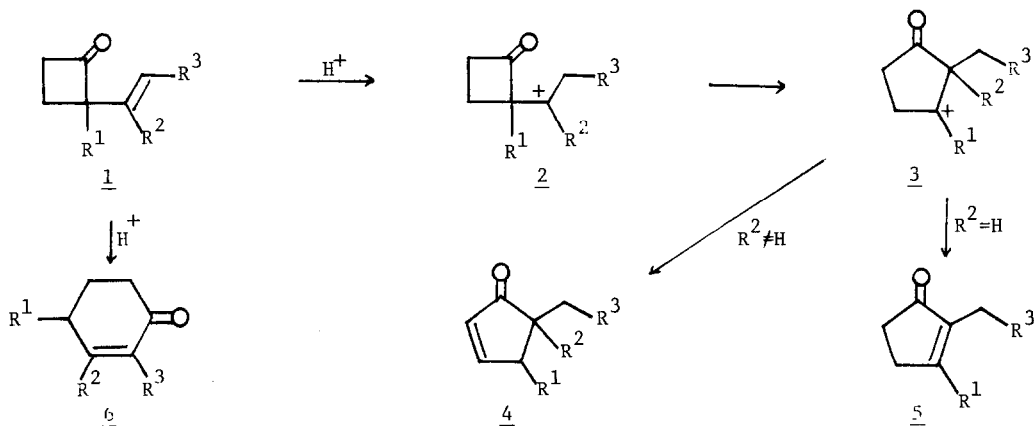
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Abstract: In the presence of acid, 2-alkyl-2-vinylcyclobutanones rearrange mainly by a 1,2-acyl migration to give cyclopentenones while 2-vinylcyclobutanones lacking 2-alkyl substituents undergo a 1,3-acyl migration to produce cyclohexenones; the former rearrangement can be used to produce angularly substituted fused bicyclic systems.

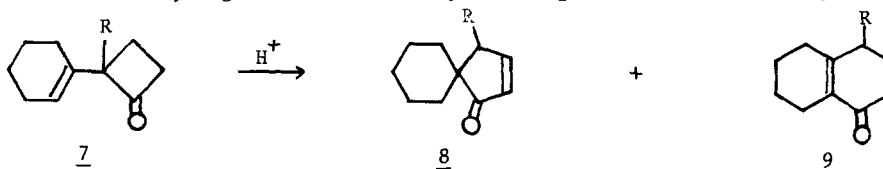
In view of the fact that reasonably general preparations of 2-vinylcyclobutanones have only recently become available,¹ it is not surprising that negligible research on their rearrangements has been performed. Nevertheless, there are a number of hints in the literature that 2-vinylcyclobutanones may undergo synthetically useful ring expansions. Aside from the rearrangements of 2-arylcyclobutanones bearing cation-stabilizing groups at the 3-positions,² we can cite the thermally-induced rearrangement of 2-alkylidenecyclobutanones to cyclohexenones in which 2-vinylcyclobutanones have been postulated as intermediates,³ the presence of the latter in a photostationary state with 3-cycloalkenones,⁴ and the acid-catalyzed rearrangement of a cyclopentenocyclobutanone to a mixture of [2.2.1]-bicyclic β,γ -unsaturated ketones.⁵

One type of rearrangement which we anticipated would be synthetically useful and which would seem *a priori* to be mechanistically and thermodynamically favorable is the acid-catalyzed conversion of 1 to 4 or 5 shown in Scheme I. Although we have not been able to find an example of this type of rearrangement in the literature, a related pinacol rearrangement, presumably proceeding through intermediates analogous to 2 and 3 ($R^1 = \text{OSiMe}_3$), has been reported⁶ and we have observed the corresponding thio analogue of this pinacolic rearrangement ($R^1 = \text{SPh}$).⁷

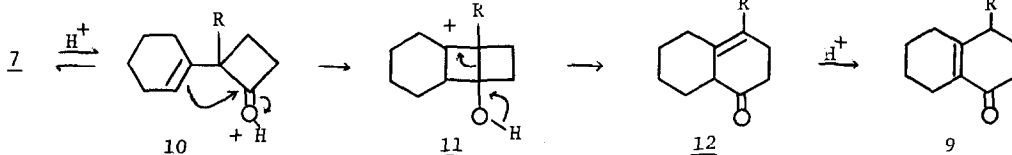


Scheme I

This type of 1,2-rearrangement (1 \rightarrow 4 or 5) was indeed observed for cases in which $R^1 =$ alkyl; however, it was accompanied by a minor but significant degree of 1,3-rearrangement (1 \rightarrow 6). For example, in the presence of 10:1 methanesulfonic acid/ P_2O_5 (Eaton's reagent)^{8,9} 7 ($R = Me$)¹ rearranged to provide 51% of 8 ($R = Me$) and 13% of 9 ($R = Me$). Furthermore, the normethyl analogue (7; $R = H$) yielded no 1,2-rearrangement product; only the 1,3-rearrangement product (9; $R = H$) was formed. As indicated in the Table, the 1,3-rearrangement is general for substrates which have a hydrogen atom on the vinyl-bearing carbon atom of the cyclobutane ring.

