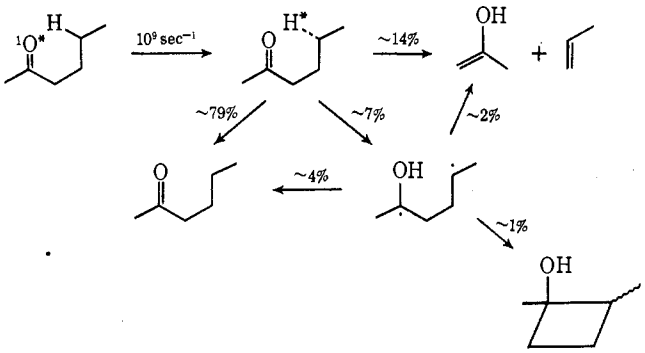
species partitions its energy. Excited-state rate constants should depend on the stretching frequency of the bond being broken. It is worthwhile exploring whether this idea can explain singlet-state type II processes.

Scheme III



Scheme III estimates how excited singlet 2-hexanone might dissipate its excitation energy *via* interaction with a γ C–H bond. The relative percentages are based on the assumption that any singlet biradical partitions itself among products in the same way as does the biradical formed from triplet 2-hexanone. Unfortunately, there is kinetic evidence both for and against such electronic–vibrational energy transfer. If both singlet and triplet ketones abstracted hydrogen atoms by the same mechanism, the 10-fold greater reactivity of singlets toward γ C–H bonds (compare Tables VI and IX) is difficult to explain in comparison with the well-documented 100-fold greater reactivity of triplets toward Sn–H bonds.[55] However, the comparison makes sense in terms of radiationless decay theory. Since the Sn–H stretching frequency is only half as large as that for C–H, transfer of electronic energy into Sn–H stretching modes would be expected to be very much slower than into C–H stretches. On the other hand, radiationless decay theory would predict huge deuterium isotope effects. Experiments indicate that γ deuteration increases singlet ketone lifetimes by a factor of only three[7] or four.[56] Hopefully, further work will soon resolve this intriguing dilemma.

Acknowledgments are due to my diligent coworkers; to the National Science Foundation; to Professors Stephenson, Lewis, Padwa, and Turro for their generous sharing of unpublished results; and to N. C. Yang for first attracting my interest to type II reactions, and for regularly reinforcing that interest.

(55) P. J. Wagner, *J. Amer. Chem. Soc.*, **89**, 2503 (1967).
(56) A. Padwa and W. Bergmark, *Tetrahedron Lett.*, 5795 (1968).

Migrations of Alkoxycarbonyl Groups

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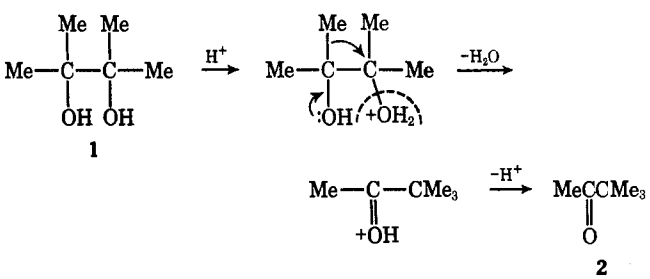
The subject of intramolecular rearrangement has fascinated chemists since the time of Fittig, who in 1860 discovered that pinacol (**1**) with sulfuric acid isomerized to pinacolone (**2**). Very many examples and types of rearrangements are now known; the tendency to form a more stable arrangement of atoms than that present in the starting material is the driving force for the reactions. This can be associated with the relief of steric strain, or the formation of aromatic or more conjugated systems, during the rearrangement.

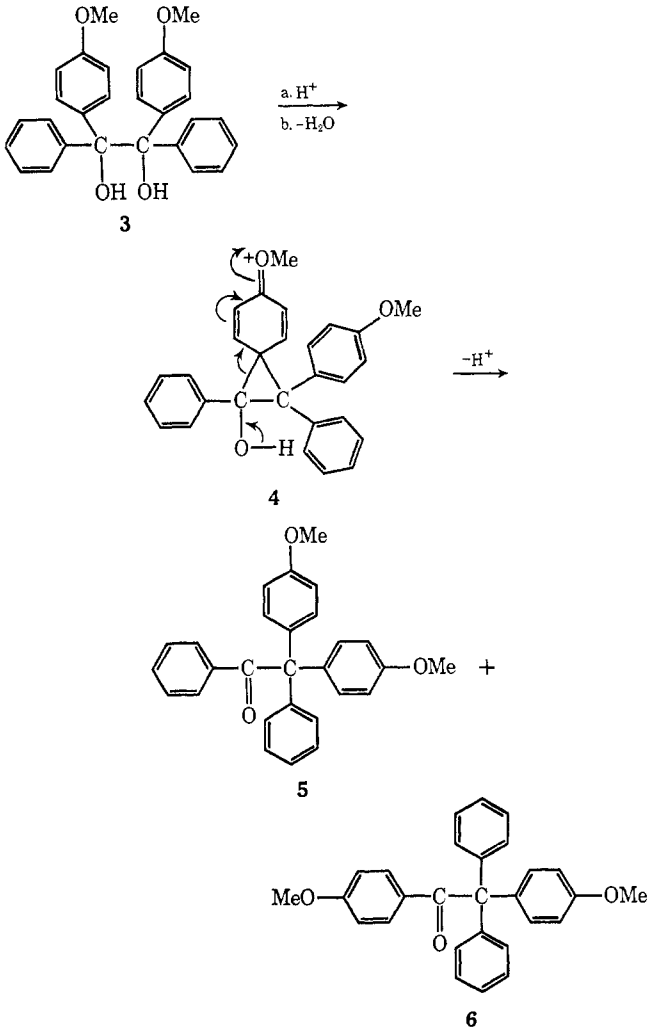
Fittig's reaction proceeds by protonation of one hydroxyl group after which a methyl group migrates as water is eliminated. A very large number of rearrangements of this general type have been discovered,



and both alkyl and aryl groups can move.[1] Relative

(1) G. W. Wheland, "Advanced Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1960, p 536 ff; P. de Mayo, Ed., "Molecular Rearrangements," Parts 1 and 2, Interscience, New York, N. Y., 1960.

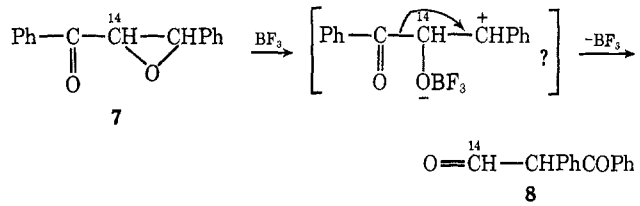
"migratory aptitudes" of different groups have been assessed in some cases. For example, when the pinacol **3** is treated with acid the 4-methoxyphenyl group migrates much more readily than the phenyl group, as **5** and **6** are formed in 500:1 ratio.[1] The methoxyl group stabilizes the intermediate phenonium ion **4**.



