

# Acid-Catalyzed Rearrangements of $\beta,\gamma$ -Unsaturated Ketones<sup>1a</sup>

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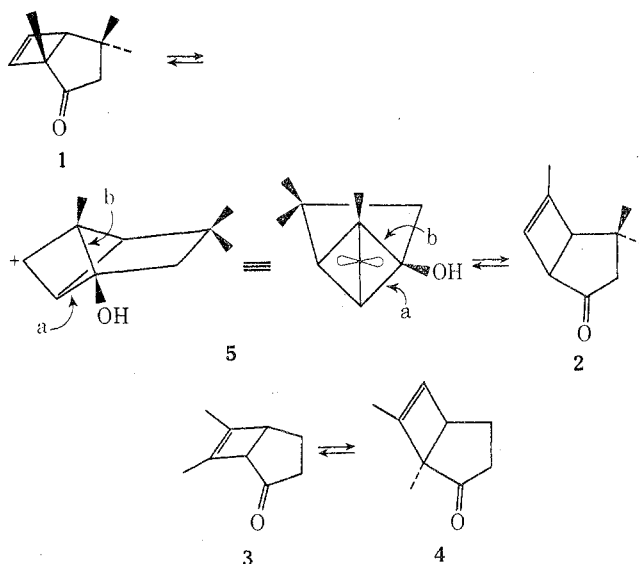
In 1960, Büchi and Burgess reported that the bicyclo[3.2.0]hept-6-en-2-one **1** was converted into its isomer **2** by the action of *p*-toluenesulfonic acid (TsOH) in hot benzene, as well as by the absorption of ultraviolet light.<sup>2</sup>

Since 1960 numerous groups have investigated the photochemical transformations of  $\beta,\gamma$ -unsaturated ketones, but far less effort has been expended in exploration of the acid-catalyzed isomerizations of these homoconjugated systems. In this Account we shall explore the rearrangements of and additions to those  $\beta,\gamma$ -unsaturated ketones in which either the carbonyl group or the double bond, or both, is held in a strained environment. Some chemistry of the corresponding saturated derivatives will also be discussed. Primary emphasis will be placed on work done by the authors at the University of South Carolina.

The isomerization **1**  $\rightarrow$  **2** is reported to be nearly quantitative; the mixture resulting from heating **1** in benzene containing TsOH contained 92.5% of **2** and 7.5% of recovered **1**. Similar treatment of **2** gave only recovered **2**. These data reflect that **1** and **2** are equilibrated by acid treatment and that the equilibrium mixture contains >90% of **2**. The greater stability of **2** may result from the removal of a 1:3 methyl-methyl interaction; however, a more likely explanation is that the enthalpy of **2** is lower than that of **1** by *ca.* 1.5 kcal/mol as a result of methyl substitution on the double bond.<sup>3</sup> The acid-catalyzed equilibration of **3** and **4** likewise provides a mixture in which the more highly substituted olefin predominates; the equilibrium mixture contains 95% of **3** and 5% of **4**.<sup>4</sup>

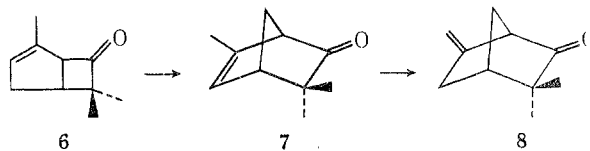
These acid-catalyzed 1,3-acyl shifts occur by donation of a pair of  $\pi$  electrons from the  $\gamma$  carbon to the electron-deficient carbonyl carbon to form the cyclobutonium ion **5**. This intermediate is probably stabilized by overlap of the vacant p orbital with the adjacent bent bonds of the bicyclo[1.1.1]pentane system.<sup>5</sup> Deactivation of **5** by cleavage of bond a regenerates **1**, and rupture of bond b yields **2**.

It is a matter of synthetic importance to note that the interconversion of  $\beta,\gamma$ -unsaturated ketones *via* the 1,3-acyl shift causes epimerization of the chiral



enone system. From another point of view, the methyl group at C-4 which is syn to the cyclobutene ring in **1** becomes anti to that ring in **2**. In general, the 1,3-acyl shift appears to be the lowest energy process available to  $\beta,\gamma$ -unsaturated ketones (see below).

The isomerization of **6** to **7** is an example of an irreversible 1,3-acyl shift. This reflects the much lower enthalpy of **7**, making the amount of **6** present at equilibrium undetectable. Further isomerization of **7** to the still more stable **8** may also affect  $K_{eq}$ .<sup>6</sup>



We have found that the tricyclic ketones **9** and **10** are rapidly equilibrated in mild acid to give a mixture containing 90% of the former and 10% of the latter.<sup>7</sup> On the other hand, **11** was recovered unchanged from treatment with TsOH in refluxing benzene,<sup>7</sup> but **12**, formed by irradiation of **11**, reverted quantitatively to **11** during all attempts at its iso-

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(1) (a) Sandoz Pharmaceuticals, Hanover, N. J.; (b) Dow Chemical Company, Midland, Mich.; (c) Tennessee Eastman Company, Kingsport, Tenn.

(2) G. Büchi and E. M. Burgess, *J. Amer. Chem. Soc.*, **82**, 433 (1960).

(3) R. B. Turner, "Theoretical Organic Chemistry, The Kekule Symposium," Butterworths, London, 1959, p 67.

