from other effects so that these other effects may be identified and evaluated. Perhaps the use of N_+ values in an equation of the form of eq 2 will be useful.

The successful application of the concepts already developed to the clarification of the selectivity–reactivity problem and to the problem of general base catalysis in cation reactions have served as demonstrations of the general scientific value of these concepts. Undoubtedly, the concepts will be found to have some limitations, and it is the goal of much of our present work to define these limitations as closely as possible.

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Spirocyclic Intermediates in Organic Reactions

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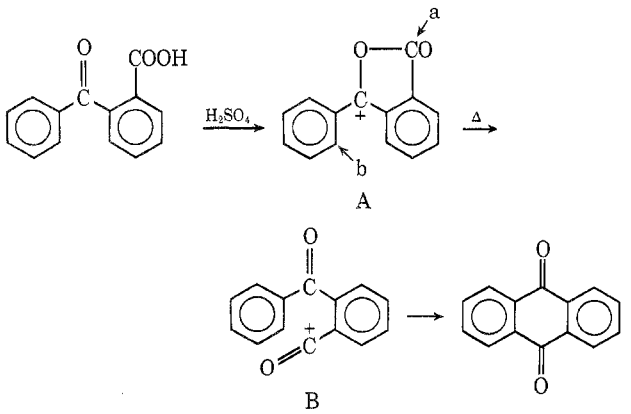
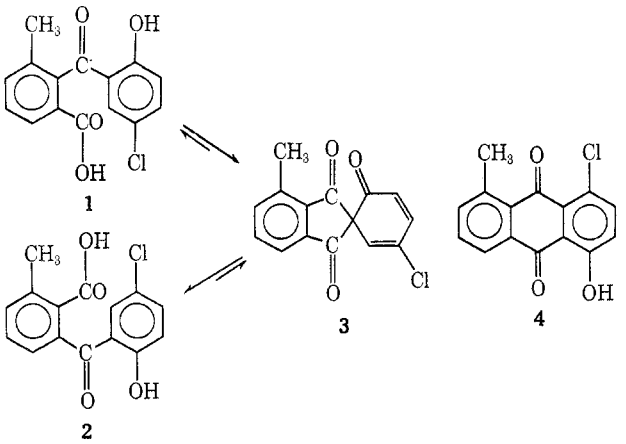
My interest in spirocyclic reaction mechanisms arose from early work on the mechanism of anthraquinone formation from *o*-benzoylbenzoic acid.[1] The proposed mechanism is shown in Scheme I.

Scheme I



It was pointed out[1] that cyclic ion A was undoubtedly produced first.[2] Ion A is stable at temperatures up to about 70°. Cyclization to anthraquinone cannot occur because carbons a and b cannot approach within bond-forming distance. However, at temperatures above 70° opening of A to B occurs readily and cyclization to anthraquinone may result.

Later, my attention was drawn to the fact that certain keto acids of the *o*-benzoylbenzoic type give rise to isomeric keto acids and to anthraquinone-type molecules which could not be explained solely by the above mechanism. Hayashi had shown[3] that 2-(2-hydroxy-5-chlorobenzoyl)-3-methylbenzoic acid (**1**) rearranges to 6-(2-hydroxy-5-chlorobenzoyl)-2-methylbenzoic acid (**2**) on warming in sulfuric acid. The rearrangement was postulated to go through the cyclohexadienone **3** shown. Both **1** and **2** give the same quinone (**4**) on warming in sulfuric acid.



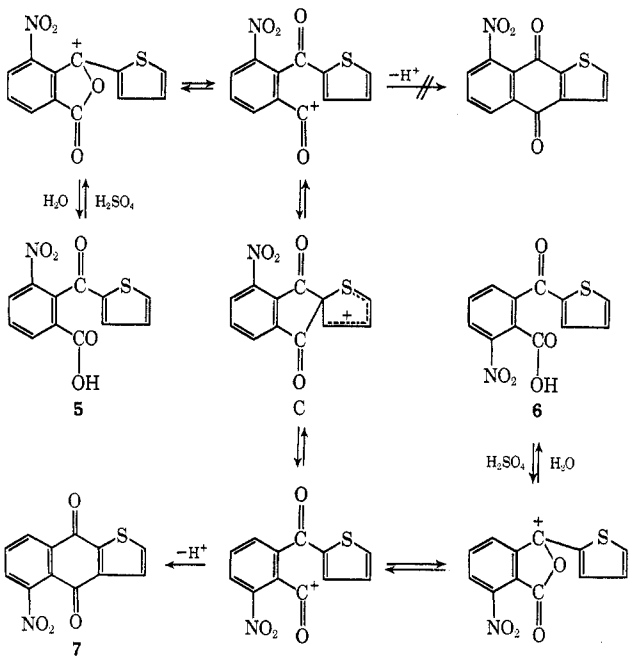
The species **3** represents a spirocyclic compound and, presumably, the phenolic hydroxyl in **1** or **2** is necessary for its formation, although this point was not mentioned in Hayashi's discussion.[3] In the present discussion, however, I do not cover reactions which yield spirocyclic compounds, rather, reactions which may proceed through a *spirocyclic intermediate* (nonisolable).

