

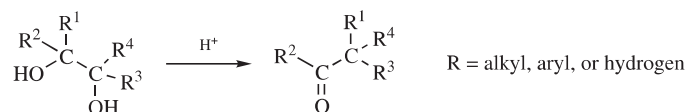
because of their complexity.¹¹⁸ Treatment of adamantane-2-¹⁴C with AlCl₃ results in total carbon scrambling on a statistical basis.¹¹⁹

As already indicated, the mechanism of the Wagner–Meerwein rearrangement is usually nucleophilic. Free-radical rearrangements are also known (see the mechanism section of this chapter), though virtually only with aryl migration. However, carbanion mechanisms (electrophilic) have also been found.⁹⁴ Thus Ph₃CCH₂Cl treated with sodium gave Ph₂CHCH₂Ph along with unrearranged products.¹²⁰ This is called the *Grovenstein–Zimmerman rearrangement*. The intermediate is Ph₃CCH₂⁻, and the phenyl moves without its electron pair. Only aryl and vinylic,¹²¹ and not alkyl, groups migrate by the electrophilic mechanism (p. \$\$\$) and transition states or intermediates analogous to **41** and **42** are likely.¹²²

OS V, 16, 194; VI, 378, 845.

18-2 The Pinacol Rearrangement

1/0-Hydro,3/hydroxy-(2/ → 3/alkyl)-migr-o-elimination



When *vic*-diols (glycols) are treated with acids,¹²³ they can be rearranged to give aldehydes or ketones, although elimination without rearrangement can also be accomplished. This reaction is called the *pinacol rearrangement*; the reaction gets its name from a prototype compound pinacol (Me₂COHCOHMe₂), which is rearranged to pinacolone (Me₃CCOCH₃).¹²⁴ In this type of reaction, reduction can compete with rearrangement.¹²⁵ The reaction has been accomplished many times, with alkyl, aryl, hydrogen, and even ethoxycarbonyl (COOEt)¹²⁶ as migrating

¹¹⁸See, for example, Engler, E.M.; Fărcașiu, M.; Sevin, A.; Cense, J.M.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1973**, *95*, 5769; Klester, A.M.; Ganter, C. *Helv. Chim. Acta* **1983**, *66*, 1200; **1985**, *68*, 734.

¹¹⁹Majerski, Z.; Liggero, S.H.; Schleyer, P.v.R.; Wolf, A.P. *Chem. Commun.* **1970**, 1596.

¹²⁰Grovenstein, Jr., E. *J. Am. Chem. Soc.* **1957**, *79*, 4985; Grovenstein, Jr., E.; Williams Jr., L.P. *J. Am. Chem. Soc.* **1961**, *83*, 412; Zimmerman, H.E.; Zweig, A. *J. Am. Chem. Soc.* **1961**, *83*, 1196. See also, Crimmins, T.F.; Murphy, W.S.; Hauser, C.R. *J. Org. Chem.* **1966**, *31*, 4273; Grovenstein, Jr., E.; Cheng, Y. *J. Am. Chem. Soc.* **1972**, *94*, 4971.

¹²¹See Grovenstein, Jr., E.; Black, K.W.; Goel, S.C.; Hughes, R.L.; Northrop, J.H.; Streeter, D.L.; VanDerveer, D. *J. Org. Chem.* **1989**, *54*, 1671, and references cited therein.

¹²²Bertrand, J.A.; Grovenstein, Jr., E.; Lu, P.; VanDerveer, D. *J. Am. Chem. Soc.* **1976**, *98*, 7835.

¹²³For a reaction initiated by iminium salts, see Lopez, L.; Mele, G.; Mazzeo, C. *J. Chem. Soc. Perkin Trans. I* **1994**, 779. For reactions initiated by radical cations, see de Sanabria, J.A.; Carrión, A.E. *Tetrahedron Lett.* **1993**, *34*, 7837. SbCl₅ has been used: see Harada, T.; Mukaiyama, T. *Chem. Lett.* **1992**, 81.