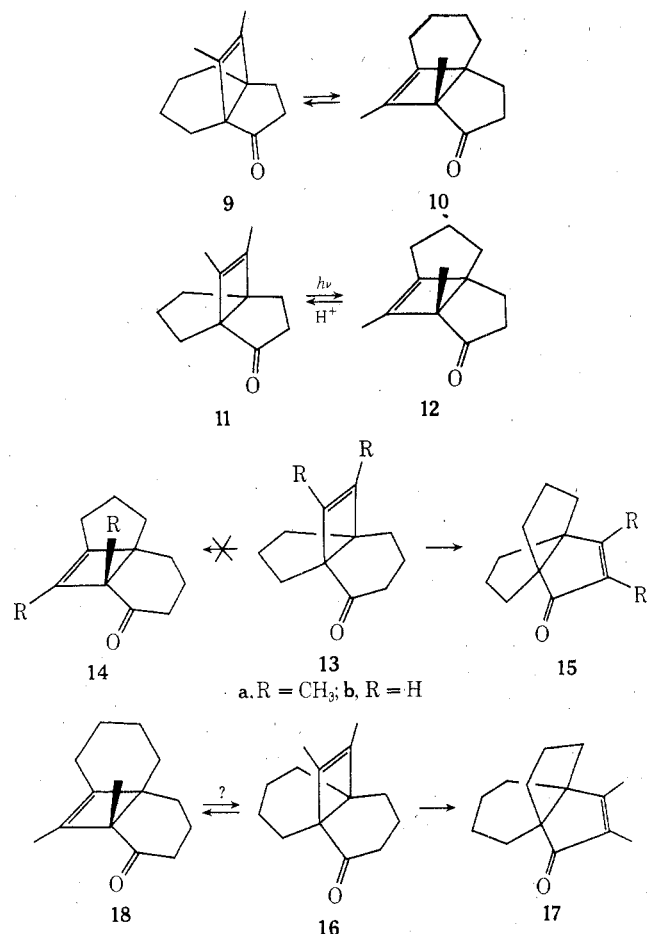
(4) R. L. Cargill, D. M. Pond, and S. O. LeGrand, *J. Org. Chem.*, **35**, 359 (1970).

(5) (a) L. Radom, J. A. Pople, V. Buss, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **92**, 6382 (1970); (b) V. Buss, R. Gleiter, and P. v. R. Schleyer, *ibid.*, **93**, 3927 (1971).

(6) J. J. Beereboom, *J. Amer. Chem. Soc.*, **85**, 3525 (1963); *J. Org. Chem.*, **30**, 4230 (1965).

(7) R. L. Cargill, M. E. Beckham, A. E. Siebert, and J. Dorn, *J. Org. Chem.*, **30**, 3647 (1965).

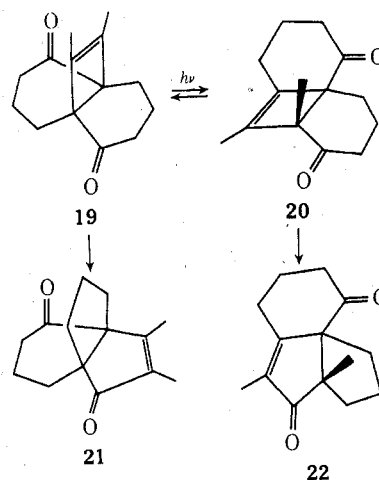
lation.<sup>8</sup> When 13 was treated with acid it gave none of the 1,3-acyl shift product 14, but instead underwent a 1,2-vinyl shift followed by a 1,2-alkyl shift to yield 15 (see below).<sup>9</sup> The absence of the 1,3-acyl shift in 11 and 13 probably results from the high enthalpy (strain) present in the bicyclo[3.2.0]hept-1(7)-ene systems of 12 and 14.<sup>8</sup>



The observation of an acid-catalyzed interconversion of 16 and 18 is precluded by the rapid isomerization of 16 to 17.<sup>10</sup> Although 18 does not suffer the instability of 12 and 14, the availability of a highly exothermic path, 16 → 17, wherein the strain of a cyclobutene ring is relieved and a conjugated enone system is formed, leaves little hope of observing 18 in an acid-catalyzed reaction. Whether irradiation of 16 will produce 18, as in the case of 11 → 12, remains to be determined. Irradiation of 13a or 13b does not appear to produce any of the corresponding 1,3-acyl shift product 14.<sup>11,12</sup>

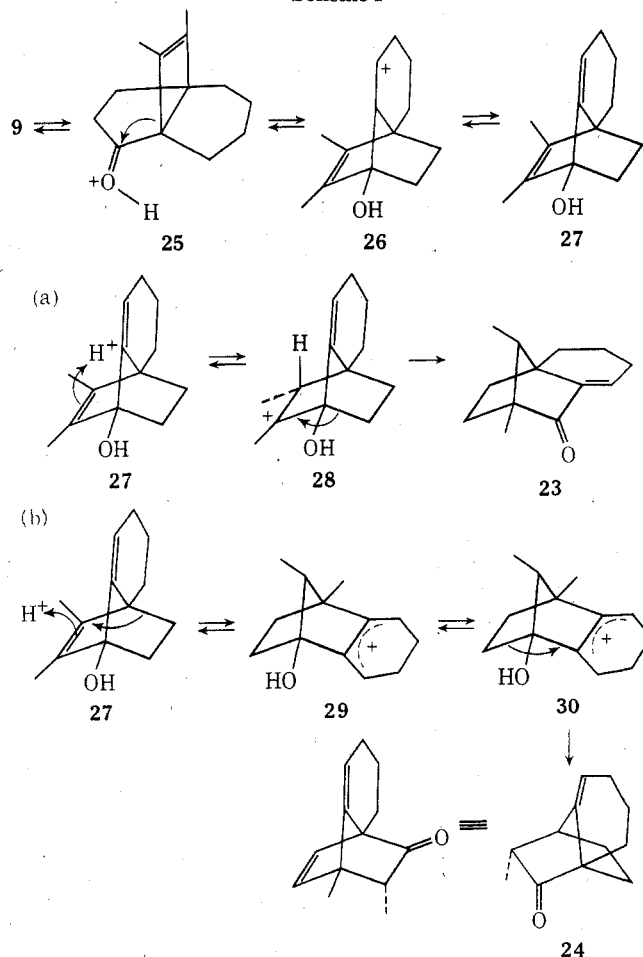
Diones 19 and 20 are interconverted (1,3-acyl shift) by ultraviolet irradiation, but not by treatment with acid. These ketones undergo acid-catalyzed 1,2-vinyl shifts to yield cyclopentenones 21 and 22, respectively. These isomerizations are sufficiently facile that they occur during normal gas chromatographic elution of 19 and 20. Dione 20 has not yet

survived gas chromatography, and its presence in the irradiation mixture (from 19) is indicated by spectroscopic data obtained from the mixture.<sup>13</sup>



The chance discovery in 1964 that ketone 10 underwent isomerization to 9 during attempts at its purification by preparative gas chromatography led us to study the behavior of 9 and 10 in hot benzene containing TsOH. Under these conditions, pure 9, or pure 10, or a mixture of the two, yielded a product mixture which contained approximately equal amounts of 23 and 24. Ketones 23 and 24 comprise 80% of the reaction mixture; two minor components

Scheme I



(8) R. L. Cargill and A. B. Sears, *Tetrahedron Lett.*, 3555 (1972).