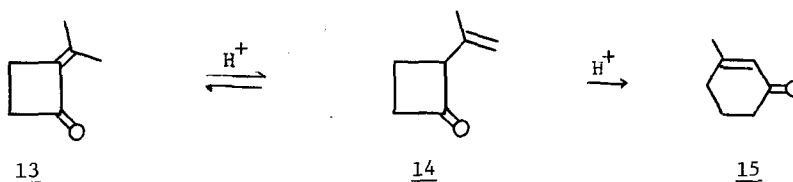


The 1,3-rearrangement (7 \rightarrow 9) is conceptually related to the one mentioned above.⁵ A reasonable mechanism for the 1,3-rearrangement (Scheme II) involves protonation of the carbonyl group and electrophilic attack of the resulting cation on the olefinic linkage to yield the strained bicyclic cation 11 which would be expected to spring open to 12; acid catalyzed migration of the double bond into conjugation then yields 9. This mechanism resembles that proposed for the 1,3-acyl migration observed upon acid treatment of certain bicyclic 3-acylcyclobutenes¹⁰ and is an interesting alternative to that involving a double bond migration in



Scheme II

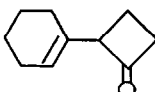
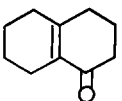
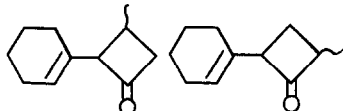
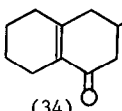
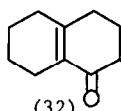
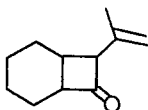
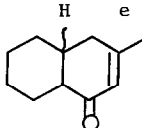
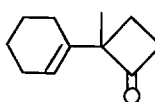
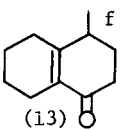
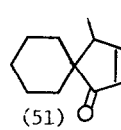
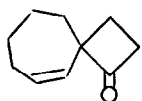
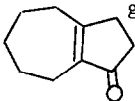
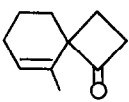
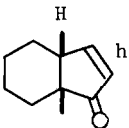
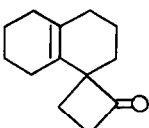
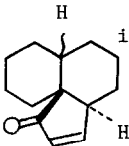
an acylium ion as proposed by Lee-Ruff, Turro, Amice, and Conia¹¹ to account for rearrangements such as 13 \rightarrow 15; all that is required is prior deconjugation as shown.¹²



The 1,3-rearrangement is interesting synthetically in that it leads to conjugated 1-octalones in which the double bond can be either in a single ring or common to both rings depending on the choice of substrate (entries 1-4). This process is presumably in competition with the 1,2-rearrangement which is depicted in Scheme I. It is reasonable to suppose that the latter is favored when $R^1 =$ alkyl so that the cation in the intermediate (2) would be tertiary rather than secondary, which it would be if $R^1 = H$.

The 1,2-rearrangement observed with 2-alkyl-2-vinylcyclobutanones is a particularly promising method of cyclopentenone annulation.^{10,13} One can completely avoid the 1,3-acyl migration by using as substrate a spiro vinylcyclobutanone, derived from a cycloalkenone¹ (entries

TABLE. Acid-Catalyzed Rearrangement of 2-Vinylcyclobutanones

| Entry | Cyclobutanone ^a | Reagent (time, min.) | Product (% Yield) ^b |
|-------|---|--|--|
| 1 |  | MeSO ₃ H/P ₂ O ₅ (15) 10:1 |  (65) ^d |
| 2 |  | " " |  (34)  (32) |
| 3 |  | " " |  (41) H e |
| 4a |  | " " |  (13)  (51) |
| 4b | " | 20% MeSO ₃ H/CH ₂ CH ₂ (600) | (8) (53) |
| 5 |  | MeSO ₃ H/P ₂ O ₅ (30) 10:1 |  (48) g |
| 6 |  | MeSO ₃ H (30) |  (52) H h |
| 7 |  | " (45) |  (33) H i |

a. For preparation see ref. 1. b. All yields are for chromatographed and distilled (Kugelrohr) material; all products are liquids. c. R. T. Conley and B. E. Nowak, *J. Org. Chem.*, **26**, 692 (1961). d. Lower yields were obtained by use of *p*-toluenesulfonic acid in benzene at reflux for 2.5 days or polyphosphorus acid at 100° for 1 h. The latter solution, which was the reagent used by Lee-Ruff,¹ was extremely viscous. e. P. DeMayo and H. Takeshita, *Can. J. Chem.*, **44**, 440 (1963). f. P. S. Wharton and B. T. Aw, *J. Org. Chem.*, **31**, 3787 (1966). g. P. A. Plattner and G. Büchi, *Helv. Chim. Acta*, **29**, 1608 (1946). h. M. Karpf and A. S. Dreiding, *ibid.*, **62**, 852 (1979). i. ₁ Appears to be a single stereoisomer according to TLC and 90 MHz NMR; a γ -lactone (IR 1770 cm⁻¹; m/e 208) was also produced in 11% yield.

5-7); the 1,3-rearrangement product would violate Bredt's rule. As demonstrated by entries 6 and 7, this rearrangement constitutes a novel method for constructing fused cyclopentenone rings with angular substituents at the α -carbon atom.^{14,15} Since the products of these rearrangements are themselves cycloalkenones, they are candidates for a subsequent cyclopentenone annulation (entry 7).

It appears likely that varying the acid conditions could lead to an improvement in the yields reported in the Table.¹⁶ Furthermore, one could envision methods of controlling the nature of the rearrangement (1,2 vs. 1,3) based on the mechanistic hypotheses outlined above. Finally, the use of electrophiles other than protonic acids could greatly increase the synthetic utility of the 1,2-rearrangement. These aspects are under active study.

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References and Notes

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