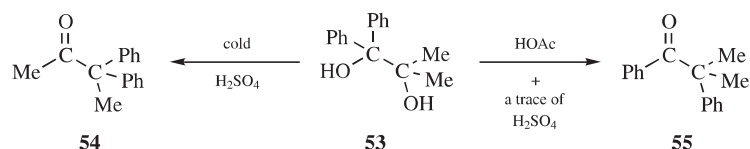
¹²⁴For reviews, see Bartók, M.; Molnár, A., in Patai, S. *The Chemistry of Functional Groups, Supplement E*, Wiley, NY, **1980**, pp. 722–732; Collins, C.J.; Eastham, J.F., in Patai, S. *The Chemistry of the Carbonyl Group*, Vol. 1, Wiley, NY, **1966**, pp. 762–771.

¹²⁵Grant, A.A.; Allukian, M.; Fry, A.J. *Tetrahedron Lett.* **2002**, *43*, 4391.

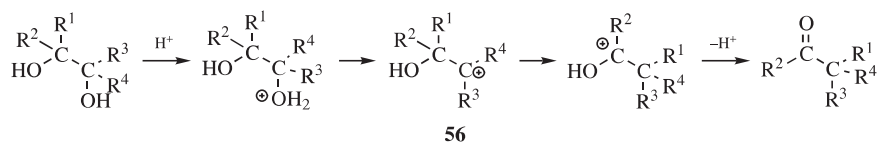
¹²⁶Kagan, J.; Agdeppa Jr., D.A.; Mayers, D.A.; Singh, S.P.; Walters, M.J.; Wintermute, R.D. *J. Org. Chem.* **1976**, *41*, 2355. COOH has been found to migrate in a Wagner–Meerwein reaction: Berner, D.; Cox, D.P.; Dahn, H. *J. Am. Chem. Soc.* **1982**, *104*, 2631.

groups. In most cases, each carbon has at least one alkyl or aryl group, and the reaction is most often carried out with tri- and tetrasubstituted glycols. As mentioned earlier, glycols in which the four R groups are not identical can give rise to more than one product, depending on which group migrates (see p. 1568 for a discussion of migratory aptitudes). A noncatalytic reaction is possible in supercritical water.¹²⁷

Stereodifferentiation is possible in this reaction.¹²⁸ When TMSOTf was used to initiate the reaction, it was shown to be highly regioselective.¹²⁹ Mixtures are often produced, and which group preferentially migrates may depend on the reaction conditions, as well as on the nature of the substrate. Thus the



action of cold, concentrated sulfuric acid on **53** produces mainly the ketone **54** (methyl migration), while treatment of **53** with acetic acid containing a trace of sulfuric acid gives mostly **55** (phenyl migration).¹³⁰ If at least one R is hydrogen, aldehydes can be produced as well as ketones. Generally, aldehyde formation is favored by the use of mild conditions (lower temperatures, weaker acids), because under more drastic conditions the aldehydes may be converted to ketones (**18-4**). The reaction has been carried out in the solid state, by treating solid substrates with HCl gas or with an organic solid acid.¹³¹



The mechanism involves a simple 1,2-shift. The ion **56** (where all four R groups are Me) has been trapped by the addition of tetrahydrothiophene.¹³² It may seem odd that a migration takes place when the positive charge is already at a tertiary position, but carbocations stabilized by an oxygen atom are even more stable than tertiary alkyl cations (p. 242). There is also the driving force supplied by the fact that the new carbocation can immediately stabilize itself by losing a proton.

It is obvious that other compounds in which a positive charge can be placed on a carbon α to one bearing an OH group can also give this rearrangement. This is true for β -amino alcohols, which rearrange on treatment with nitrous acid (this is called

¹²⁷Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama, T.; Arai, M. *J. Am. Chem. Soc.* **2000**, *122*, 1908.

¹²⁸Paquette, L.A.; Lanter, J.C.; Johnston, J.N. *J. Org. Chem.* **1997**, *62*, 1702.

¹²⁹Kudo, K.; Saigo, K.; Hashimoto, Y.; Saito, K.; Hasegawa, M. *Chem. Lett.* **1992**, 1449.

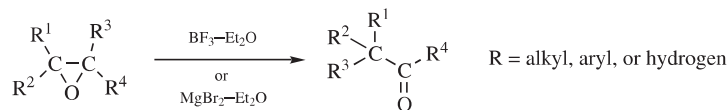
¹³⁰Ramart-Lucas, P.; Salmon-Legagneur, F. *C. R. Acad. Sci.* **1928**, *188*, 1301.

¹³¹Toda, F.; Shigemasa, T. *J. Chem. Soc. Perkin Trans. 1* **1989**, 209.