(9) R. L. Cargill and J. W. Crawford, *Tetrahedron Lett.*, 169 (1967); *J. Org. Chem.*, 35, 356 (1970).

(10) N. P. Peet and R. L. Cargill, unpublished results.

(11) N. P. Peet, R. L. Cargill, and J. W. Crawford, *J. Org. Chem.*, 38, 1222 (1973).

(12) J. W. Crawford, Ph.D. Thesis, University of South Carolina, Columbia, S. C., 1969.

(13) N. P. Peet and R. L. Cargill, *J. Org. Chem.*, 38, 4281 (1973).

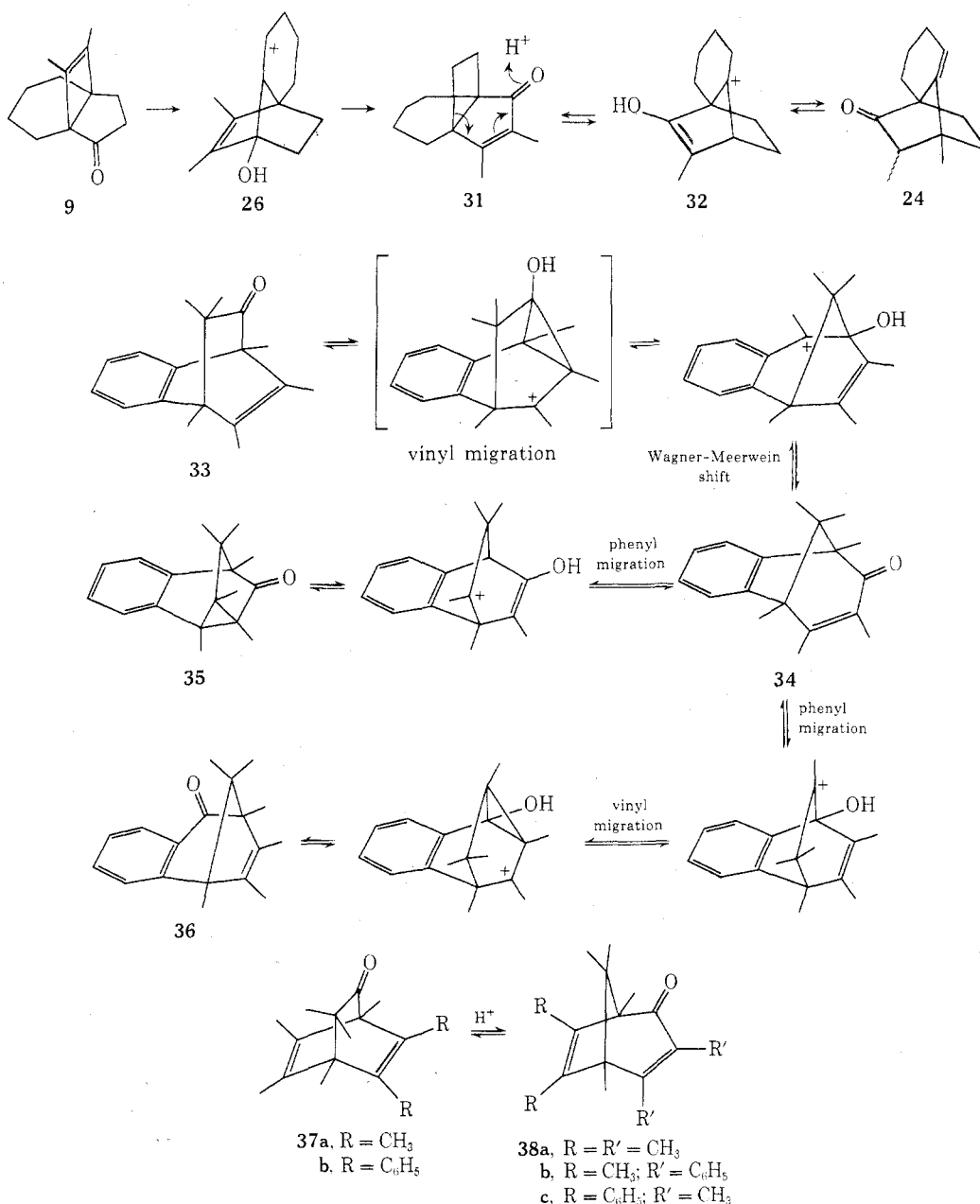
have not been further investigated. The structures of the two major ketones were divined from spectral data and mechanistic reasoning by Professor G. Büchi.<sup>14</sup> Structures **23** and **24** were eventually confirmed by X-ray crystallographic analysis.<sup>15</sup> Both **23** and **24** probably arise from **9** as indicated in Scheme I. Thus, a 1,2-vinyl shift in protonated ketone **25** and loss of a proton in the resulting ion **26** provide dienol **27**. Conversion of **27** into **23** requires only protonation (exo) and an alkyl shift (**27** → **28** → **23**, path a). Protonation (path b) of **27** (again exo) and an alkyl shift gives allylic ion **29**. Isomerization of **29** to **30** followed by a second alkyl shift provides **24**.

An alternative path leading from **9** to **24** involves the isomerization of **9** via **26** to **31**, a change analogous to **13** → **15**. Subsequent isomerization of **31** would provide **32**, the enol of **24**, by migration of a cyclobutane bond to the  $\gamma$  carbon of **31**. Synthetic

**31**, however, was recovered unchanged from treatment with TsOH in boiling *o*-dichlorobenzene, showing this alternate path to be incorrect.<sup>15</sup>

It is interesting to note that even the driving force of cyclopentenone formation is insufficient to cause detectable conversion of ion **26** into **31**. A similar situation holds in the acid-catalyzed hydrations of **3** and **4**, as well as in the isomerization of **11**. On the other hand, solvolysis of *syn*-7-norbornenyl tosylate does yield bicyclo[3.2.0]hept-3-en-2-ol.<sup>16</sup> This is a case where alternate reaction paths are not readily apparent.