The spirocyclic mechanism for anthraquinone formation is best illustrated by the work done on 3-nitro-2-(2-thenoyl)benzoic acid (**5**)[4] (Scheme II). On

Melvin S. Newman did both undergraduate and graduate study at Yale, where he received his Ph.D. in 1932, and then spent 4 years in postdoctoral positions at Yale, Columbia, and Harvard. In 1936 he joined the faculty of The Ohio State University, and in 1965 assumed his present position of Regents Professor. His interests range widely over the areas of reaction mechanisms involving bicyclic transition states, carbenes, and unsaturated carbonium ions, to the synthesis of carcinogens.

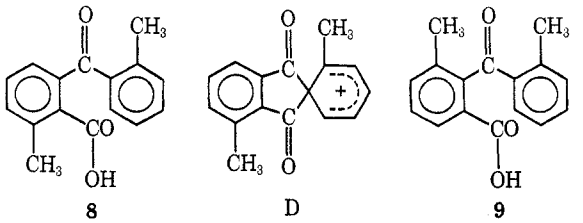
(1) M. S. Newman, *J. Amer. Chem. Soc.*, **64**, 2324 (1942).
(2) D. S. Noyce and P. A. Kittle, *J. Org. Chem.*, **30**, 1899 (1965), give uv data in favor of A in 100% H_2SO_4.
(3) M. Hayashi, *J. Chem. Soc.*, 2516 (1927); see also M. Hayashi, *ibid.*, 1513, 1520, 1524 (1930).
(4) M. S. Newman and K. G. Ihrman, *J. Amer. Chem. Soc.*, **80**, 3652 (1958).

Scheme II



heating **5** in 100% sulfuric acid at 70° for 30 min, the only water-insoluble acid produced is 6-nitro-2-(2-thenoyl)benzoic acid (**6**).[4,5] Because there is no phenolic OH on the thiophene moiety, a species such as **3** cannot be formed. However, an analogous spirocyclic intermediate (C) was postulated to account for the results. Heating either **5** or **6** in sulfuric acid at 135° forms only 5-nitrothiophanthraquinone (**7**). The results obtained depend on the temperatures and length of time of heating prior to quenching the sulfuric acid solutions in water.

In a study[6] on 6-methyl-2-(*o*-toluyl)benzoic acid (**8**) and 3-methyl-2-(*o*-toluyl)benzoic acid (**9**), the composition of mixtures of the two acids formed on heating either with sulfuric acid was shown to depend mainly on the strength of the sulfuric acid used. In 96% sulfuric acid **8** was the only product, whereas in 70% sulfuric acid **9** was the main product. These results were explained by assuming a spirocyclic carbenium[7] ion (D) as before.[4,5]

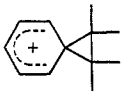


To summarize, the spirocyclic intermediates C and D provide examples of spirocyclic carbenium ions. For classification purposes, C is called a [4.4]spirocyclic intermediate, because there are four atoms in each ring comprising the spiro structure, not counting the carbon common to each ring, and D is a [5.4]spirocyclic intermediate.

One might ask what advantage there is to calling attention to one more postulated reaction intermediate. I believe it important to realize how generally this type of intermediate is involved so that caution will be exercised in assigning structures to compounds formed in many reactions which might involve such intermediates. Furthermore, new syntheses and new reactions can be predicted with intelligent use of the principles involved. Accordingly, in the remainder of this Account I will discuss briefly a few (by no means, all) reactions which *may* involve spirocyclic intermediates. In certain cases, alternate explanations are possible, and are given in the literature references. However, only the spirocyclic intermediate possibility will be offered in this discussion. It is realized that in most of the examples cited no definite decision regarding the question of whether a transition state or an intermediate is involved can be made. Hence, for the sake of brevity, all will be pictured as intermediates.

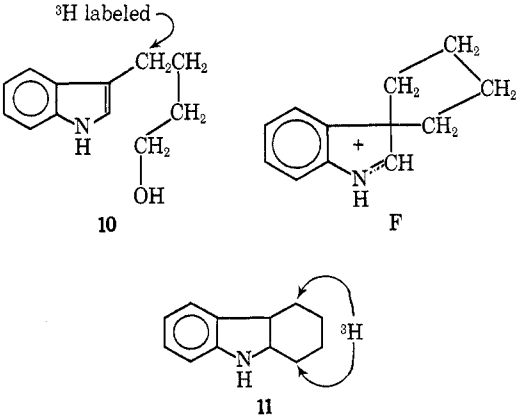
Carbenium[7] Ions

Perhaps the best known spirocyclic carbenium ion is the [5.2] species, the phenonium ion E.[8] Much has



been said and done in this area (including the arguments against the phenonium ion); no discussion will be offered.

When 4-(3-indolyl)-1-butanol (**10**) containing tritium in the 4 position is cyclized to hexahydrocarbazole (**11**), tritium is found in both the 1 and 4 positions.[9] The cationic [4.4]spirocyclic intermediate F is undoubtedly involved.