¹³²Bosshard, H.; Baumann, M.E.; Schetty, G. *Helv. Chim. Acta* **1970**, *53*, 1271.

the *semipinacol* rearrangement), iodohydrins, for which the reagent is mercuric oxide or silver nitrate, β -hydroxyalkyl selenides, $R^1R^2C(OH)C(SeR^5)R^3R^4$,¹³³ and allylic alcohols,¹³⁴ which can rearrange on treatment with a strong acid that protonates the double bond.

A similar rearrangement is given by epoxides,¹³⁵



when treated with acidic¹³⁶ reagents, such as BF_3 -etherate or $MgBr_2$ -etherate, 5 M $LiClO_4$ in ether,¹³⁷ $InCl_3$,¹³⁸ $Al(OC_6F_3)_3$,¹³⁹ $Bi(OTf)_3$,¹⁴⁰ $VO(OEt)Cl_2$,¹⁴¹ or sometimes by heat alone.¹⁴² Epoxides are converted to aldehydes or ketones on treatment with certain metallic catalysts¹⁴³ including treatment with iron complexes in refluxing dioxane,¹⁴⁴ $IrCl_3$,¹⁴⁵ or with $BiOClO_4$ in dichloromethane.¹⁴⁶ A related rearrangement called the *Meinwald rearrangement* was induced by the enzyme pig liver esterase.¹⁴⁷ It has been shown that epoxides are intermediates in the pinacol rearrangements of certain glycols.¹⁴⁸ Among the evidence for the mechanism given is that $Me_2COHCOHMe_2$, $Me_2COHCNH_2Me_2$, and $Me_2COHCCiMe_2$ gave the reaction at different rates (as expected), but yielded the *same mixture* of two products pinacol and pinacolone indicating a common intermediate.¹⁴⁹

¹³³For a review, see Krief, A.; Laboureur, J.L.; Dumont, W.; Labar, D. *Bull. Soc. Chim. Fr.* **1990**, 681.

¹³⁴See Wang, B.M.; Song, Z.L.; Fan, C.A.; Tu, Y.Q.; Chen, W.M. *Synlett* **2003**, 1497; Hurley, P.B.; Dake, G.R. *Synlett* **2003**, 2131.

¹³⁵For a discussion of the mechanism, see Hodgson, D.M.; Robinson, L.A.; Jones, M.L. *Tetrahedron Lett.* **1999**, *40*, 8637.

¹³⁶Epoxides can also be rearranged with basic catalysts, though the products are usually different. For a review, see Yandovskii, V.N.; Ershov, B.A. *Russ. Chem. Rev.* **1972**, *41*, 403, 410.

¹³⁷Sudha, R.; Narashimhan, K.M.; Saraswathy, V.G.; Sankararaman, S. *J. Org. Chem.* **1996**, *61*, 1877; Sankararaman, S.; Nesakumar, J.E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3173.

¹³⁸Ranu, B.C.; Jana, U. *J. Org. Chem.* **1998**, *63*, 8212.

¹³⁹Kita, Y.; Furukawa, A.; Futamura, J.; Ueda, K.; Sawama, Y.; Hamamoto, H.; Fujioka, H. *J. Org. Chem.* **2001**, *66*, 8779.

¹⁴⁰Bhatia, K.A.; Eash, K.J.; Leonard, N.M.; Oswald, M.C.; Mohan, R.S. *Tetrahedron Lett.* **2001**, *42*, 8129.

¹⁴¹Martínez, F.; del Campo, C.; Llama, E.F. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1749.

¹⁴²For a list of reagents that accomplish this transformation, with references, see Larock, R.C. *Comprehensive Organic Transformations*; 2nd ed., Wiley-VCH, NY, **1999**, pp. 1277–1280.

¹⁴³For example, see Alper, H.; Des Roches, D.; Durst, T.; Legault, R. *J. Org. Chem.* **1976**, *41*, 3611; Milstein, D.; Buchman, O.; Blum, J. *J. Org. Chem.* **1977**, *42*, 2299; Prandi, J.; Namy, J.L.; Menoret, G.; Kagan, H.B. *J. Organomet. Chem.* **1985**, *285*, 449; Miyashita, A.; Shimada, T.; Sugawara, A.; Nohira, H. *Chem. Lett.* **1986**, 1323; Maruoka, K.; Nagahara, S.; Ooi, T.; Yamamoto, H. *Tetrahedron Lett.* **1989**, *30*, 5607.