Hart and Love<sup>17</sup> have discovered a more complex series of isomerizations of  $\beta,\gamma$ -unsaturated ketones contained in bicyclo[2.2.2]- and bicyclo[3.2.1]octane systems. An equilibrium mixture of ketones **33**–**36** was obtained when any one of the four was heated in trifluoroacetic acid. When the starting ketone was



(14) G. Büchi, personal communication, Feb 23, 1965.

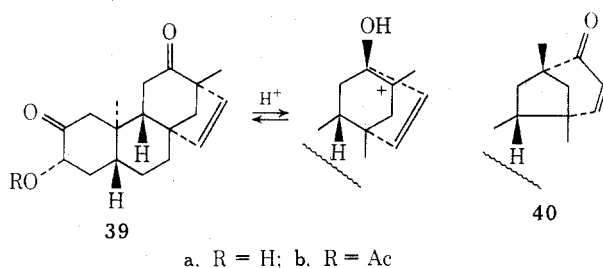
(15) R. L. Cargill, M. E. Beckham, J. R. Damewood, D. M. Pond, W. A. Bundy, and J. Bordner, *J. Org. Chem.*, **37**, 78 (1972).

(16) S. Winstein and E. T. Stafford, *J. Amer. Chem. Soc.*, **79**, 505 (1957).

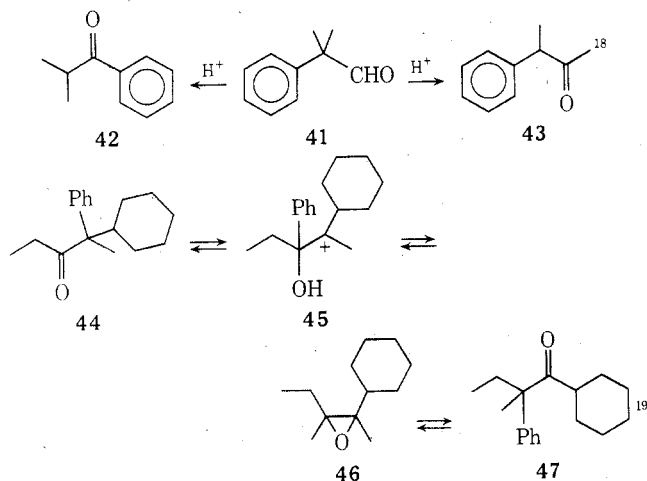
(17) H. Hart and G. M. Love, *Tetrahedron Lett.*, 2267 (1971); *J. Amer. Chem. Soc.*, **93**, 6264 (1971).

33, 34 was formed first, and 35 and 36 were formed from 34. The conversion of 33 into 34 is analogous to the 13 → 15 isomerization already discussed. Formation of the cyclopropyl ketone 35 involves phenyl migration to the  $\beta$  carbon of the enone system of 34 and ring closure between the resulting electron-deficient carbon and the enol, whereas phenyl migration to the carbonyl carbon of 34 (protonated) followed by vinyl migration leads to 36. The acid-catalyzed isomerizations of 37a to 38a and of 37b to 38b and 38c are analogous to the 33 → 34 change. In these isomerizations the absence of cyclopropyl ketones probably reflects their relative thermodynamic instability with respect to 37 and 38. Whether 38b and 38c are interconverted in acid, a process analogous to the interconversion of 34 and 36, was not reported in the preliminary communication.<sup>17</sup>

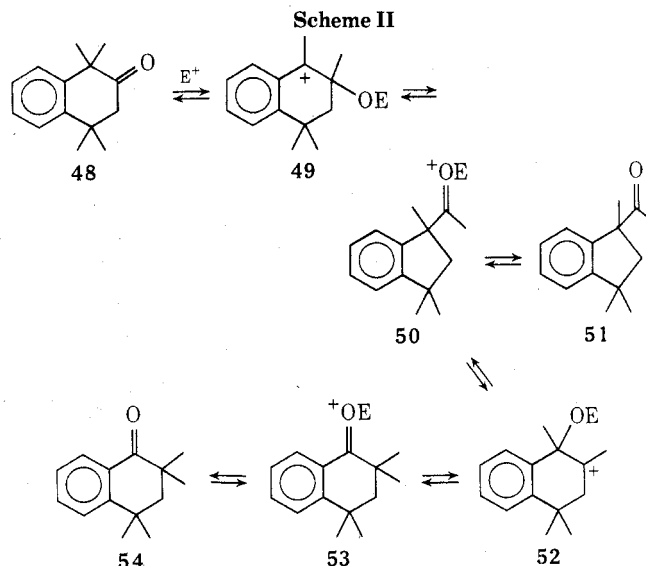
A further example of the 1,2-vinyl shift, followed by a 1,2-alkyl shift, is shown in the conversion 39 → 40.<sup>18</sup>



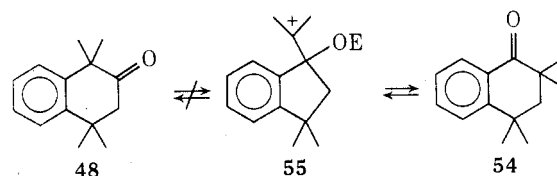
When the  $\beta, \gamma$  unsaturation is incorporated into an aromatic ring, aryl and/or alkyl migrations may be observed, as shown below.<sup>19,20</sup> The examples here are illustrative; numerous other examples are presented in Fry's review.<sup>21</sup>



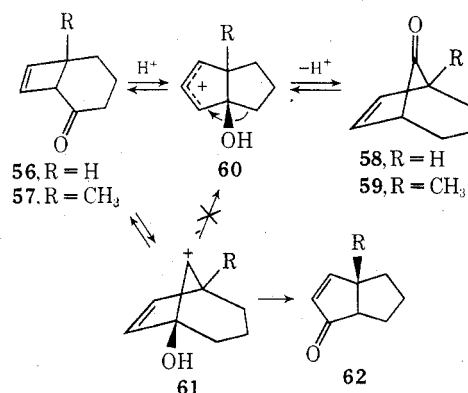
The tetralone 48 is converted into 51 by the action of Lewis acids such as aluminum chloride, ferric chloride, and hydrogen fluoride. Ketone 51 undergoes further isomerization to yield 54. The course of these changes is outlined in Scheme II.<sup>22</sup>