Treatment of 1,2-diphenyl-2-*p*-deuteriophenylthiovinyl 2,4,6-trinitrobenzenesulfonate (**12**) with boron fluoride etherate affords about a 1:1 mixture of 5- and

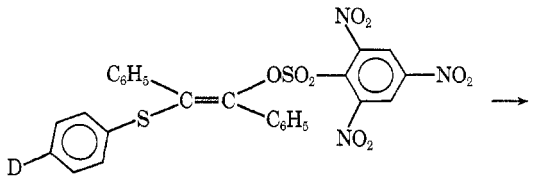
(5) See R. B. Sandin, R. Melby, R. Crawford, and D. McGreer, *J. Amer. Chem. Soc.*, **78**, 3817 (1956), for examples and pertinent discussion.

(6) S. J. Cristol and M. L. Caspar, *J. Org. Chem.*, **33**, 2020 (1968).

(7) The preferred nomenclature for what has hitherto been termed a carbonium ion. See G. Olah, *J. Amer. Chem. Soc.*, **94**, 808 (1972).

(8) D. J. Cram, *ibid.*, **71**, 3863 (1949).

(9) A. H. Jackson and P. Smith, *Chem. Commun.*, 264 (1967).



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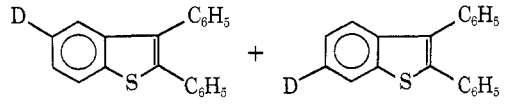
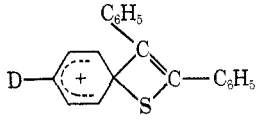


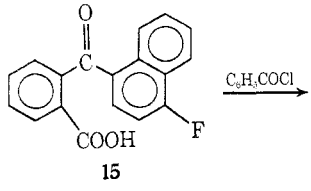
13 14



G

6-deuterio-2,3-diphenylbenzo[*b*]thiophenes (**13** and **14**).[10] The involvement of a [5.3]spirocyclic intermediate G is used to account for the results (in part).

Treatment of 2-(4-fluoro-1-naphthoyl)benzoic acid (**15**) with benzoyl chloride affords 5-chloro-7,12-benz[*a*]anthraquinone (**16**).[11] The exchange of halogens undoubtedly occurs in the (pictured as localized) [5.4]-spirocyclic intermediate H.



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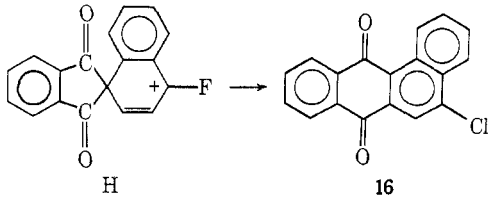
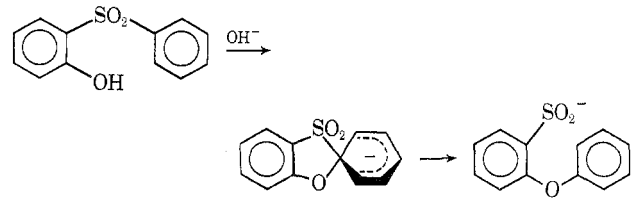


H 16

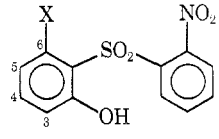
The lack of exchange of fluorine under similar conditions in analogs of **15** containing the fluorine in the meta position to the ketonic carbonyl is readily understood because the positive charge cannot be localized on the same carbon that holds the fluorine.

Carbanions

Perhaps the most frequently studied reaction which proceeds by a spirocyclic carbanion mechanism is the Smiles rearrangement,[12] which involves the rearrangement of an *o*-hydroxydiphenyl sulfone to a diphenyl ether sulfinic acid on heating with alkali. The rearrangement is pictured as going through a [5.4]spirocyclic anion as shown.



Many examples of such a rearrangement are given.[12] The fact that sulfones of type **17** rearrange 10^5 to 10^6



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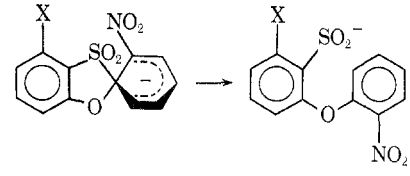
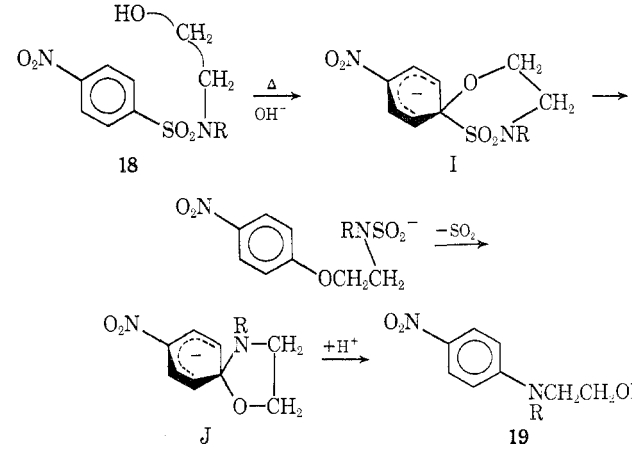


times faster than comparable sulfones without substituents in the 6 position was explained[13] by assuming that the rate enhancement was mainly due to conformational factors leading to the transition state (which was not specifically shown as a spirocyclic intermediate). The argument that another important factor is the relief of strain in going from the spirocyclic intermediate H to product can also be made. The original article[13] should be consulted for a discussion of the polar and steric effects involved.