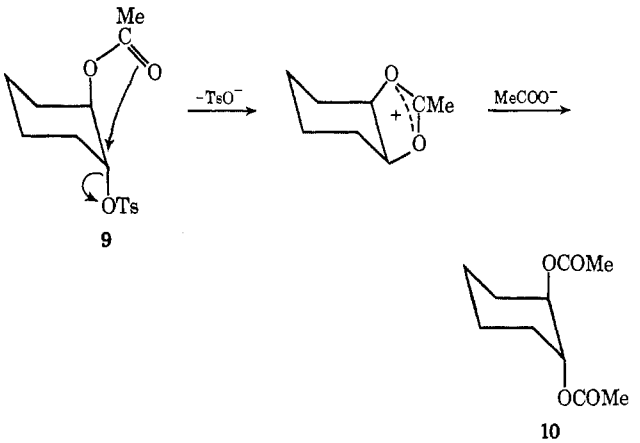
This type of ion has been detected in other reactions.[2]

Whitmore in 1932 put forward[3] a general theory of "1,2 shifts." This includes the pinacol–pinacolone and Beckmann rearrangements, the Hofmann degradation of amides to amines, and a number of other rearrangements of the same mechanistic type. These rearrangements are characterized by their intramolecular nature, which has been demonstrated in some cases by rearranging a mixture of two compounds which separately rearrange similarly and at comparable rates. The lack of formation of "crossed products," which can only be built up from parts of both of the original compounds, indicates the intramolecular nature of the rearrangements. Retention of the configuration of the moving group and the inversion of the center to which it moves can be demonstrated in suitable cases using optically active materials.[1] It is not clear whether these rearrangements are precisely concerted or not, but it is certain that the moving group never becomes free from the influence of the rest of the molecule during the rearrangements.

Migrations of acyl groups to positive centers are exemplified[4] by the boron trifluoride catalyzed rearrangement of the oxirane **7** to the ketone **8**, the movement of the acyl group being established by the path of the labeled atom shown. Electrophilic attack on the



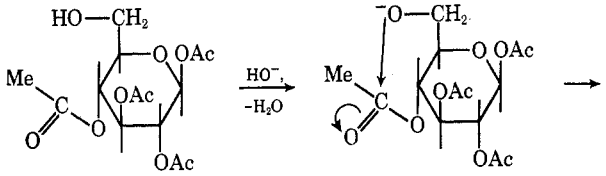
carbonyl oxygen atom of an acyloxy group, which can occur in certain types of neighboring group participation,[5] also leads to migration as in the solvolysis of (+)-*trans*-2-acetoxycyclohexyl tosylate (**9**) by sodium acetate in acetic acid to (±)-*trans*-1,2-cyclohexyl diacetate (**10**). The intermediate possesses a plane of symmetry.



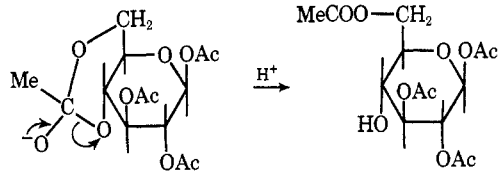
Migrations of acyl groups to negative centers through the formation of cyclic intermediates, for example[6] the base-catalyzed rearrangement of tetraacetylglucose **11** to the isomer **12**, are also well known.

In view of the easy movement of alkyl, aryl, and acyl groups from one position to another in a suitable molecule under suitable conditions, it is remarkable that so very few rearrangements involving the migration of intact alkoxycarbonyl groups have been discovered. No discussion of this type of rearrangement is made in any textbook or review article with which the author is familiar. The first alkoxycarbonyl shift was reported by Ranson[7] in 1900, who showed that 2-amino-

(2) R. J. Jabonski and E. I. Snyder, *Tetrahedron Lett.*, 1103 (1968).
(3) F. C. Whitmore, *J. Amer. Chem. Soc.*, **54**, 3274 (1932).
(4) H. O. House, *ibid.*, **78**, 2298 (1956).
(5) B. Capon, *Quart. Rev., Chem. Soc.*, **18**, 45 (1964).
(6) B. Helferick and W. Klein, *Justus Liebigs Ann. Chem.*, **450**, 219 (1926).
(7) J. H. Ransom, *Ber.*, **33**, 199 (1900).

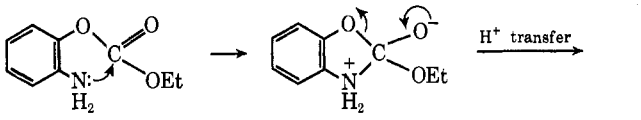


11



12

phenyl ethyl carbonate (**13**) isomerized to the urethane **14** on standing at room temperature for 12 hr. Presumably cyclization occurs as indicated, and the



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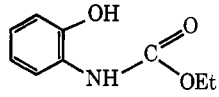


14

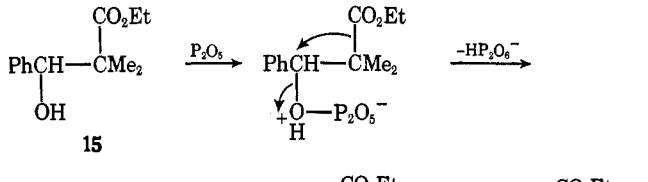
newly formed ring opens in the opposite direction as in the rearrangement of **11** to **12**.

Blaise and Courtot[8] in 1906 made the next very intriguing observation in this area by showing that an ethoxycarbonyl group could move more readily than a methyl group to a positive center (**15** → **16**). In the next 50 years one further example of an alkoxycarbonyl shift was found. Since then a relatively small number of ester shifts have been discovered, but nevertheless it is established that the migration of alkoxycarbonyl groups can be so facile as to take precedence over the possible migration of both alkyl and aryl groups. It is the purpose of the present Account to classify the rather meager and scattered data available and to draw attention to the known alkoxycarbonyl shifts with the expectation that many more examples will come to light in the future.

Migrations of Ester Groups with Their Bonding Electrons

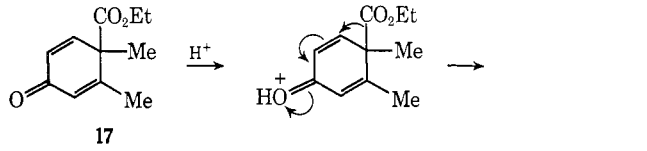
Carbonium Ion Type Rearrangements. Blaise and Courtot's ester shift,[8] the conversion of the hydroxy ester **15** to the unsaturated ester **16** by the action of phosphorus pentoxide, appears to be of this type. Presumably the hydroxyl group is phosphorylated, and during its removal the ester group undergoes a 1,2 shift with its bonding electrons as indicated.

Conversion of the ketones **17**[9,10] and **19**[11] by about

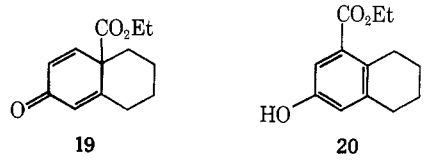


15 16

50% aqueous sulfuric acid to the phenols **18** and **20** presumably takes place by protonation of the carbonyl group and migration of the ester group to the electron-

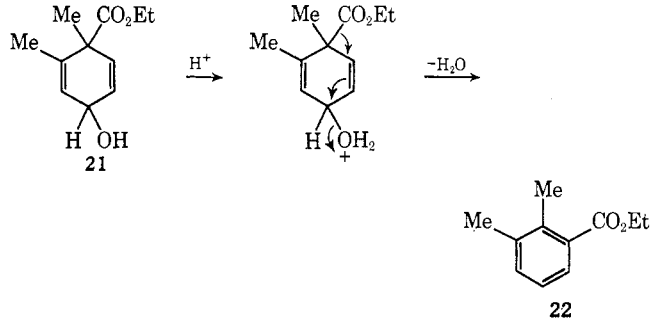


17 18



19 20

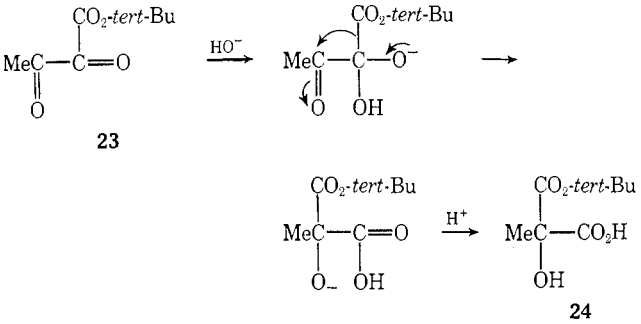
deficient β position as indicated. In a similar way the alcohol **21** is dehydrated[10] by dilute acid to **22**. The noteworthy feature of these and other rearrangements considered later is that the ester group can migrate in preference to an alkyl group.