The direct formation of 54 from 48 via 55 was discounted by the authors, who showed that an initial increase in the concentration of 51 corresponded to the decrease in concentration of 48. A subsequent decrease in concentration of 51 was accompanied by a corresponding increase in the amount of 54 present.<sup>22</sup>



Most of the previous discussion has dealt with the chemistry of 3-acylcyclobutenes in which the carbonyl group is part of a cyclopentanone. When the ketone function is incorporated into a six-membered ring, isomerizations may be observed which only indirectly involve the double bond. Thus, the bicyclo[4.2.0]oct-7-en-2-ones 56 and 57 undergo acid-catalyzed isomerization to 58 and 59,<sup>9</sup> respectively. These changes occur via migration of the C<sub>1</sub>-C<sub>6</sub> bond to the carbonyl carbon, followed by collapse of the resulting allylic ion 60 to the observed products. The isomerization which we had originally expected, based on the earlier conversion of 13 into 15 (namely, 1,2-vinyl shift and subsequent collapse of ion 61 to yield 62), was not observed. Furthermore, formation of 60 from an initially formed 61 is ruled out since, in this case, the methyl group from 57 would appear on



(18) M. Laing, P. Sommerville, D. Hanouskova, K. H. Pegel, L. P. L. Picacenza, L. Phillips, and E. S. Waigant, *J. Chem. Soc., Chem. Commun.*, 196 (1972).

(19) J. W. Huffman and L. E. Browder, *J. Org. Chem.*, 27, 3208 (1962).

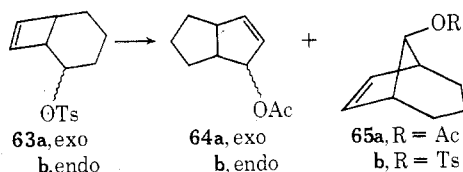
(20) B. Calas and L. Giral, *Bull. Soc. Chim. Fr.*, 2895 (1972).

(21) A. Fry in "Mechanisms of Molecular Migrations," B. S. Thyagarajan, Ed., Wiley-Interscience, New York, N. Y., 1971, pp 113-196.

(22) L. R. C. Barclay, R. H. Young, K. L. Adams, and H. M. Foote, *Can. J. Chem.*, 51, 1598 (1973).

the double bond of **59** rather than at the bridgehead position.

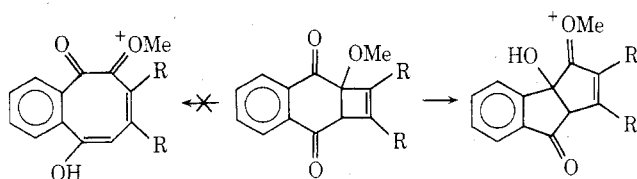
The isomerizations of **56** and **57** may be contrasted with the solvolyses of the corresponding bicyclooctenyl and bicyclooctyl tosylates (brosylates). The crude mixture of epimeric tosylates **63**, obtained from reduction of **56** and conversion to the sulfonate esters, was solvolyzed in acetic acid to yield acetates **64** and **65a** (2:8, respectively).<sup>23</sup> Since the object of this work was to obtain **65b** for solvolytic studies, no analysis of the solvolysis of **63** was reported. It appears, however, that in this solvolysis the major reaction path is that of 1,2-vinyl migration,<sup>23</sup> a result in direct contrast to that observed in the rearrangements of **56** and **57**.



In the solvolyses of the 2-bicyclo[4.2.0]octyl brosylates, most of the product may be reasonably accounted for by migration of the C<sub>1</sub>-C<sub>8</sub> bond to the initial carbonium ion center. Migration of the C<sub>1</sub>-C<sub>6</sub> bond accounts for *ca.* one-third of the product from the endo brosylate.<sup>24</sup> Solvolyses of the 2-bicyclo[3.2.0]heptyl or -hept-6-enyl tosylates, however, yield only products of C<sub>1</sub>-C<sub>7</sub> bond migration and unrearranged material.<sup>25,26</sup>

An electron-donating substituent such as O or N attached to C-6 of a bicyclo[4.2.0]octanone or to C-5 of a bicyclo[3.2.0]heptanone exerts a powerful influence on the course of the acid-catalyzed reactions of these compounds. Thus, the C<sub>1</sub>-C<sub>5</sub> bond in the bicycloheptyl series and the C<sub>1</sub>-C<sub>6</sub> bond in the bicyclooctyl series is cleaved (reverse aldol) in each of the cases listed in Table I.<sup>27-32</sup>

That the 1,2-alkyl shift predominates over the alternative reverse aldol reaction in entries **10** and **11** in Table I probably results from the greater stability



(23) B. A. Hess, *J. Amer. Chem. Soc.*, **93**, 1000 (1971). Surely the major epimeric tosylate is **59b**. A 1,2-vinyl shift in the solvolysis of **59b** cannot occur in concert with departure of tosylate ion; therefore, a free carbonium ion is probably generated in this case.

(24) A. C. Cope, R. W. Gleason, S. Moon, and C. H. Park, *J. Org. Chem.*, **32**, 942 (1967).

(25) S. C. Lewis and G. H. Whitham, *J. Chem. Soc. C*, 274 (1967).

(26) S. Winstein, F. Gadiant, E. T. Stafford, and P. E. Kleindinst, *J. Amer. Chem. Soc.*, **80**, 5895 (1958).

(27) O. L. Chapman and D. J. Pasto, *J. Amer. Chem. Soc.*, **82**, 3642 (1960).

(28) O. L. Chapman, D. J. Pasto, G. W. Borden, and A. A. Griswold, *J. Amer. Chem. Soc.*, **84**, 1220 (1962).

(29) B. D. Challand, H. Hikino, G. Kornis, G. Lange, and P. de Mayo, *J. Org. Chem.*, **34**, 794 (1969). Several examples of the overall transformation of 5-acetoxycyclo[3.2.0]heptan-2-ones into the seven-membered-ring products during treatment with base are also reported in this paper.