The fact that certain sulfonamides (**18**) yield 2-arylaminoethanols (**19**) on treatment with alkali has been explained by assuming that two spirocyclic intermediates, I [5.5] and J [5.4], are involved, as shown.[14]



18 I J 19

The analogy to the Smiles rearrangement was pointed out.[14]

Other reactions in which different sulfur-containing functions are displaced in Smiles-type rearrangements by anionic oxygen-, nitrogen-, and carbon-containing

(10) G. Capozzi, G. Melloni, and G. Modena, *J. Org. Chem.*, **35**, 1217 (1970), and references therein to compounds containing substituents other than D in the para positions.

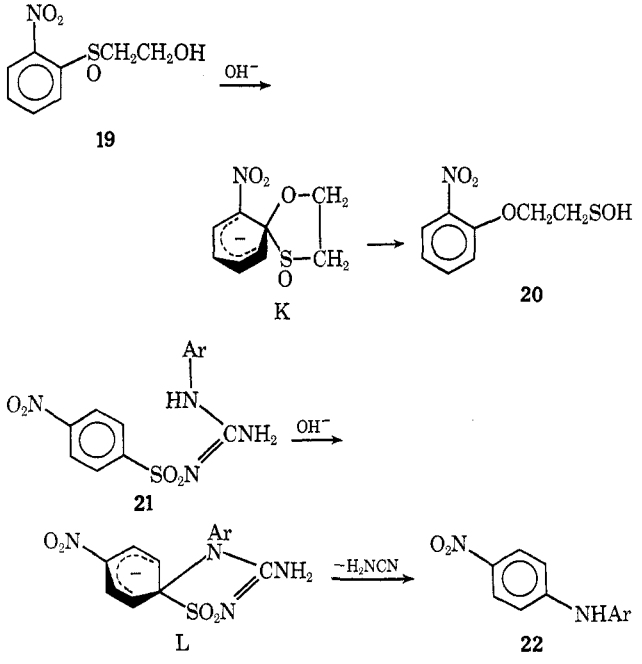
(11) E. D. Bergmann, J. Blum, and S. Butanaro, *ibid.*, **26**, 3211 (1961).

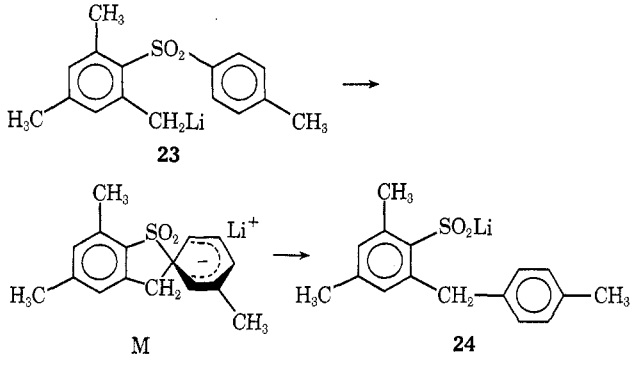
(12) J. F. Bunnett and R. F. Zahler, *Chem. Rev.*, **49**, 362 (1951).

(13) J. F. Bunnett and T. Okamoto, *J. Amer. Chem. Soc.*, **78**, 5563 (1956).

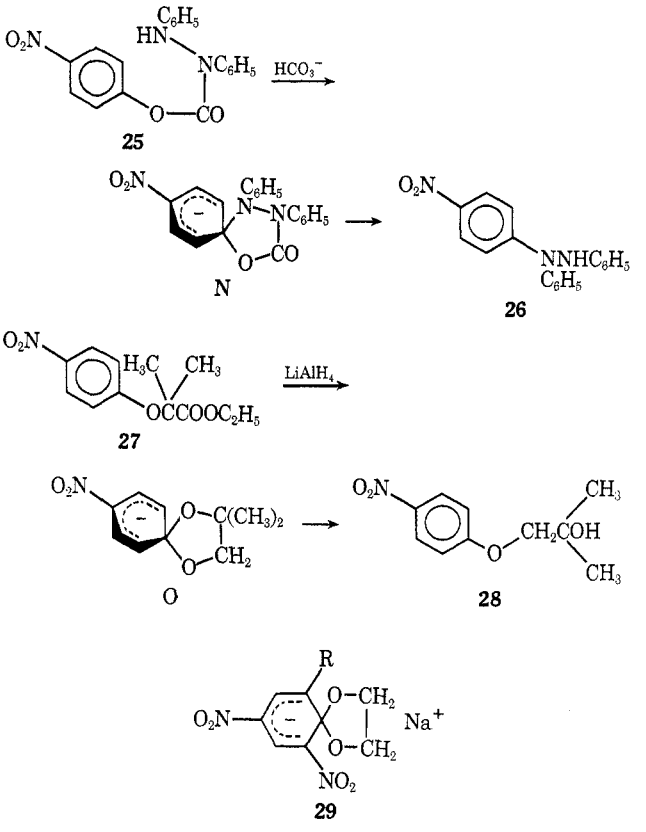
(14) K. G. Kleb, *Angew. Chem., Int. Ed. Engl.*, **7**, 291 (1968).

functions are shown in the reactions of **19**,[15] **21**,[16] and **23**[17] to **20**, **22**, and **24**, respectively. The sulfone corresponding to **19** also rearranged rapidly to the sulfenic acid analogous to **20**. The spirocyclic intermediates, K [5.4], L [5.4], and M [5.4], are shown.