¹⁴⁴Suda, K.; Baba, K.; Nakajima, S.-I.; Takanami, T. *Tetrahedron Lett.* **1999**, *40*, 7243.

¹⁴⁵Karamé, I.; Tommasino, M.L.; LeMaire, M. *Tetrahedron Lett.* **2003**, *44*, 7687.

¹⁴⁶Anderson, A.M.; Blazek, J.M.; Garg, P.; Payne, B.J.; Mohan, R.S. *Tetrahedron Lett.* **2000**, *41*, 1527.

¹⁴⁷Niwayama, S.; Noguchi, H.; Ohno, M.; Kobayashi, S. *Tetrahedron Lett.* **1993**, *34*, 665.

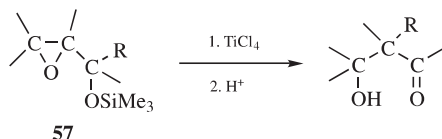
¹⁴⁸See, for example, Matsumoto, K. *Tetrahedron* **1968**, *24*, 6851; Pocker, Y.; Ronald, B.P. *J. Am. Chem. Soc.* **1970**, *92*, 3385; *J. Org. Chem.* **1970**, *35*, 3362; Tamura, K.; Moriyoshi, T. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2942.

¹⁴⁹Pocker, Y. *Chem. Ind. (London)*, **1959**, 332. See also, Herlihy, K.P. *Aust. J. Chem.* **1981**, *34*, 107.

A good way to prepare β -diketones consists of heating α,β -epoxy ketones at 80–140°C in toluene with small amounts of $(\text{Ph}_3\text{P})_4\text{Pd}$ and 1,2-bis(diphenylphosphino)ethane.¹⁵⁰ Epoxides are converted to 1,2-diketones with Bi, DMSO, O_2 , and a catalytic amounts of $\text{Cu}(\text{OTf})_2$ at 100°C.¹⁵¹ α,β -Epoxy ketones are also converted to 1,2-diketones with a ruthenium catalyst¹⁵² or an iron catalyst.¹⁵³ Epoxides with an α -hydroxyalkyl substituent give a pinacol rearrangement product in the presence of a ZnBr_2 ¹⁵⁴ or $\text{Tb}(\text{OTf})_3$ ¹⁵⁵ catalyst to give a γ -hydroxy ketone.

Oxaziridines are converted to ring-expanded lactams under photochemical conditions.¹⁵⁶ *N*-Tosyl aziridines with an α -hydroxyalkyl substituent give a pinacol rearrangement product in the presence of Lewis acids, such as SmI_2 , in this case a keto-*N*-tosyl amide.¹⁵⁷

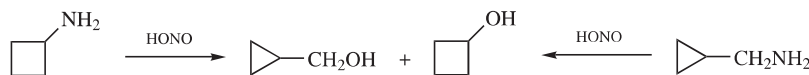
β -Hydroxy ketones can be prepared by treating the silyl ethers (**57**) of α,β -epoxy alcohols with TiCl_4 .¹⁵⁸



OS I, 462; II, 73, 408; III, 312; IV, 375, 957; V, 326, 647; VI, 39, 320; VII, 129. See also, OS VII, 456.

18-3 Expansion and Contraction of Rings

Demyanov ring contraction; Demyanov ring expansion



When a positive charge is formed on an alicyclic carbon, migration of an alkyl group can take place to give ring contraction, producing a ring that is one carbon smaller than the original, as in the interconversion of the cyclobutyl cation and the

¹⁵⁰Suzuki, M.; Watanabe, A.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 2095.

¹⁵¹Antonietti, S.; Duñach, E. *Chem. Commun.* **2001**, 2566.

¹⁵²Chang, C.-L.; Kumar, M.P.; Liu, R.-S. *J. Org. Chem.* **2004**, *69*, 2793.

¹⁵³Suda, K.; Baba, K.; Nakajima, S.; Takanami, T. *Chem. Commun.* **2002**, 2570.

¹⁵⁴Tu, Y.Q.; Fan, C.A.; Ren, S.K.; Chan, A.S.C. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3791.

¹⁵⁵Bickley, J.F.; Hauer, B.; Pena, P.C.A.; Roberts, S.M.; Skidmore, J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1253.