21 22

Benzil–Benzilic Acid Type Rearrangements. The *tert*-butyl ester **23** with alkali appears to undergo[12] a benzil–benzilic acid type of rearrangement[13] with the formation of **24**; similar reactions can occur with amides.[12] Tracer studies with the ethyl ester corresponding to **23** have excluded the possibility of the methyl group moving position.[14]

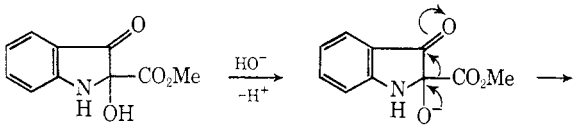
(8) E. E. Blaise and A. Courtot, *Bull. Soc. Chim. Fr.*, [3] **35**, 360, 589 (1906).
(9) H. Plieninger and T. Suehiro, *Chem. Ber.*, **89**, 2789 (1956).
(10) H. Plieninger, L. Arnold, and W. Hoffmann, *ibid.*, **101**, 981 (1968).
(11) S. Inayama and M. Yanagita, *J. Org. Chem.*, **27**, 1465 (1962).
(12) H. Dahn, M. Ballenegger, and H. P. Schlunke, *Chimia*, **18**, 59 (1964).
(13) S. Selmon and J. F. Eastham, *Quart. Rev., Chem. Soc.*, **14**, 221 (1961).
(14) H. W. Davis, E. Grovenstein, and O. K. Neville, *J. Amer. Chem. Soc.*, **75**, 3304 (1953).



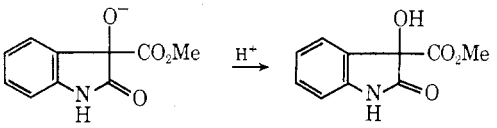
23

24

In 1911 Kalb[15] showed that the indoxyl **25** with aqueous sodium hydroxide was converted in excellent yield to the oxindole **26**. When ^{18}O-enriched water was used[16] as solvent the incorporation of ^{18}O into the product was far too low for the sequence of ring opening to a diketo ester (*cf.* **23**), rearrangement (*cf.* **23** → **24**), and ring closure to be possible. The ester group therefore appears to move with its bonding electrons as

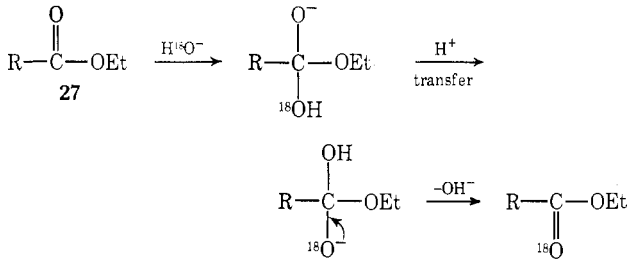


25



26

indicated. The small incorporation of ^{18}O probably occurs at the carbonyl groups, for Bender[17] has shown that the ester group can undergo oxygen exchange, **27** → **28**, in the presence of base.

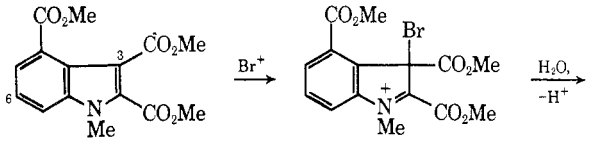


27 28

Trimethyl 1-methylindole-2,3,4-tricarboxylate (**29**) with bromine in anhydrous acetic acid yields the 6-bromo derivative, but if water is present the oxindole **31** (R = Br) is formed.[18] The key steps in sequence are the addition of a bromonium ion at position 3, nucleophilic attack by water at position 2, and substitution of bromine in the ring to give **30**. Loss of the 2-hydroxy proton followed by a probably concerted movement of the ester group with its bonding electrons and expulsion of the bromine ion from position 3 leads to **31** (R = Br).

(15) L. Kalb, *Ber.*, **44**, 1455 (1911).
(16) R. M. Acheson and S. R. G. Booth, *J. Chem. Soc C*, 30 (1968).
(17) M. L. Bender, *J. Amer. Chem. Soc.*, **73**, 1626 (1951).
(18) R. M. Acheson, R. W. Snaith, and J. M. Vernon, *J. Chem. Soc.*, 614 (1964).

Attempts to detect the suspected intermediate **30** by spectral methods have failed, but the substitution of an intermediate must take place as **31** (R = H) does not brominate under the reaction conditions.



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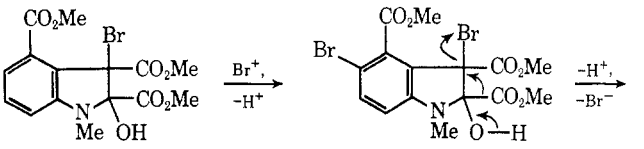

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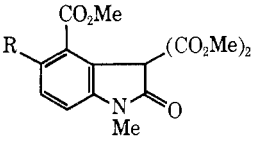
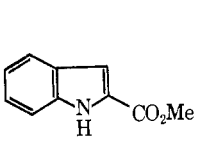


31

Methyl indole-2-carboxylate (**32**) undergoes[19] a similar reaction with ethyl *N*,*N*-dichlorocarbamate in aqueous acetic acid, yielding a mixture of **34** and its 7-chloro derivative. Treatment of **33**,[20] the structure of which has been established by an X-ray diffraction investigation,[21] with refluxing 50% aqueous acetic acid gave the oxindole **35**.



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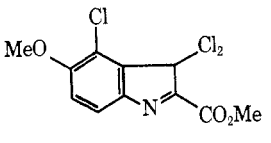

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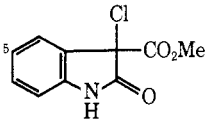


34, 5-Cl
35, 4-Cl-5-MeO

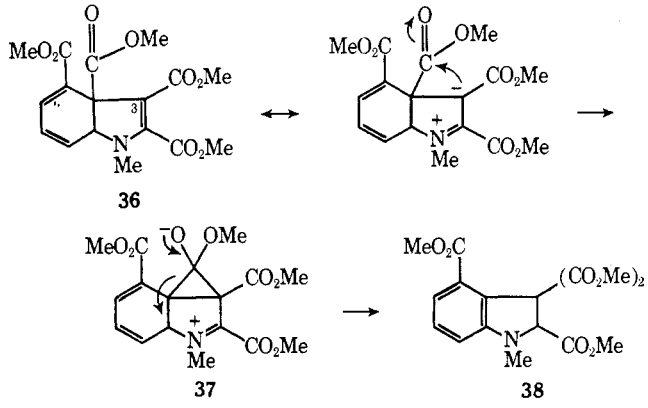
Migrations of Ester Groups to a Nucleophilic Center

Nucleophilic attack at the carbonyl carbon atom of the moving ester group to form a ring, followed by release of the electrons originally bonding the ester group to the rest of the molecule, has been suggested as the mode through which the ester group migrates in a series of reactions considered to take place through the formation of three- to six-membered rings.