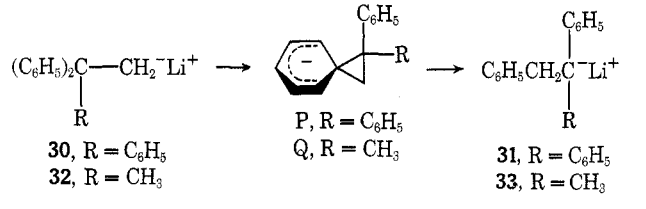




The displacement of oxygen by nitrogen or oxygen species in Smiles-type reactions is illustrated by the conversion of **25** to **26**[18] and of **27** to **28**[19] under basic conditions. The spirocyclic intermediates N [5.4] and O [5.4] are shown. Evidence in favor of the existence of O is provided by the fact that several Meisenheimer complexes of the general structure **29** have been isolated.[20]

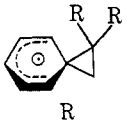


The rearrangement of carbanions *via* spirocyclic intermediates has been postulated. For example, the rearrangement of 2,2,2-triphenylethyllithium (**30**, R = C_6H_5) to 1,1,2-triphenylethyllithium (**31**, R = C_6H_5) has been postulated to proceed by way of the [5.2]-spirocyclic anion P.[21] Similarly, **32** (R = CH_3) yields **33** *via* the similar anion Q (R = CH_3).[22] The rate of these rearrangements is markedly affected by the metal used to prepare the organometallic reagent.



Free Radicals

The literature of 1,2-aryl shifts in free-radical reactions has been reviewed.[23] In certain cases aryl groups, such as 1-naphthyl and biphenyl, have a migration aptitude greater than phenyl. This fact supports the hypothesis that a [5.2]spirocyclic intermediate R is involved in such shifts.[24]



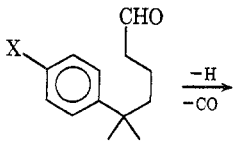
(15) B. A. Kent and S. Smiles, *J. Chem. Soc.*, 422 (1934).
(16) H. J. Backer and S. K. Wadman, *Recl. Trav. Chim. Pay-Bas*, **68**, 595 (1949).
(17) W. E. Truce, W. J. Ray, Jr., O. L. Norman, and D. B. Eickemeyer, *J. Amer. Chem. Soc.*, **80**, 3625 (1958), and later papers, *ibid.*, **81**, 481, 484 (1959).
(18) P. Baudet, M. Calin, and E. Cherbuliez, *Helv. Chim. Acta*, **47**, 1047 (1964).
(19) M. Harfenist and E. Thom, *Chem. Commun.*, 730 (1969).
(20) *Annu. Rep., Chem. Soc.*, **65**, 99 (1968).
(21) E. Grovenstein, Jr., and L. P. Williams, Jr., *J. Amer. Chem. Soc.*, **83**, 412, 2537 (1961).
(22) H. E. Zimmerman and A. Zweig, *ibid.*, **83**, 1196 (1961).
(23) C. Walling in P. de Mayo, "Molecular Rearrangements," Part 1, Wiley-Interscience, New York, N. Y., 1963 p 409 ff.
(24) See ref 20, p 428, for several references.

An excellent example of this type of rearrangement is the conversion of 3,3,3-triphenylpropanal (**34**) to 1,1,2-triphenylpropane (**35**) on heating with di-*tert*-butyl peroxide.[25] In this example, the R groups are C_6H_5 in the spirocyclic intermediate R.

$$(C_6H_5)_3CCH_2CHO \xrightarrow[\Delta,\ -CO]{(C_4H_9O)_2} (C_6H_5)_2CHCH_2C_6H_5$$

34 **35**

In the similar decarbonylation of 5-*p*-substituted-phenyl-5-methylhexanal (**36**) the formation of 5-*p*-substituted-phenyl-2-methylpentane (**37**) probably involves the [5.4]spirocyclic intermediate S.[26]



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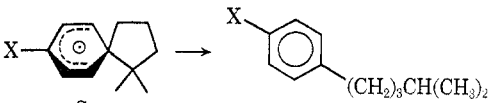
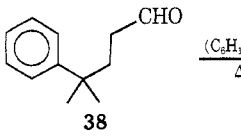


S **37**

A ketonic [5.4]spirocyclic intermediate T was postulated to account for the formation of **39** from **38**.[27]



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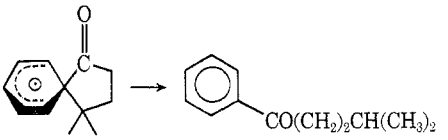
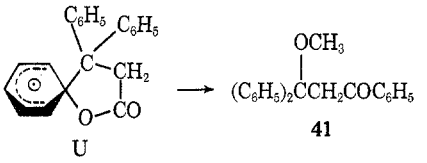


T **39**

The formation of the phenyl ester **41** on electrolysis of sodium 3,3,3-triphenylpropanoate (**40**) in methanol indicates the involvement of the [5.4]spirocyclic radical intermediate U.[28]