¹⁵⁶Bourguet, E.; Baneres, J.-L.; Girard, J.-P.; Parello, J.; Vidal, J.-P.; Lusinchi, X.; Declerqz, J.-P. *Org. Lett.* **2001**, *3*, 3067.

¹⁵⁷Wang, B.M.; Song, Z.L.; Fan, C.A.; Tu, Y.Q.; Shi, Y. *Org. Lett.* **2002**, *4*, 363.

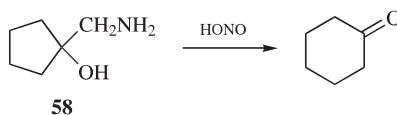
¹⁵⁸Maruoka, K.; Hasegawa, M.; Yamamoto, H.; Suzuki, K.; Shimazaki, M.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 3827. For a different rearrangement of **53**, see Maruoka, K.; Ooi, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 6431.

cyclopropylcarbinyl cation.



Note that this change involves conversion of a secondary to a primary carbocation. In a similar manner, when a positive charge is placed on a carbon atom in an alicyclic ring, ring expansion can take place.¹⁵⁹ The new carbocation, and the old one, can then give products by combination with a nucleophile (e.g., the alcohols shown above), or by elimination, so that this reaction is a special case of **18-1**. Often, both rearranged and unrearranged products are formed, so that, for example, cyclobutylamine and cyclopropylmethylamine give similar mixtures of the two alcohols shown above on treatment with nitrous acid (a small amount of 3-buten-1-ol is also produced). When the carbocation is formed by diazotization of an amine, the reaction is called the *Demyanov rearrangement*,¹⁶⁰ but of course similar products are formed when the carbocation is generated in other ways. The expansion reaction has been performed on rings of C₃–C₈,¹⁶¹ but yields are best with the smaller rings, where relief of small-angle strain provides a driving force for the reaction. The contraction reaction has been applied to four-membered rings and to rings of C₆–C₈, but contraction of a cyclopentyl cation to a cyclobutylmethyl system is generally not feasible because of the additional strain involved. Strain is apparently much less of a factor in the cyclobutyl–cyclopropylmethyl interconversion (for a discussion of this interconversion, see p. 450). The influence of substituents on this rearrangement has been examined.¹⁶²

Ring expansions of certain hydroxyamines, such as **58**



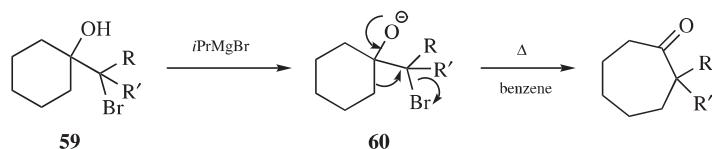
¹⁵⁹For monographs on ring expansions, see Hesse, M. *Ring Enlargement in Organic Chemistry*, VCH, NY, **1991**; Gutsche, C.D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*, Academic Press, NY, **1968**. For a review of ring contractions, see Redmore, D.; Gutsche, C.D. *Adv. Alicyclic Chem.* **1971**, *3*, 1. For reviews of ring expansions in certain systems, see Baldwin, J.E.; Adlington, R.M.; Robertson, J. *Tetrahedron* **1989**, *45*, 909; Stach, H.; Hesse, M. *Tetrahedron* **1988**, *44*, 1573; Dolbier Jr., W.R. *Mech. Mol. Migr.* **1971**, *3*, 1. For reviews of expansions and contractions of three- and four-membered rings, see Salaün, J., in Rappoport, Z. *The Chemistry of the Cyclopropyl Group*, pt. 2, Wiley, NY, **1987**, pp. 809–878; Conia, J.M.; Robson, M.J. *Angew. Chem. Int. Ed.* **1975**, *14*, 473. For a list of ring expansions and contractions, with references, see Larock, R.C. *Comprehensive Organic Transformation*, 2nd ed., Wiley-VCH, NY, **1999**, pp. 1283–1302.

¹⁶⁰For a review, see Smith, P.A.S.; Baer, D.R. *Org. React.* **1960**, *11*, 157. See also, Chow, L.; McClure, M.; White, J. *Org. Biomol. Chem.* **2004**, *2*, 648.