Structures containing a three-membered ring (*e.g.*, **37**), analogous to intermediate structures suggested in the Favorskii rearrangement, are considered likely in the thermal conversion[22] of tetramethyl 1-methyl-3a,-

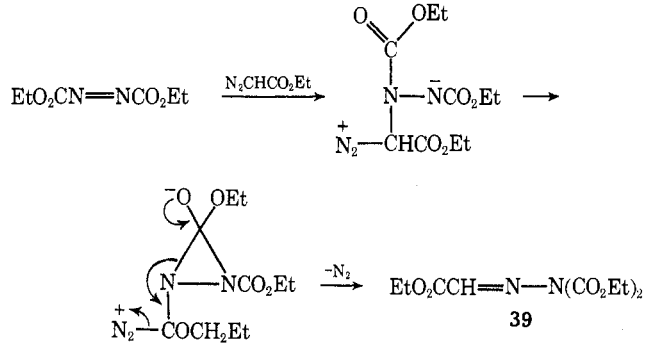
(19) J. M. Muchowski, *Can. J. Chem.*, **48**, 422 (1970).
(20) R. J. Bass, personal communications.
(21) D. Rogers, personal communications.
(22) R. M. Acheson and J. M. Vernon, *J. Chem. Soc.*, 1907 (1963).

7a-dihydroindole-2,3,3a,4-tetracarboxylate (**36**) to the dihydroindole **38**, and in the reaction[23] between diethyl azodicarboxylate and ethyl diazoacetate which yields the ester **39**. The attack of the 3a-ester group of the dihydroindole **36** at the 3 position is exactly analogous to electrophilic attack at the β-carbon atom of an enamine.

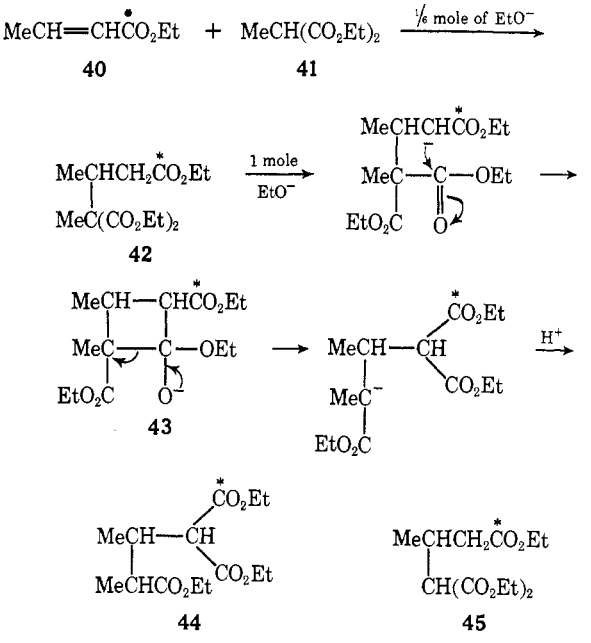


36 **37** **38**

Michael discovered the addition reaction,[24] which now bears his name, in 1887. This reaction consists of the addition of a carbanion, such as that formed from diethyl methylmalonate (**41**) with base, to a double bond activated by an electron-attracting substituent which can be an ester group. Thus the addition of **40** to **41** is expected to give **42** and does so in the presence of a limited quantity of base. However the use of 1 mole of sodium ethoxide causes an "abnormal" Michael reaction to occur, yielding the "abnormal" product **44**. It was first thought that **42** was produced initially, and that a methyl group moved subsequently

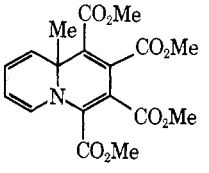


to give **44**. However Holden and Lapworth[25] in 1931 pointed out that migration of the ester group was much more plausible on mechanistic grounds, and they accounted for the formation of the product through an intermediate cyclobutanone (*cf.* **43**). Experiments with ^{14}C- and ^{18}O-carboxyl-labeled ethyl crotonate, followed by the determination of position of the label in the products, have established the correctness of Lapworth's ideas. The driving force for the reaction is clearly the formation of the product which can give the more stable anion. The "abnormal" product **44** possesses a proton activated by two ester groups, while **42** does not. This interpretation is strongly supported



40 **41** **42** **43** **44** **45**

by the fact that the product from ^{14}C-carboxyl-labeled ethyl crotonate, diethyl malonate, and 1 mole of sodium ethoxide was **45**, it being established that no unlabeled ester had been transferred to the carbon atom bearing the labeled group.[26] A normal Michael addition had therefore taken place, and as **45**, in contrast to **42**, possesses a hydrogen atom activated by two ester groups, no thermodynamic advantage would be gained by an ester shift.