(30) Y. Tamura, Y. Kita, H. Ishibashi, and M. Ikeda, *Chem. Commun.*, 1167 (1971); *J. Chem. Soc., Chem. Commun.*, 101 (1973).

(31) Y. Tamura, Y. Kita, H. Ishibashi, and M. Ikeda, *Tetrahedron Lett.*, 1977 (1972).

(32) S. P. Pappas, B. C. Pappas, and N. A. Portnoy, *J. Org. Chem.*, **34**, 520 (1969).

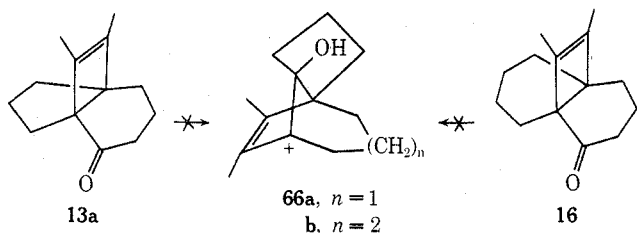
**Table I**  
Acid-Catalyzed Reactions of Heteroatom-Substituted Ketones

Reaction	Reactant	Product	Ref
1			27
2			28
3			27
4			27
5			29
6			30
7			30
8			31
9			31
10			32
11			32

(in the respective transition states) of the incipient cyclopentenone system *vs.* the cyclooctatrienedione system.

Rearrangement of the propellanes **13** and **16** by migration of the C<sub>1</sub>-C<sub>6</sub> bond, as in **56** → **58** would yield a highly strained bridgehead carbonium ion **66**; therefore, isomerization of these tricycles must proceed *via* an alternate path, *e.g.*, **13** → **15**.<sup>8</sup>

We may compare the acid-catalyzed isomeriza-



tions of some saturated  $[m.n.2]$ propellaneones with those of the unsaturated analogs discussed above. In all cases (Table II<sup>10,13,33,34</sup>) it is the cyclobutane bond equivalent to the C<sub>1</sub>-C<sub>8</sub> bond of a bicyclo[4.2.0]octan-2-one which shifts. The relative rates of rearrangement of 67 and 68 reflect the greater increase in steric crowding in passing from 68 to the intermediate ion compared with that in the isomerization of 67. The sole product obtained from 74 results, as expected, from migration of that carbon which is better able to accommodate electron deficiency. The final step in Corey's synthesis of  $\alpha$ -caryophyllene alcohol (apollanol, 77)<sup>34</sup> is included in Table II because of its close similarity to the rearrangements of the ketones listed there.

**Table II**  
Isomerizations of  $[m.n.2]$ Propellaneones

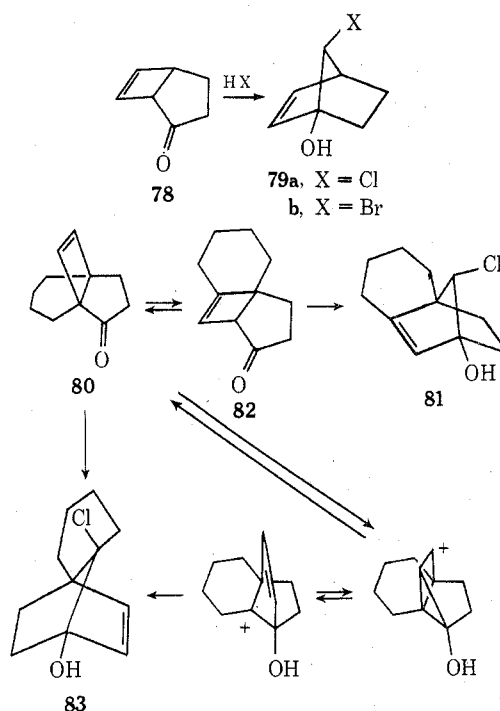
	Ref
	33
	33
	13
	10
	34

When the acidic medium was changed from the nonnucleophilic TosOH-benzene system to aqueous

(33) N. P. Peet, R. L. Cargill, and D. F. Bushey, *J. Org. Chem.*, **38**, 1218 (1973).

(34) E. J. Corey and S. Nozoe, *J. Amer. Chem. Soc.*, **87**, 5733 (1965).

hydrochloric acid-ether, new types of products began to appear. Thus, stirring 78 in 6 *N* hydrochloric acid-ether gave the rearranged chloro alcohol 79a.<sup>4</sup> A similar addition of hydrogen bromide to 78 has been reported.<sup>35</sup> Reaction of 80 with aqueous hydrochloric acid gave a mixture of chloro alcohols 81 and 83. The former was easily obtained as a crystalline substance; the latter was found in a subsequent reinvestigation of the reaction mixture.<sup>36</sup> The formation of 83 from 80 involves a 1,2-vinyl shift to a 7-norbornenyl ion and capture of the latter ion by chloride ion. Chloro alcohol 81 must arise in a similar manner from 82, the product of a 1,3-acyl shift in 80. Of course, a 1,3-acyl shift in 78 would provide only recovered starting material (in the absence of labels or of optically active ketone); thus, no indication of whether the 1,3-acyl shift precedes addition is available.

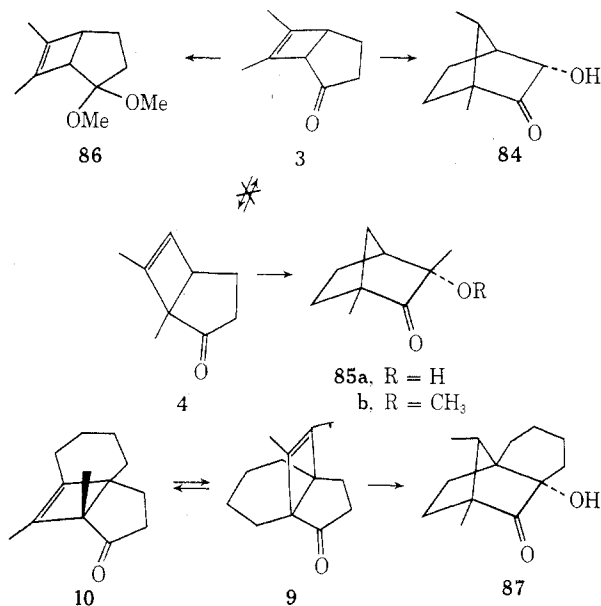


The nature of the acid-catalyzed additions to the bicyclo[3.2.0]hept-6-en-3-one system changes drastically when the double bond is substituted. When ketone 3 was stirred with aqueous hydrochloric acid, as above, a single keto alcohol, 84, was obtained.<sup>4</sup> Similar treatment of 4 gave only 85a.<sup>4</sup> The acid-catalyzed rearrangement-addition in these cases is faster than the 1,3-acyl shift. In methanolic hydrogen chloride 4 gave 85b, and 3 gave the stable ketal 86.<sup>4</sup> From similar hydration of a mixture of 9 and 10 only 87 was isolated as a major product.<sup>15</sup>