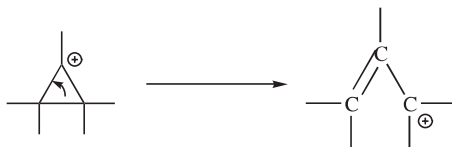
¹⁶¹For a review concerning three-membered rings, see Wong, H.N.C.; Hon, M.; Tse, C.; Yip, Y.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165, see pp. 182–186. For a review concerning three- and four-membered rings, see Breslow, R., in Mayo, P. *Molecular Rearrangements*, Vol. 1, Wiley, NY, **1963**, pp. 233–294.

¹⁶²Wiberg, K.B.; Shobe, D.; Nelson, G.C. *J. Am. Chem. Soc.* **1993**, *115*, 10645.

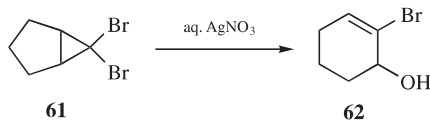
are analogous to the semipinacol rearrangement (18-2). This reaction is called the *Tiffeneau–Demyanov ring expansion*. These have been performed on rings of C₄–C₈ and the yields are better than for the simple Demyanov ring expansion. A similar reaction has been used to expand rings of from five to eight members.¹⁶³ In this case, a cyclic bromohydrin of the form **59** is treated with a Grignard reagent which, acting as a base, removes the OH proton to give the alkoxide **60**. Refluxing of **60** brings about the ring enlargement. The reaction has been accomplished for **59** in which at least one R group is phenyl or methyl,¹⁶⁴ but fails when both R groups are hydrogen.¹⁶⁵



A positive charge generated on a three-membered ring gives “contraction” to an allylic cation.¹⁶⁶



We have previously seen (p. 487) that this is the reason nucleophilic substitutions are not feasible at a cyclopropyl substrate. The reaction is often used to convert cyclopropyl halides and tosylates to allylic products, especially for the purpose of ring expansion, an example being the conversion of **61–62**.¹⁶⁷ The stereochemistry of these cyclopropyl cleavages is governed by the principle of orbital symmetry conservation (for a discussion, see p. 1644).



Three-membered rings can also be cleaved to unsaturated products in at least two other ways. (1) On pyrolysis, cyclopropanes can undergo “contraction” to

¹⁶³Sisti, A.J. *Tetrahedron Lett.* **1967**, 5327; *J. Org. Chem.* **1968**, *33*, 453. See also, Sisti, A.J.; Vitale, A.C. *J. Org. Chem.* **1972**, *37*, 4090.

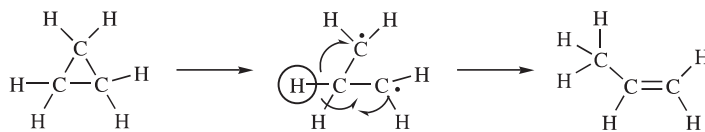
¹⁶⁴Sisti, A.J.; Meyers, M. *J. Org. Chem.* **1973**, *38*, 4431; Sisti, A.J.; Rusch, G.M. *J. Org. Chem.* **1974**, *39*, 1182.

¹⁶⁵Sisti, A.J. *J. Org. Chem.* **1968**, *33*, 3953.

¹⁶⁶For reviews, see Marvell, E.N. *Thermal Electrocyclic Reactions*, Academic Press, NY, **1980**, pp. 23–53; Sorensen, T.S.; Rauk, A., in Marchand, A.P.; Lehr, R.E. *Pericyclic Reactions*, Vol. 2, Academic Press, NY, **1977**, pp. 1–78.

¹⁶⁷Skell, P.S.; Sandler, S.R. *J. Am. Chem. Soc.* **1958**, *80*, 2024.

propenes.¹⁶⁸ In the simplest case, cyclopropane gives propene when heated to 400–500°C. The mechanism is generally regarded¹⁶⁹ as involving a diradical



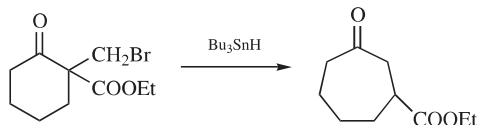
intermediate¹⁷⁰ (recall that free-radical 1,2 migration is possible for diradicals, p. 1574). (2) The generation of a carbene or carbenoid carbon in a three-membered ring can lead to allenes, and allenes are often prepared in this



way.¹⁷¹ Flash vacuum pyrolysis of 1-chlorocyclopropane thermally rearranges to chloroallene.¹⁷² One way to generate, such a species is treatment of a 1,1-dihalo-cyclopropane with an alkyllithium compound (**12-39**).¹⁷³ In contrast, the generation of a carbene or carbenoid at a cyclopropylmethyl carbon gives ring expansion.¹⁷⁴