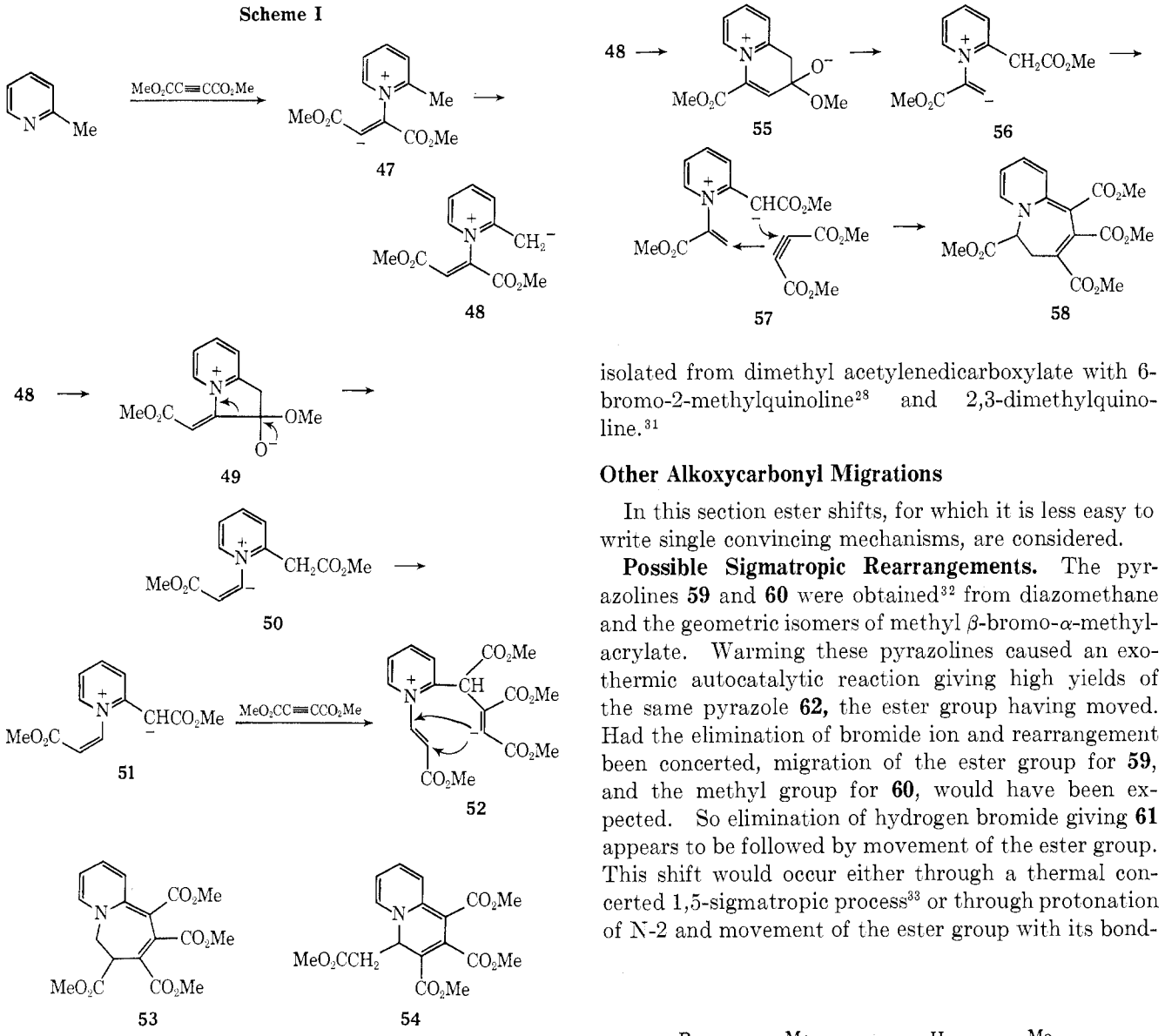
46

Five- and six-membered cyclic intermediates, such as **49** and **55**, have been put forward[27,28] to account for the formation of certain types of products from reactions of acetylenedicarboxylic esters with heterocycles which possess a methyl group activated by a pyridine-type nitrogen atom in the "ortho" position. Although 2-methylpyridine itself only gives 9a*H*-quinolizines (*e.g.*, **46**) with dimethyl acetylenedicarboxylate,[29] 6-bromo-2-methylquinoline yields compounds of type **53** and **58**, and 1-methylisoquinoline products of type **53** and **54**, concurrently with the formation of 9a*H*-quinolizines.[27]

In the first stage of Scheme I nucleophilic addition of the pyridine to the activated triple bond of the acety-

(23) E. Fahr and F. Scheckenbach, *Justus Liebigs Ann. Chem.*, **655**, 86 (1962).
(24) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. React.*, **10**, 179 (1959).
(25) N. E. Holden and A. Lapworth, *J. Chem. Soc.*, 2368 (1931).
(26) G. A. Swan, *ibid.*, 1039 (1955).
(27) R. M. Acheson, J. M. F. Gagan, and D. R. Harrison, *ibid.*, *C*, 362 (1968).
(28) R. M. Acheson, R. T. Aplin, J. M. F. Gagan, D. R. Harrison, and G. R. Miller, *Chem. Commun.*, 451 (1966).
(29) R. M. Acheson, R. S. Feinberg, and J. M. F. Gagan, *J. Chem. Soc.*, 948 (1965).

Scheme I



lenic ester gives **47**. While not rigorously established, this reaction is highly likely on the basis of many analogies.[30] Proton transfer yielding **48** can then follow as an intermolecular process or as an intramolecular process involving a six-membered cyclic transition state. Nucleophilic attack by the carbanion on either ester group could now proceed. Cyclization to the five-membered intermediate **49** could be followed by ring opening in the opposite sense to **50**, and proton transfer would then lead to species **51**. Nucleophilic addition of **51** to another molecule of the acetylenic ester would give a new carbanion **52** which by cyclization at the alternative positions indicated, followed by proton transfer, would give structures of types **53** and **54**.

An alternative cyclization of **48** to the six-membered intermediate **55** could be followed by a similar series of transformations through **56** and **57**, leading to **58**.

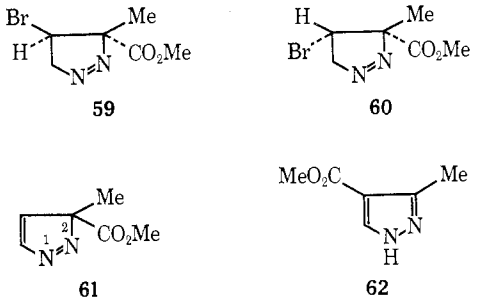
Isomeric azepines of types **53** and **58** have been isolated from dimethyl acetylenedicarboxylate with 6-bromo-2-methylquinoline[28] and 2,3-dimethylquinoline.[31]

(30) R. M. Acheson, *Advan. Heterocycl. Chem.*, 1, 125 (1963); R. M. Acheson and A. O. Plunkett, *J. Chem. Soc.*, 2676 (1964).

Other Alkoxycarbonyl Migrations

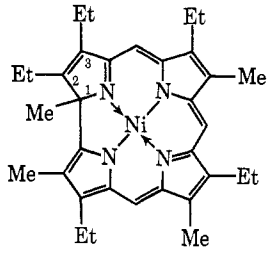
In this section ester shifts, for which it is less easy to write single convincing mechanisms, are considered.

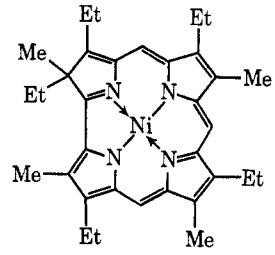
Possible Sigmatropic Rearrangements. The pyrazolines **59** and **60** were obtained[32] from diazomethane and the geometric isomers of methyl β-bromo-α-methylacrylate. Warming these pyrazolines caused an exothermic autocatalytic reaction giving high yields of the same pyrazole **62**, the ester group having moved. Had the elimination of bromide ion and rearrangement been concerted, migration of the ester group for **59**, and the methyl group for **60**, would have been expected. So elimination of hydrogen bromide giving **61** appears to be followed by movement of the ester group. This shift would occur either through a thermal concerted 1,5-sigmatropic process[33] or through protonation of N-2 and movement of the ester group with its bond-



ing electrons. Heating the nickel 1-methyl-2,3-diethyltetrahydrocorrin **63** in 1,2,4-trichlorobenzene causes rearrangement to the 2-methyl-3,3-diethyl isomer **65**. This probably takes place through two successive 1,5-sigmatropic shifts, **63** → **64** → **65**. A similar process could account for the thermal conversion of the 1-ethoxycarbonylcorrin **66** (R = Me and Et) to the 3 isomer **68**, although the movement of the

(31) R. M. Acheson and D. F. Nisbet, unpublished observation.
(32) D. E. McGreer and Y. Y. Wigfield, *Can. J. Chem.*, **47**, 2095 (1969).
(33) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, 1, 17 (1968).


63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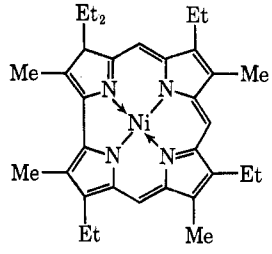
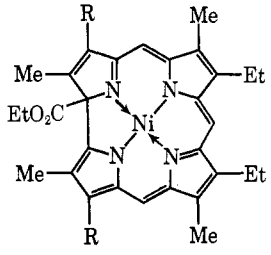
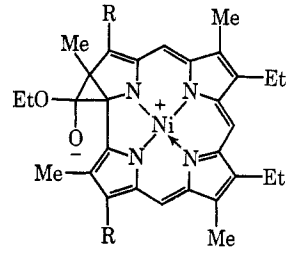

65

ester group *via* two cyclopropane intermediates (*e.g.*, **67**; *cf.* **37**) cannot be excluded.[34]


66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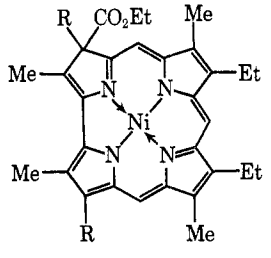
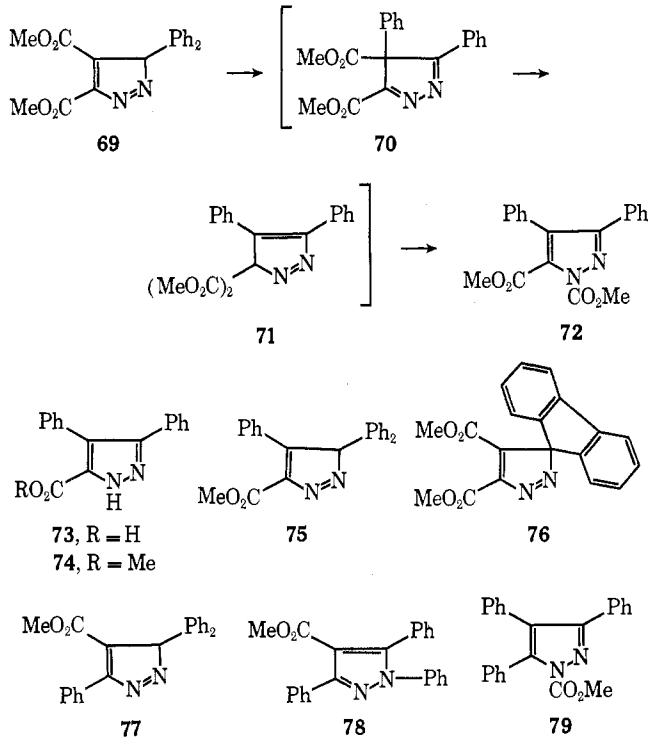