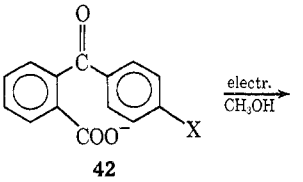
$$(C_6H_5)_3CCH_2COO^-Na \xrightarrow[\text{electr.}]{CH_3OH}$$

40



U **41**

Similarly, the electrolysis of a series of *o*-benzoylbenzoic acids (**42**) in methanolic sodium methoxide yielded aryl methyl phthalates (**43**) *via* the postulated [5.5]spirocyclic intermediate V.[29]



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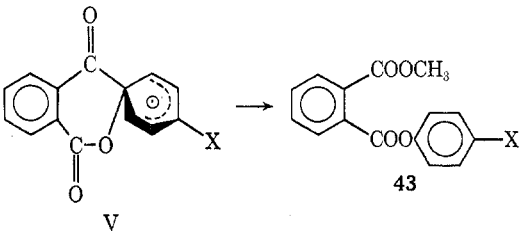
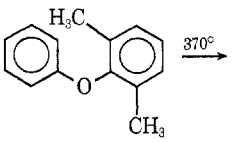


V **43**

In the preceding examples of radical reactions a phenyl group has migrated to carbon or oxygen. However, pyrolysis of 2,6-dimethylphenyl phenyl ether (**44**) at 370° produced 2-benzyl-6-methylphenol (**45**).[30] This is reported as the first case in which an aromatic group migrates from oxygen to an aliphatic carbon.[30] A mechanism involving the formation of a free benzyl-type radical was suggested.[30] The rearrangement may be pictured as involving the [5.4]spirocyclic intermediate W.



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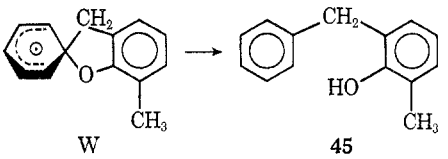
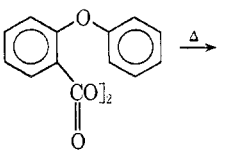
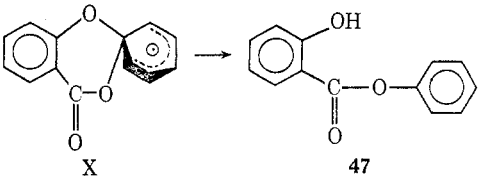


W **45**

Rearrangement of a phenyl group from an ether oxygen to a carboxyl oxygen has been demonstrated. Pyrolysis of 2-phenoxybenzoyl peroxide (**46**) yields phenyl salicylate (**47**) *via* the [5.5]spirocyclic radical X.[31]



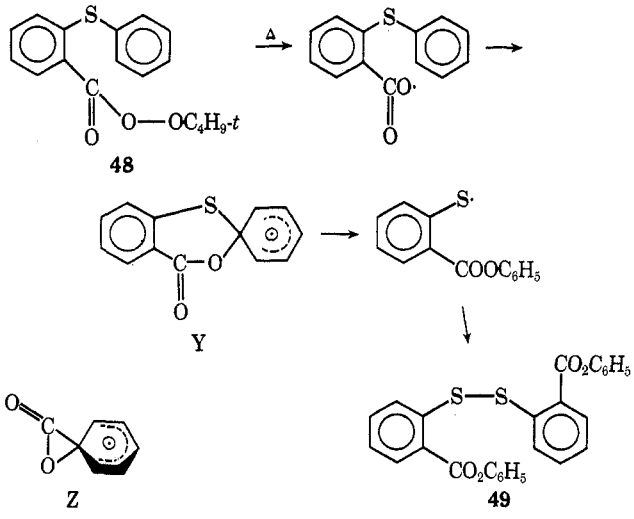
46



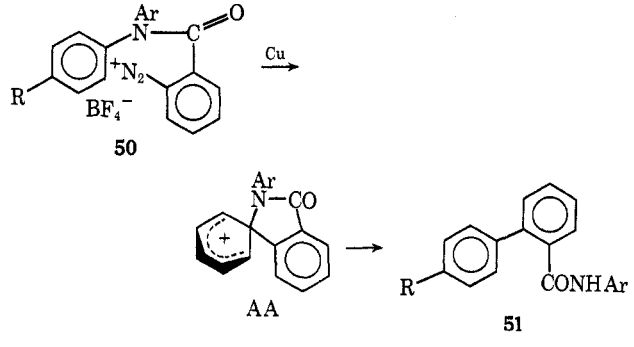
X **47**

(25) D. Y. Curtin and M. J. Hurwitz, *J. Amer. Chem. Soc.*, **74**, 5381 (1952).
(26) S. Winstein, R. Heck, S. Laporte, and R. Baird, *Experientia*, **12**, 138 (1956).
(27) W. H. Urry, D. J. Trecker, and H. D. Hartzler, *J. Org. Chem.*, **29**, 1663 (1964).
(28) H. Breederveld and E. C. Kooyman, *Recl. Trav. Chim. Pays-Bas*, **76**, 297 (1957). See also J. W. Witt and L. J. Finnerty, *J. Org. Chem.*, **26**, 2173 (1961), and references therein.
(29) P. J. Bunyan and D. H. Hey, *J. Chem. Soc.*, 324 (1962).
(30) A. Factor, H. Finkbeiner, R. A. Jerussi, and D. M. White, *J. Org. Chem.*, **35**, 57 (1970).