Some free-radical ring enlargements are also known, an example being:¹⁷⁵



¹⁶⁸For reviews, see Berson, J.A., in de Mayo, P. *Rearrangements in Ground and Excited States*, Vol. 1, Academic Press, NY, **1980**, pp. 324–352; *Ann. Rev. Phys. Chem.* **1977**, 28, 111; Bergman, R.G., in Kochi, J.K. *Free Radicals*, Vol. 1, Wiley, NY, **1973**, pp. 191–237; Frey, H.M. *Adv. Phys. Org. Chem.* **1966**, 4, 147, see pp. 148–170.

¹⁶⁹For evidence that diradical intermediates may not be involved, at least in some cases, see Fields, R.; Haszeldine, R.N.; Peter, D. *Chem. Commun.* **1967**, 1081; Parry, K.A.W.; Robinson, P.J. *Chem. Commun.* **1967**, 1083; Clifford, R.P.; Holbrook, K.A. *J. Chem. Soc. Perkin Trans. 2* **1972**, 1972; Baldwin, J.E.; Grayston, M.W. *J. Am. Chem. Soc.* **1974**, 96, 1629, 1630.

¹⁷⁰We have seen before that such diradicals can close up to give cyclopropanes (**17-34**). Therefore, pyrolysis of cyclopropanes can produce not only propenes, but also isomerized (cis → trans or optically active → inactive) cyclopropanes. See, for example, Berson, J.A.; Balquist, J.M. *J. Am. Chem. Soc.* **1968**, 90, 7343; Bergman, R.G.; Carter, W.L. *J. Am. Chem. Soc.* **1969**, 91, 7411.

¹⁷¹For reviews, see Schuster, H.F.; Coppola, G.M. *Allenes in Organic Synthesis*, Wiley, NY, **1984**, pp. 20–23; Kirmse, W. *Carbene Chemistry*, 2nd ed., Academic Press, NY, **1971**, pp. 462–467.

¹⁷²Billups, W.E.; Bachman, R.E. *Tetrahedron Lett.* **1992**, 33, 1825.

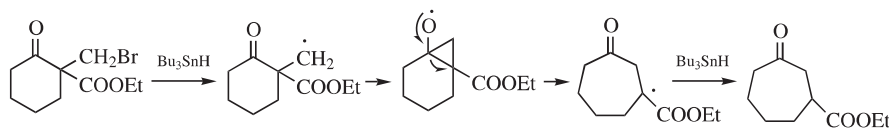
¹⁷³See Baird, M.S.; Baxter, A.G.W. *J. Chem. Soc. Perkin Trans. 1* **1979**, 2317, and references cited therein.

¹⁷⁴For a review, see Gutsche, C.D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*, Academic Press, NY, **1968**, pp. 111–117.

¹⁷⁵Dowd, P.; Choi, S. *Tetrahedron Lett.* **1991**, 32, 565; *Tetrahedron* **1991**, 47, 4847. For a related ring expansion, see Baldwin, J.E.; Adlington, R.M.; Robertson, J. *J. Chem. Soc., Chem. Commun.* **1988**, 1404.

1592 REARRANGEMENTS

This reaction has been used to make rings of 6, 7, 8, and 13 members. A possible mechanism is

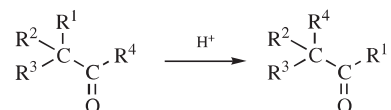


This reaction has been extended to the expansion of rings by three or four carbons, by the use of a substrate containing $(\text{CH}_2)_n\text{X}$ ($n = 3$ or 4) instead of CH_2Br .¹⁷⁶ By this means, 5-, 6-, and 7-membered rings were enlarged to 18–11-membered rings.

OS **III**, 276; **IV**, 221, 957; **V**, 306, 320; **VI**, 142, 187; **VII**, 12, 114, 117, 129, 135; **VIII**, 179, 467, 556, 578.

