

---

---

# QUARTERLY REVIEWS

---

---

## REARRANGEMENTS OF PINANE DERIVATIVES

By D. V. BANTHORPE

(WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,  
UNIVERSITY COLLEGE, LONDON)

AND D. WHITTAKER

(ROBERT ROBINSON LABORATORIES, UNIVERSITY OF LIVERPOOL)

### 1. Introduction

THE outstanding feature of the chemistry of monoterpenes with the pinane skeleton (1), a class of compound occurring in the wood and leaf oils of numerous plants, is the ease of skeletal rearrangement. Such inter-conversions much confused the pioneer investigators,<sup>1</sup> and an understanding of them was essential for the elucidation of the structure of these and related natural products.

In this Review we include within the scope of rearrangement: (a) Wagner-Meerwein conversion into another bicyclic skeleton; (b) ring-opening to acyclic or monocyclic derivatives; and (c) migration of double bonds in allylic systems. Such reactions have previously been only briefly summarised.<sup>2</sup> Fragmentations such as are caused by powerful oxidants and acid- or base-catalysed epimerisation of alcohols and ketones are not discussed as these exhibit no particularly novel features.

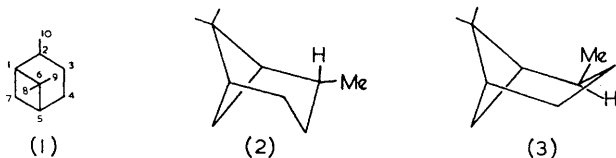
The configurations of most pinane derivatives are well established, but little is known concerning the preferred conformations, although these govern the direction of certain rearrangements. Early workers considered the skeleton to be a bridged chair, but thermochemical comparisons with cyclobutyl and cyclohexyl compounds have shown the bulk of the strain energy of the bicyclic system to be accommodated in the six-membered ring,<sup>3</sup> and departures from the chair conformation of the unstrained cyclohexane ring must be considerable. Models and calculations suggest that *trans*-pinanes take up a bridged half-chair (2) as a stable conformation such that five carbons simulate a cyclopentyl system with C(3) probably slightly displaced towards the methylene bridge below the plane of the others. The epimeric *cis*-compounds probably pucker in the opposite direction such that the 2-methyl group becomes pseudo-equatorial, and so minimises its interactions with the *gem*-dimethyl bridge (e.g., as in 3). These favoured conformations appear consistent with chemical, nuclear

<sup>1</sup> J. L. Simonsen and L. N. Owen, "The Terpenes", Cambridge Univ. Press, London, 2nd edn., 1949, p. 100.

<sup>2</sup> J. A. Berson in P. de Mayo's "Molecular Rearrangements", Interscience, New York, part I, 1963, p. 111.

<sup>3</sup> F. H. Seubold, *Chem. and Ind.*, 1954, 1389.

magnetic resonance, and optical results,<sup>4</sup> but electron-diffraction studies are urgently needed. So far such studies have been incomplete or restricted to pinyl derivatives with endocyclic double-bonds.<sup>4a</sup>



Rearrangements of only a few types of pinyl compound have been studied under a limited range of conditions. We first describe predominantly homolytic processes that are common to all the family (sections 2 and 3) and then outline reactions of three sub-classes that proceed through carbonium ions. Kinetic and product studies have led to the general opinion that often these intermediates are mesomeric and non-classical,<sup>2</sup> although the observed phenomena have also been attributed to the operation of steric effects in a system of rapidly interconverting classical ions.<sup>5</sup>

## 2. Thermal Rearrangements

Early workers showed that (+)- $\alpha$ -pinene (4) decomposed to isoprene and *p*-cymene on passage of the vapour through a heated tube, but these are almost certainly secondary products.<sup>6</sup> Gas-phase decomposition at 375° gives 42% dipentene (5),\* 40% allo-ocimene (6), and 12%  $\alpha$ - and  $\beta$ -pyronene (7, 8) but the distribution of products depends on the heating time and the last three products are formed in sequence from ocimene (9)<sup>7</sup> which primary product can be obtained in excellent yield at 175° by use of a flow-reaction vessel with a low contact time.<sup>8</sup> The stereochemistry of (6) is probably as shown.<sup>9</sup>  $\beta$ -Pyronene is generally given the structure (8a), but it may be a mixture.<sup>10</sup> Although we will sometimes represent the relative orientations of certain bonds by full or dotted lines, this convention can lead to confusion for mesomeric molecules or for species possessing partially formed bonds (cf. 10 or 35). In such cases we will usually not attempt to depict the stereochemistry.

The liquid-phase pyrolysis of (+)- $\alpha$ -pinene, either alone or in the presence of water, gives similar products together with a dimer of allo-oci-

<sup>4</sup> M. P. Hartshorn and A. F. A. Wallis, *Tetrahedron*, 1965, **21**, 273; G. Zweifel and H. C. Brown, *J. Amer. Chem. Soc.*, 1964, **86**, 393.