68

van Alphen in 1943 discovered[35] a number of rearrangements of 3*H*-pyrazoles involving ester shifts. Treating the pyrazole **69**, obtained from dimethyl acetylenedicarboxylate and diphenyldiazomethane, with either cold concentrated sulfuric acid or hot methanolic potassium hydroxide caused a rearrangement to occur with the formation of **73** and **74**, respectively. The 3*H*-pyrazole with hot acetic acid, or acetic anhydride, or even in maleic anhydride at 100°, gave **72**. This compound could be an intermediate in the previous rearrangements, for on further reaction with potassium hydroxide or with concentrated sulfuric acid **73** and **74** were obtained.

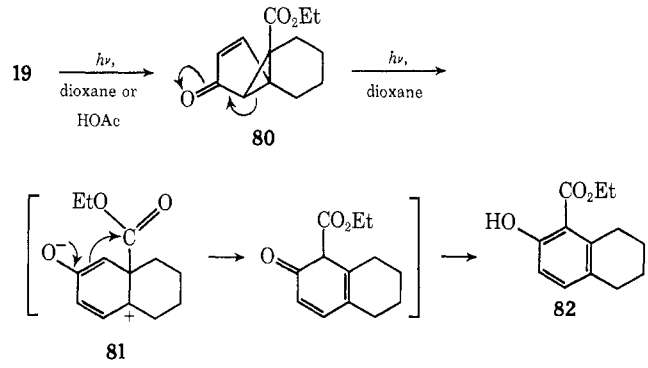
An exactly similar series of transformations is reported[35] for **75**, and also for **76**[36] and **77**[37] where migration of an aryl substituent to nitrogen, for example, giving **78**, also occurs. **79** is formed from both **75** and **77**, and an attempt[37] has been made to ascertain the relative amounts of migration of phenyl to nitrogen and carbon under various conditions in the case of **77**.


69 70 71 72 73, R = H 74, R = Me 75 76 77 78 79

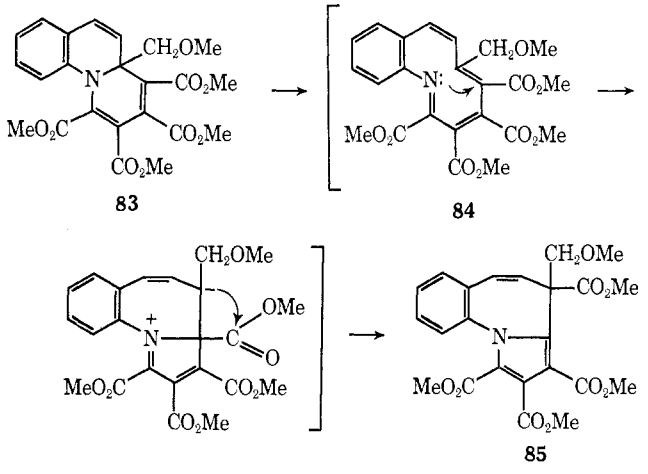
The broad features of the rearrangement are clear. It can be brought about by cold concentrated acid, heat, or hot alkali. The fact that methyl 3,3-diphenylpyrazole-5-carboxylate rearranges to methyl 3,4-diphenylpyrazole-5-carboxylate even on attempted recrystallization from methanol[35] shows that a 3-phenyl group can readily move to the 4 position. This and the formation of **79** from **77** are strongly suggestive that the rearrangement can take place through a series of sigmatropic shifts, *e.g.*, **69** → **70** → **71** → **72**, but does not exclude a similar scheme preceded by protonation when sulfuric acid is involved. It can also be concluded that an ester group can migrate in preference to a phenyl group.

Photochemical Rearrangements. Two photochemical shifts of ester groups have been described. Irradiation[38] of the ketone **19** in dioxane or aqueous acetic acid caused first the "lumiketone" rearrangement giving **80**. A subsequent photolytic reaction yielded the tetralin **82** in 90% yield, possibly *via* the ionic intermediate **81** and a 1,2 shift of the ester group. It is interesting that the ester group, and not the methylene chain attached to the carbon bearing the ester group in **81**, migrates. One of the products from the irradiation of **83** is thought[39] to be **85** formed by ring opening to the annulene **84**, cyclization as indicated, and an ester shift

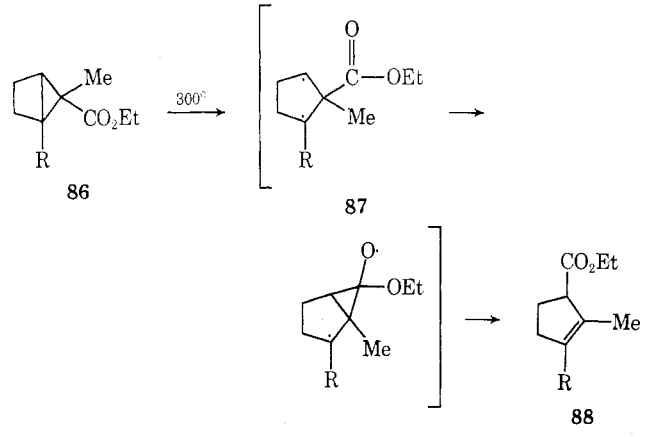
(34) R. Grigg, A. W. Johnson, K. Richardson, and M. J. Smith, *J. Chem. Soc. C*, 1289 (1970).
(35) J. van Alphen, *Recl. Trav. Chim. Pays-Bas*, **62**, 485 (1943).
(36) J. van Alphen, *ibid.*, **62**, 491 (1943).
(37) R. Hüttel, K. Franke, H. Martin, and J. Riedel, *Chem. Ber.*, **93**, 1433 (1960).
(38) P. J. Kropp, *Tetrahedron Lett.*, 3647 (1964).
(39) R. M. Acheson and J. K. Stubbs, *J. Chem. Soc. C*, 2316 (1969).



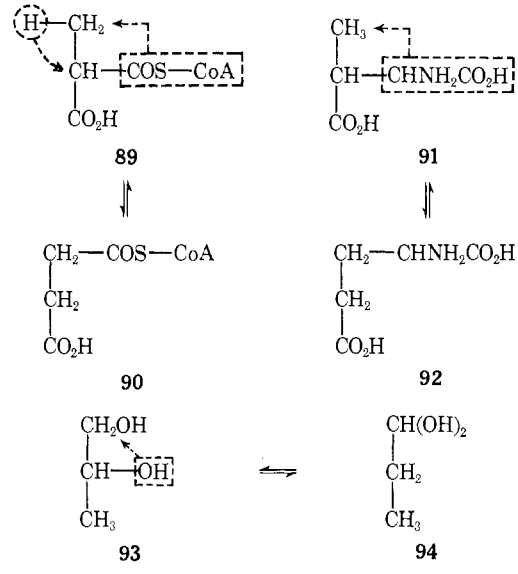
taking place through a cyclopropane intermediate (*cf.* **37**).