18-4 Acid-Catalyzed Rearrangements of Aldehydes and Ketones

1/Alkyl,2/alkyl-interchange, and so on



Rearrangements of this type, where a group α to a carbonyl "changes places" with a group attached to the carbonyl carbon, occur when migratory aptitudes are favorable.¹⁷⁷ The R^2 , R^3 , and R^4 groups may be alkyl or hydrogen. Certain aldehydes have been converted to ketones, and ketones to other ketones (though more drastic conditions are required for the latter), but no rearrangement of a ketone to an aldehyde ($\text{R}^1 = \text{H}$) has so far been reported. There are two mechanisms,¹⁷⁸ each beginning with protonation of the oxygen and each involving two migrations. In one pathway, the migrations are in opposite directions:¹⁷⁹



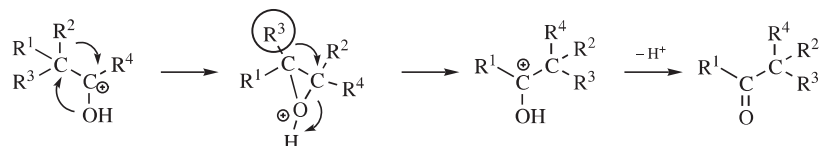
¹⁷⁶Dowd, P.; Choi, S. *J. Am. Chem. Soc.* **1987**, *109*, 6548; *Tetrahedron Lett.* **1991**, 32, 565.

¹⁷⁷For reviews, see Fry, A. *Mech. Mol. Migr.* **1971**, *4*, 113; Collins, C.J.; Eastham, J.F., in Patai, S. *The Chemistry of the Carbonyl Group*, Vol. 1, Wiley, NY, **1966**, pp. 771–790.

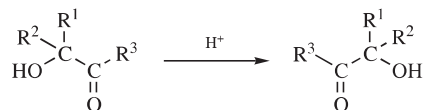
¹⁷⁸Favorskii, A.; Chilingaren, A. *C. R. Acad. Sci.* **1926**, *182*, 221.

¹⁷⁹Kendrick Jr., L.W.; Benjamin, B.M.; Collins, C.J. *J. Am. Chem. Soc.* **1958**, *80*, 4057; Rothrock, T.S.; Fry, A. *J. Am. Chem. Soc.* **1958**, *80*, 4349; Collins, C.J.; Bowman, N.S. *J. Am. Chem. Soc.* **1959**, *81*, 3614.

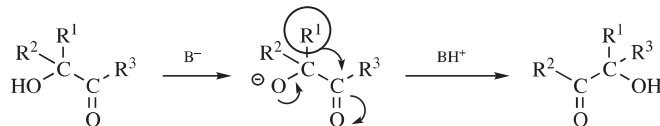
In the other pathway, the migrations are in the same direction. The actual mechanism of this pathway is not certain, but an epoxide (protonated) intermediate¹⁸⁰ is one possibility:¹⁸¹



If the reaction is carried out with ketone labeled in the C=O group with ¹⁴C, the first pathway predicts that the product will contain all the ¹⁴C in the C=O carbon, while in the second pathway the label will be in the α carbon (demonstrating migration of oxygen). The results of such experiments¹⁸² have shown that in some cases only the C=O carbon was labeled, in other cases only the α carbon, while in still others both carbons bore the label, indicating that in these cases both pathways were in operation. With α -hydroxy aldehydes and ketones, the process may stop after only one migration (this is called the α -ketol rearrangement).

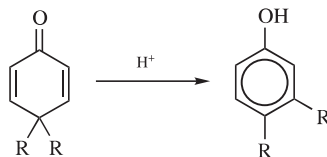


The α -ketol rearrangement can also be brought about by base catalysis, but only if the alcohol is tertiary, since if R¹ or R² = hydrogen, enolization of the substrate is more favored than rearrangement.



18-5 The Dienone-Phenol Rearrangement

2/C \rightarrow 5/O-Hydro, 1/C \rightarrow 2/C-alkyl-bis-migration



¹⁸⁰Zook, H.D.; Smith, W.E.; Greene, J.L. *J. Am. Chem. Soc.* **1957**, *79*, 4436.

¹⁸¹Some such pathway is necessary to account for the migration of oxygen that is found. It may involve a protonated epoxide, a 1,2-diol, or simply a [1,2]-shift of an OH group.

¹⁸²See, for example, Barton, S.; Porter, C.R. *J. Chem. Soc.* **1956**, 2483; Zalesskaya, T.E.; Remizova, T.B. *J. Gen. Chem. USSR* **1965**, *35*, 29; Fry, A.; Oka, M. *J. Am. Chem. Soc.* **1979**, *101*, 6353.