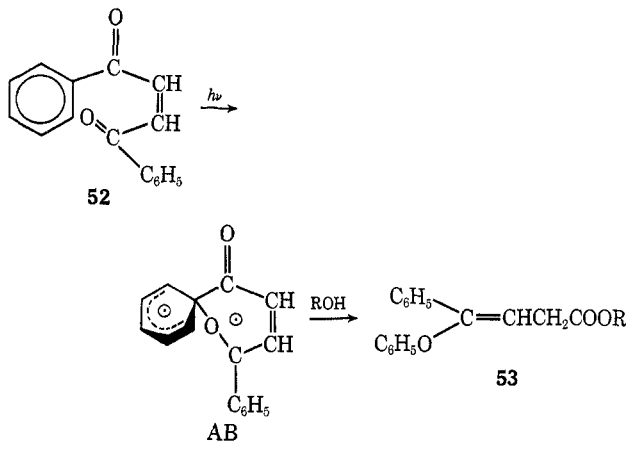
An analogous reaction involving migration of phenyl from sulfur to oxygen is found in the formation of the disulfide **49** on pyrolysis of **48**. The [5.5]intermediate Y offers an alternate explanation to that in the paper.[32] In this paper[32] the suggestion previously made[33] that a [5.2]spirocyclic radical Z may be involved in the decomposition of benzyloxy radicals was discussed.



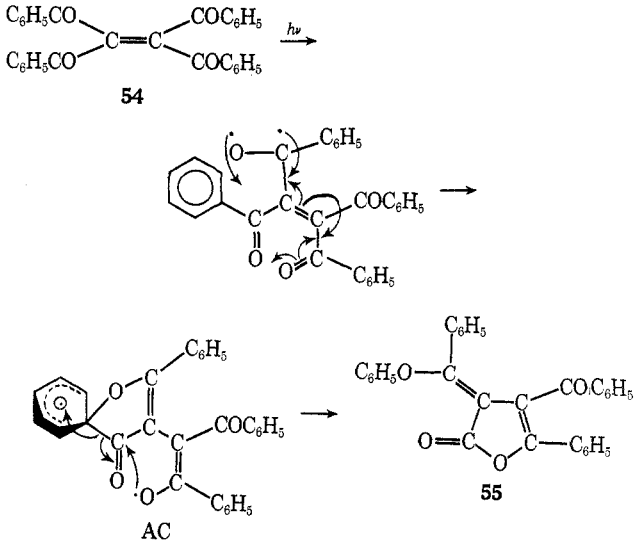
In all of the above examples of spirocyclic free radicals, the free radical, generated at a nonaromatic site, attacks an aromatic ring carbon. In a different type of reaction, the aromatic free radical generated by treating the diazonium fluoroborate **50** with copper forms the [5.4]spirocyclic intermediate AA which opens and yields **51**.[34]



Examples of photochemical rearrangements are included in concluding the discussion of free-radical rearrangements. The rearrangement of *cis*-dibenzoylethylene (**52**) on irradiation in alcohols to give alkyl 4-phenoxy-4-phenyl-3-butenoates (**53**) was explained by postulating the [5.5]spirocyclic diradical AB as an intermediate.[35,36]



A different reaction course which may involve the [5.4]spirocyclic diradical AC is pictured in the photochemical rearrangement of tetrabenzoylethylene (**54**) to **55**[37] as shown.



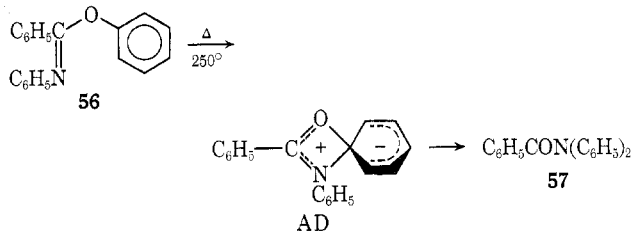
Dipolar Ionic Intermediates

Perhaps the best studied rearrangement reactions which have been assumed to proceed *via* spirocyclic dipolar ions are the Chapman[38] rearrangement and the thermal rearrangement of *O*-aryl dialkylthiocarbamates to *S*-aryl dialkylthiocarbamates.[39,40] In each of these cases, the rate of reaction has been shown to be unimolecular, increased by electron-attracting substituents in the ring, which becomes negatively charged, and affected in complicated ways by ortho groups.[41,42]

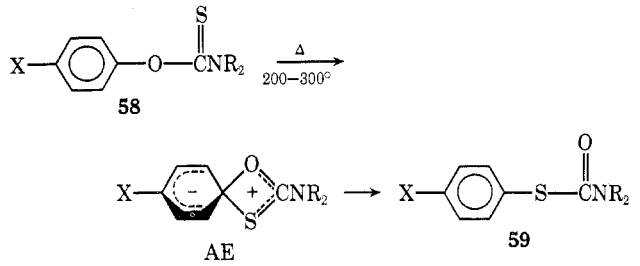
A typical example of the Chapman rearrangement is illustrated by the pyrolysis of phenyl benzanil imino