Pyrolytic Rearrangement. Pyrolyses of the [2.1.0]-pentanes **86** (R = H and Me) yield[40] as main products the cyclopentenes **88**, the formation of which has been rationalized *via* the diradicals **87**, although ionic intermediates and the possibility of a concerted reaction are not excluded. It is again interesting that the ester group moves in preference to the methyl group.



Enzyme-Mediated Alkylthiocarbonyl Migration. The general structural picture of the cobalt-containing B_{12} coenzyme (*d*-dimethylbenzimidazolyl-*Co*-5′-deoxyadenosylcobamide) mediated rearrangement of methylmalonyl coenzyme A (**89**) to succinyl coenzyme A (**90**) has been convincingly established.[41] Only one[42] of the optically active isomers of **89** can be converted to **90** by the mutase, and a series of experiments with ^{13}C- and ^{14}C-labeled **89** have shown that the thiol ester, and not the carboxyl group, migrates through an intramolecular process.[43,44] When the hydrogen atoms of the methyl group of **89** are all replaced by deuterium, and the compound is isomerized, 85–95% of the original deuterium is present[45] in the resulting **90**. Apparently no tritium is lost when the methyl group of **89** is partially tritiated and the compound converted to **90**, but there is a large isotope effect against the movement of the tritium. The thiol ester replaces the moving hydrogen atom with retention of the original configuration.[46] The coenzyme is also involved[41] in the isomerization[47] of β-methylaspartic acid (**91**) to glutamic acid (**92**) and in the conversion[48] of 1,2-propanediol (**93**) to propionaldehyde (**94**), but in these reactions inversion of the configuration of the carbon atom bearing the hydrogen

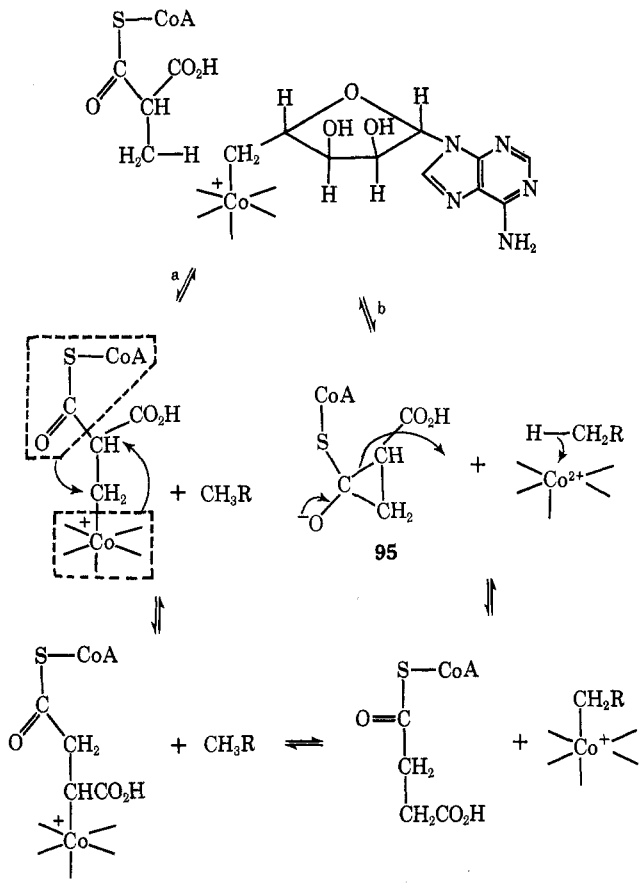


atom which moves takes place. Up to two atoms of tritium have been transferred[49] to the 5′ position of the *Co*-5′-deoxyadenosylcobamide part of the enzyme from [1-^{3}H]1,2-propanediol, and the labeled enzyme when used to convert methylmalonyl coenzyme A to succinyl coenzyme A caused incorporation[50] of tritium in the succinyl residue of the product. Further elegant

(40) M. J. Jorgenson and T. J. Clark, *J. Amer. Chem. Soc.*, **90**, 2188 (1968).

(41) H. A. Barker, *Biochem. J.*, **105**, 1 (1967).
(42) R. Mazumder, T. Sasakawa, Y. Kaziro, and S. Ochoa, *J. Biol. Chem.*, **237**, 3065 (1962).
(43) H. G. Wood, R. W. Kellermeyer, R. Stjernholm, and S. H. G. Allen, *Ann. N. Y. Acad. Sci.*, **112**, 661 (1964).
(44) E. F. Phares, M. V. Long, and S. F. Carson, *ibid.*, **112**, 680 (1964).
(45) J. D. Erfle, J. M. Clark, and B. C. Johnson, *ibid.*, **112**, 684 (1964).
(46) M. Sprecher, M. J. Clark, and D. B. Sprinson, *J. Biol. Chem.*, **241**, 872 (1966).
(47) M. Sprecher, R. L. Switzer, and D. B. Sprinson, *ibid.*, **241**, 864 (1966).
(48) B. Zagalak, P. A. Frey, G. L. Karabatsos, and R. H. Abeles, *ibid.*, **241**, 3028 (1966).
(49) P. A. Frey and R. H. Abeles, *ibid.*, **241**, 2732 (1966).
(50) J. Retey and D. Arigoni, *Experientia*, **22**, 783 (1966); C. J. Cardinale and R. H. Abeles, *Biochim. Biophys. Acta*, **132**, 517 (1967).

Scheme II

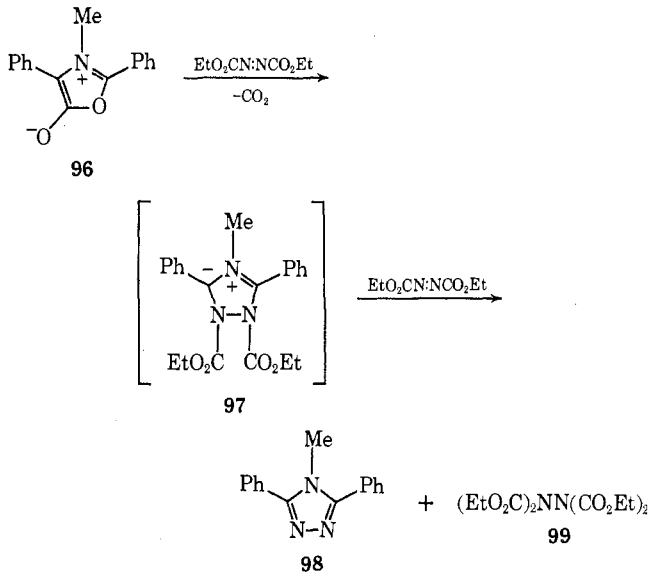


studies[51] on partitioning of deuterium between residual starting material and the various deuteriated succinic acids, formed from the enzyme with a mixture of methylmalonyl coenzyme A and [4,4,4-$^2H_3$]methylmalonyl coenzyme A, have led to the conclusion that the hydrogen atom lost to the enzyme becomes one of three equivalent hydrogen atoms before being returned to give succinyl coenzyme A and that the initial proton abstraction is at least in part rate determining. Two types of reaction pathway, a and b, accounting for these results are given in Scheme II, which differs in the first stage from that originally proposed[51] in that the 4′-hydrogen atom of the deoxyribose moiety is not removed. Another possibility is that removal of the proton from methylmalonyl coenzyme A by the cobamide enzyme gives a carbanion which cyclizes to a cyclopropane intermediate, **95**, of the type proposed for other 1,2 shifts of esters. The opening of cyclopropanols by protons proceeds with retention of configuration in some cases.[52] Both of these schemes require 5′-deoxyadenosine as an intermediate, and as yet there is no evidence on this point. In the enzymic conversion of 1,2-propanediol to propionaldehyde a diradical is formed,[53] so the details of Scheme II may need some modification. Although it is tempting to propose a common mechanism for the three B_{12}-mediated reactions outlined here, the retention of stereochemistry at the position losing the hydrogen atom in the methylmalonyl–succinyl coenzyme A reaction, and the inversion in the other two cases, highlights an important difference, although it may only be in a matter of detail.