These acid-catalyzed rearrangement-additions proceed as depicted in Scheme III. A 1,2-vinyl shift in protonated ketone 88 leads to ion 89, which is rapidly hydrated from the anti side to yield diol 90. Slow protonation (exo side) of the double bond in 90 followed by an alkyl shift leads to the observed hydroxy ketones 92. When the double bond bears no

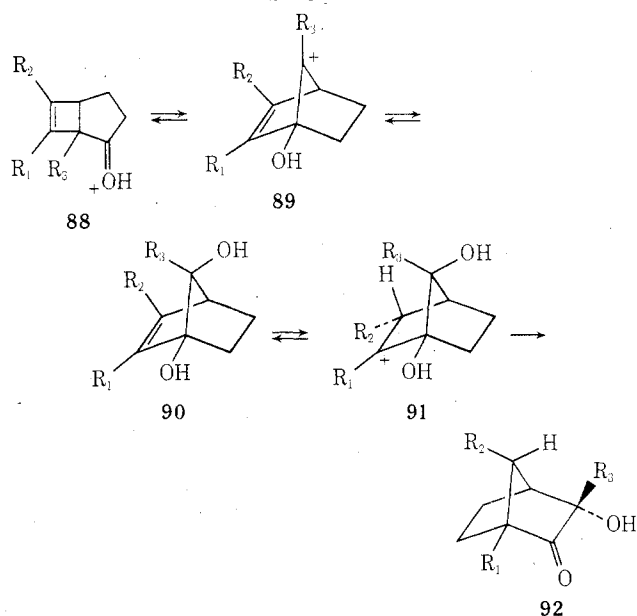
(35) H. H. Grootveld, C. Blomberg, and F. Bickelhaupt, *Tetrahedron Lett.*, 1999 (1971).

(36) R. L. Cargill and J. C. Boehm, unpublished results. Similar results have been indicated in preliminary studies with 13b: R. L. Cargill and J. C. Preston, unpublished results.



alkyl (or other electron donor) groups protonation of diol **90c** is very slow (formation of secondary *vs.* tertiary cation). This slow protonation of **90c** allows ion **89c** to be captured by chloride ion to produce **79a**, which is inert under the reaction conditions.

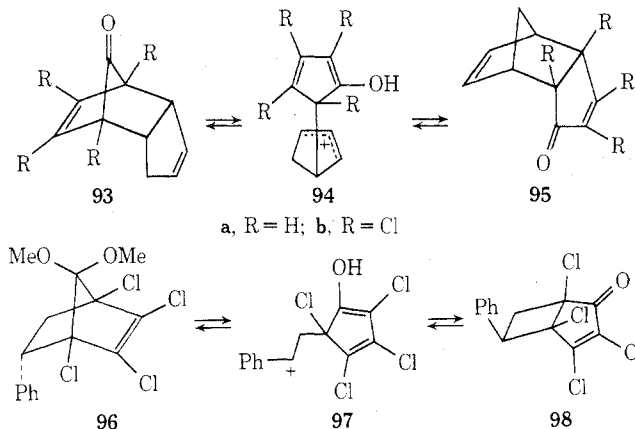
Scheme III



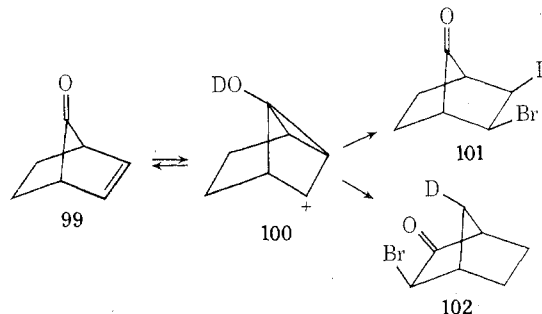
- a.  $R_1 = \text{Me}; R_2 = \text{Me}; R_3 = \text{H}$   
 b.  $R_1 = \text{Me}; R_2 = \text{H}; R_3 = \text{Me}$   
 c.  $R_1 = R_2 = R_3 = \text{H}$

When the carbonyl group of a  $\beta,\gamma$ -unsaturated ketone occupies a more strained position than the double bond, then acid-catalyzed reactions such as  $\beta$  fragmentation often occur. For example, the rearrangement of **93** to **95**<sup>37,38</sup> involves fragmentation of the  $\text{C}_1\text{-C}_2$  bond to yield intermediate **94** which may reclose to give either **93** or **95**. A similar isomerization of **96** to **98** has also been reported.<sup>39,40</sup> These

processes clearly depend upon the ability of C-2 to accommodate a positive charge (here the charges are stabilized in allylic or benzylic systems). The  $\beta,\gamma$  double bond participates here in the stabilization of the enol resulting from bond fragmentation.



The addition of deuterium bromide and related acids to 7-ketonorbornene (**99**) to yield **101** and **102** probably proceeds *via* an intermediate such as **100**<sup>15</sup> rather than as depicted earlier.<sup>41</sup> Thus, in **99** the  $\beta,\gamma$ -unsaturated carbonyl system as a whole probably does participate in this addition.