(31) D. F. DeTar and A. Hlynsky, *J. Amer. Chem. Soc.*, **77**, 4411 (1955).
(32) W. G. Bentrude and J. C. Martin, *ibid.*, **84**, 1561 (1962); J. C. Martin and W. G. Bentrude, *Chem. Ind. (London)*, 192 (1959).
(33) C. Walling and E. S. Saras, *J. Amer. Chem. Soc.*, **82**, 1738 (1960).
(34) D. H. Hey, C. W. Rees, and A. R. Todd, *J. Chem. Soc.*, 1518 (1967).
(35) G. W. Griffin and E. J. O'Connell, *J. Amer. Chem. Soc.*, **84**, 4148 (1962).
(36) H. E. Zimmerman, H. C. G. Durr, R. G. Lewis, and S. Bram, *ibid.*, **84**, 4149 (1962).
(37) H. Schmid, M. Hochweber, and H. von Halban, *Helv. Chim. Acta*, **30**, 1135 (1947).
(38) A. W. Chapman, *J. Chem. Soc.*, 1992 (1925); 2296 (1926); 1749 (1927).
(39) M. S. Newman and H. A. Karnes, *J. Org. Chem.*, **31**, 3980 (1966).
(40) H. Kwart and E. R. Evans, *ibid.*, **31**, 410 (1966).
(41) K. B. Wiberg and B. I. Rowland, *J. Amer. Chem. Soc.*, **77**, 2205 (1955).
(42) H. M. Relles, *J. Org. Chem.*, **33**, 2245 (1968); H. M. Relles and G. Pizzolato, *ibid.*, **33**, 2249 (1968).

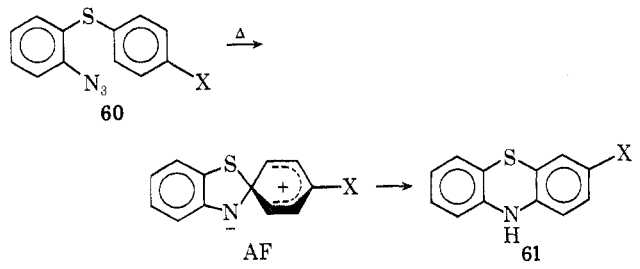
ether (**56**) to yield *N*-phenylbenzanilide (**57**) *via* the [5.3]spirocyclic dipolar ion AD.[38]



The rearrangement[39,40] of *O*-aryl dialkylthiocarbamates (**58**) to *S*-aryl dialkylthiocarbamates (**59**) may involve the [5.3]spirocyclic dipolar ion AE as shown.



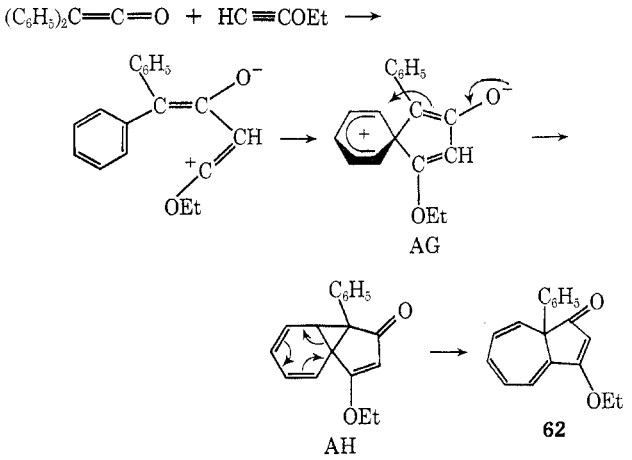
A closely related reaction which also probably involves a spirocyclic intermediate is the Schonberg rearrangement of diaryl thiocarbonates to diaryl thiocarbonates.[43]



(43) D. H. Powers and D. S. Tarbell, *J. Amer. Chem. Soc.*, **78**, 70 (1956), and references therein.

On pyrolysis a variety of diphenyl thioethers (**60**) are converted to phenothiazines (**61**) of rearranged structure. These reactions are pictured as proceeding *via* the [5.4]spirocyclic dipolar ions AF, as shown.[44,45]

A more complicated reaction mechanism which is pictured as involving the spirocyclic dipolar intermediate, AG, was postulated to account for the formation of **62** from the reaction of diphenylketene with ethoxyacetylene.[46]



In conclusion, it should be emphasized that reactions which involve spirocyclic intermediates are general. Such reactions may be expected whenever a compound containing a suitably substituted aromatic ring is subjected to reaction conditions which allow for aromatic participation. Furthermore, aromatic participation is shown to involve 1,3, and 1,4, and 1,5 examples in addition to the better known 1,2 examples. The numerous examples which involve [5.2]-, [5.3]-, [5.4]-, and [5.5]spirocyclic species cited in this paper suggest that many more examples remain to be discovered.

(44) M. Messer and D. Farge, *Bull. Soc. Chim. Fr.*, 2832 (1968).
(45) J. I. G. Cadogan and S. Kulik, *Chem. Commun.*, 436 (1970).
(46) J. Druey, E. F. Jenny, K. Scheuker, and R. B. Woodward, *Helv. Chim. Acta*, **45**, 600 (1962).