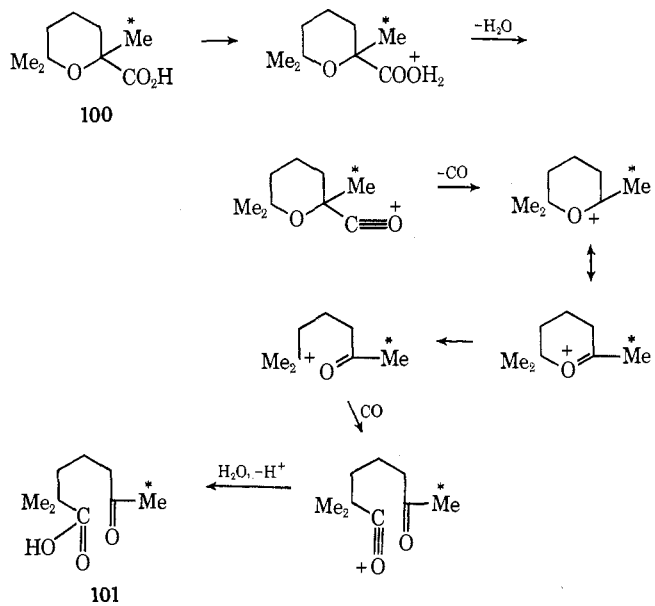
(51) W. W. Miller and J. H. Richards, *J. Amer. Chem. Soc.*, **91**, 1498 (1969).
(52) C. H. DePuy, *Accounts Chem. Res.*, **1**, 33 (1968).
(53) S. A. Cockle, S. Davies, M. A. Foster, H. A. O. Hill, and R. J. P. Williams, *Symp. Biochem. Soc.*, **30**, in press.

Intermolecular Alkoxycarbonyl and Carboxyl Shifts

The sydnone **96** with diethyl azodicarboxylate at 0° loses carbon dioxide to give the triazole **98** and tetraethyl hydrazinetetracarboxylate (**99**) in 83 and 87% yields, respectively.[54] It is suggested that two ethoxycarbonyl groups are transferred from the postulated intermediate **97** to the second mole of the azo ester which takes part in the reaction.



From a structural standpoint, the conversion of α-cinenic acid (**100**) to geronic acid (**101**) by cold, concentrated sulfuric acid appears to be a carboxyl migra-

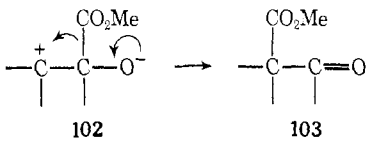


(54) R. Huisgen, *Chem. Soc., Spec. Publ.*, **No. 21**, 67 (1966).

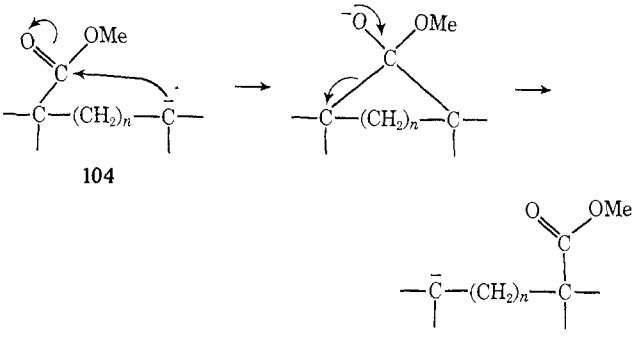
tion. However, the mechanism outlined has been established by following the movement of the ^{14}C-labeled methyl group, indicated by an asterisk, and by the incorporation of ^{14}C-labeled carbon monoxide bubbled through the reaction mixture.[55] Similar apparent migrations of ester groups are clearly possible but do not appear to have been recorded.

Conclusions

The idea that ester groups can migrate has been put forward to account for the formation of particular structures from others under the influence of conditions inducing chemical change. Although detailed mechanistic studies need to be carried out on all the rearrangements described in this Account before one can be certain of exactly what is going on, it is possible, on the basis of commonly accepted theory, to make two generalizations. Ester groups can undergo 1,2 shifts with their bonding electrons to adjacent positive centers (**102** → **103**). Ester groups can also move to nucleophilic centers, through the formation of three- to six-membered rings (**104** → **105**), relinquishing their original bonding electrons in the process.



102 103



104 105

Photolysis can also induce ester shifts, and ester groups appear to undergo 1,5-sigmatropic shifts and to move through processes involving radicals. One B_{12}-containing enzyme catalyzes a reversible thiol ester shift (**89** → **90**) which must occur in most living systems. Ester groups also can migrate in preference to both alkyl and aryl groups. The migration of ester groups, although rare, is therefore a widespread phenomenon, and it is already clear that great care should be taken in interpreting experimental results which indicate that either an ester group, or another substituent, could migrate.

(55) J. Meinwald, H. C. Hwang, D. Christman, and A. P. Wolf, *J. Amer. Chem. Soc.*, **82**, 483 (1960).

Decomposition of Acylarylnitrosamines. A Multipathway Reaction

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Received November 13, 1970

The behavior of acylarylnitrosamines in solution, exemplified by *N*-nitrosoacetanilide ($C_6H_5N(NO)COCH_3$), has puzzled generations of chemists since its synthesis in 1876[1] and Bamberger's discovery, 20 years later,[2] that it decomposed easily in benzene at room temperature to give biphenyl and acetic acid (eq 1). This apparently simple reaction, quite apart

$$C_6H_5N(NO)COCH_3 + C_6H_6 \longrightarrow C_6H_5C_6H_5 + N_2 + CH_3CO_2H \quad (1)$$

from its synthetical utility, played a major part in the development in the 1930's of the concept of the transient existence of radicals in solution.[3] It thus became the subject of much research into the mechanism of its decomposition into phenyl radicals, *via* the isomeric benzenediazo acetate.[4,5]

In the late sixties the demonstration that the decomposition also involved stable radicals,[6-8] detectable by esr spectroscopy, and unstable species such as the aryl carbonium ion and benzyne,[9] sharpened interest

(1) O. Fischer, *Chem. Ber.*, **9**, 463 (1876).
(2) E. Bamberger, *ibid.*, **30**, 360 (1897).
(3) W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.*, 1797 (1934).
(4) R. Huisgen and H. Nakaten, *Justus Liebigs Ann. Chem.*, **573**, 181 (1951).
(5) D. H. Hey, J. Stuart-Webb, and G. H. Williams, *J. Chem. Soc.*, 4657 (1952).
(6) G. Binsch and C. Rüchardt, *J. Amer. Chem. Soc.*, **88**, 173 (1966).
(7) G. R. Chalfont and M. J. Perkins, *ibid.*, **89**, 3054 (1967).
(8) J. I. G. Cadogan, R. M. Paton, and C. Thomson, *Chem. Commun.*, 614 (1969).
(9) (a) J. I. G. Cadogan and P. G. Hibbert, *Proc. Chem. Soc. (London)*, 338 (1964); (b) D. L. Brydon, J. I. G. Cadogan, D. M. Smith, and J. B. Thomson, *Chem. Commun.*, 727 (1967).