The acid-catalyzed isomerizations of chrysanthenone (**103**) and filifolone (**104**) provide further intriguing consequences of strain at the carbonyl group. Chrysanthenone undergoes  $\beta$  fragmentation to ion **105**, which then leads to a variety of thymol-related products (Scheme IV).<sup>42-44</sup> Recently, Erman and Wenkert<sup>45,46</sup> showed that **103** undergoes isomerization to **104** *via* the cyclopropanol **106**. Further interconversion of **104** and **108** *via* cyclopropanol **107** was also observed. In the latter transformation the double bond plays no part, and the reaction is typical of cyclobutanones.<sup>47,48</sup>

Formation of ion **106** is enhanced by the  $\beta,\gamma$  double bond (allylic stabilization), but even here the double bond is not required. Thus, **109** is converted

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(39) L. S. Besford, R. C. Cookson, and J. Cooper, *J. Chem. Soc. C*, 1385 (1967).

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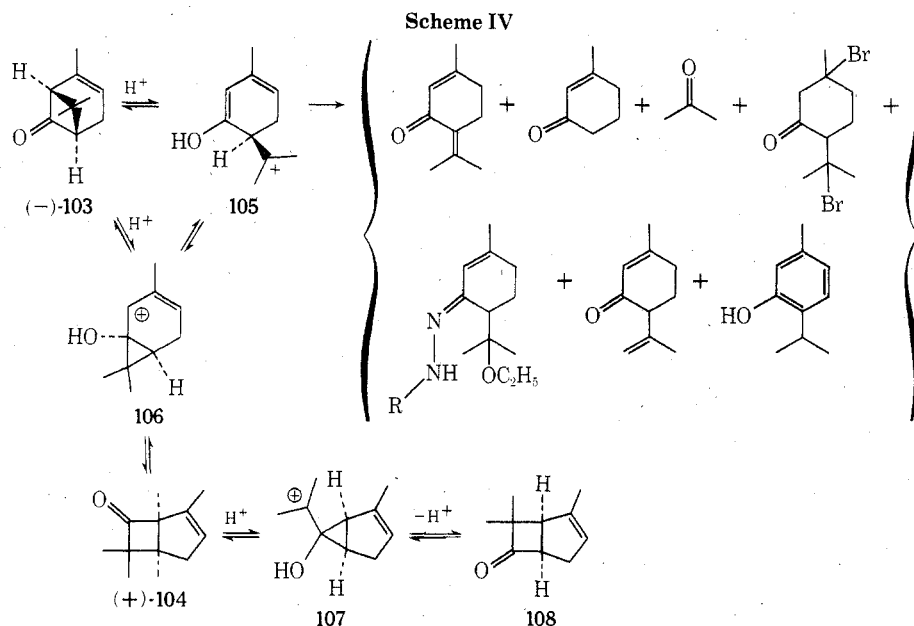
(44) M. Kotake and H. Nonaka, *Justus Liebigs Ann. Chem.*, 607, 153 (1957).

(45) W. F. Erman, *J. Amer. Chem. Soc.*, 91, 779 (1969).

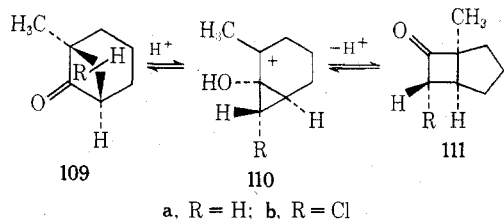
(46) W. F. Erman, R. S. Treptow, R. Bakuzis, and E. Wenkert, *J. Amer. Chem. Soc.*, 93, 657 (1971).

(47) T. J. Katz and P. Dessau, *J. Amer. Chem. Soc.*, 85, 2172 (1963).

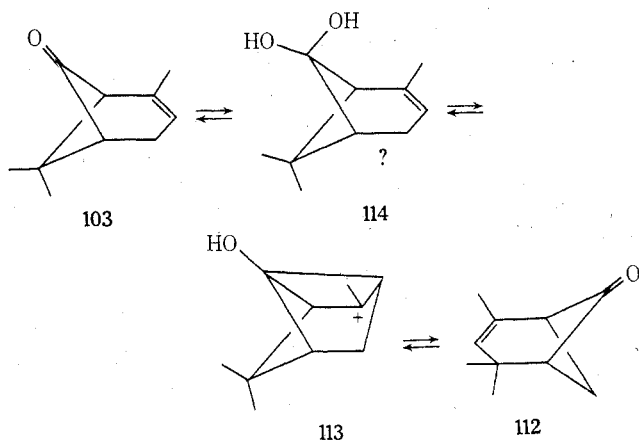
(48) See J. M. Conia and J. R. Salaun, *Accounts Chem. Res.*, 5, 33 (1972), for a review of cyclobutanone rearrangements which do not involve carbonium ions.



into 111 via 110, albeit more slowly than 103 yields 104.<sup>46,49</sup>



The absence of 112 (from 1,3-acyl shift) in the boron trifluoride catalyzed isomerization of 103 may reflect either the strain of ion 113 and/or the necessary intermediacy of a hemiketal or ketone hydrate, e.g., 114, in the 1,3-acyl shifts.<sup>46</sup> In nearly every case



(49) Y. Tsuda, T. Tanno, A. Ukai, and K. Isobe, *Tetrahedron Lett.*, 2009 (1971).

cited in the discussion of 1,3-acyl shifts the catalyst was *p*-toluenesulfonic acid hydrate.

In summary we note that the most extensive investigations of the acid-catalyzed reactions, both rearrangements and additions, of  $\beta,\gamma$ -unsaturated ketones have been largely confined to those systems in which either the carbonyl group or the double bond, or both, are contained in a strained environment. Except when other processes are highly competitive, e.g., 103  $\rightarrow$  105,  $\beta,\gamma$ -unsaturated ketones undergo reactions in which electron donation from the double bond to the electron-deficient carbonyl carbon is the first step (after protonation of the carbonyl oxygen). Usually either 1,3-acyl or 1,2-vinyl shifts are encountered, with various subsequent steps possible as appropriate, given the reaction conditions and substrate structure. Although our present understanding does not allow infallible prediction of reaction paths, the results discussed in this Account clearly demonstrate the synthetic utility of the acid-catalyzed isomerizations, etc., of unsaturated (and saturated) carbonyl compounds. We continue to explore, with a view to using them in projected syntheses, the isomerizations and additions of cyclobutyl and cyclobutenyl ketones related to those discussed above. The reader may find many other examples of acid-catalyzed rearrangements of ketones in a 1971 review by Fry.<sup>21</sup>

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