<sup>4a</sup> B. A. Arbuzov and V. A. Naumov, *Doklady Akad. Nauk S.S.S.R.*, 1964, **158**, 376.

<sup>5</sup> H. C. Brown, "The Transition State", *Chem. Soc. Special Publ.* No. 16, London, 1962, p. 140.

<sup>6</sup> H. Staudinger and H. W. Kleuer, *Ber.*, 1942, **75**, 2059.

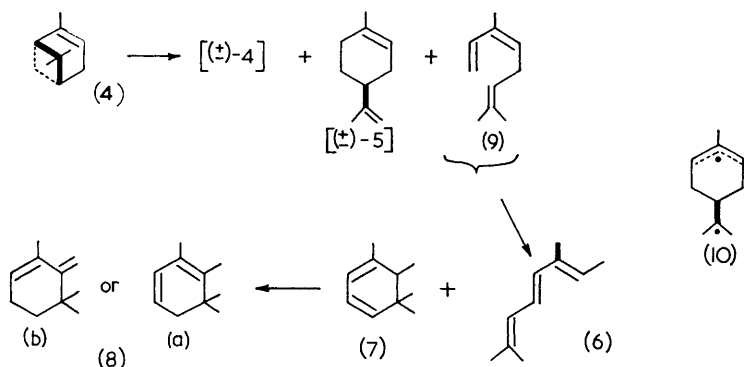
<sup>7</sup> J. E. Hawkins and H. G. Hunt, *J. Amer. Chem. Soc.*, 1951, **73**, 5379.

<sup>8</sup> J. E. Hawkins and W. A. Burnis, *J. Org. Chem.*, 1959, **24**, 1507.

<sup>9</sup> K. Alder, A. Dreike, H. Ergenbach, and V. Wicket, *Annalen*, 1957, **609**, 1.

<sup>10</sup> D. V. Tishchenko and N. Summ, *Zhur. obshehei Khim.*, 1957, **27**, 379.

\* Dipentene is ( $\pm$ )-limonene. The occurrence of optically active products will only be noted in cases of especial interest: often optical readings have not been recorded.



mene.<sup>11</sup> Unchanged substrate is partially racemised and as limonene is optically stable under these conditions (this point was not checked for the gas-phase reaction) the dipentene must have been formed directly. The decomposition is of the first order in  $\alpha$ -pinene<sup>12</sup> and the rate is unaffected by the addition of benzoic acid, antioxidants, or dipentene.<sup>13</sup> This suggests that mechanisms requiring protonation of an olefin to form a carbonium ion, catalysis by peroxides, or radical chains are unimportant; and as the products of both gas- and liquid-phase reactions are similar, a common mechanism is likely. All the results are consistent with the formation of a biradical (10) with one electron forming part of an allylic system.<sup>14</sup> Although this view has been commonly accepted, concerted electronic reorganisation leading directly to the primary products cannot be ruled out.<sup>15</sup>

The vapour-phase decomposition of  $(-)\beta$ -pinene (11) at 160° forms 70% myrcene (12), 13%  $(-)$ -limonene (13), and 10% myrcene-dimer together with smaller amounts of 1,(7),8-*p*-menthadiene (14) and  $\alpha$ -myrcene (15).<sup>16</sup> The main product can be obtained in nearly quantitative yield at 580–750°, and this reaction is of considerable industrial importance.<sup>17</sup> Similar products result from liquid-phase pyrolysis except that the myrcene is almost completely polymerised,<sup>18</sup> and the kinetics and effect of additives are similar to the situation for  $\alpha$ -pinene (except that benzoic acid causes extensive conversion of the substrate into the more stable  $\alpha$ -isomer before ring-opening). The biradical mechanism is again consistent with all the observations and successfully predicted the forma-

<sup>11</sup> R. E. Fuguitt and J. E. Hawkins, *J. Amer. Chem. Soc.*, 1945, **67**, 242; T. R. Savich and L. A. Goldblatt, *J. Amer. Chem. Soc.*, 1945, **67**, 2027.

<sup>12</sup> R. E. Fuguitt and J. E. Hawkins, *J. Amer. Chem. Soc.*, 1947, **69**, 319.

<sup>13</sup> H. G. Hunt and J. E. Hawkins, *J. Amer. Chem. Soc.*, 1950, **72**, 5618.

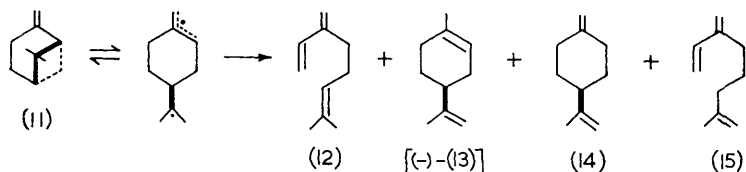
<sup>14</sup> R. L. Burwell, *J. Amer. Chem. Soc.*, 1951, **73**, 4461.

<sup>15</sup> T. H. Bates and T. F. Williams, *Nature*, 1960, **187**, 665.

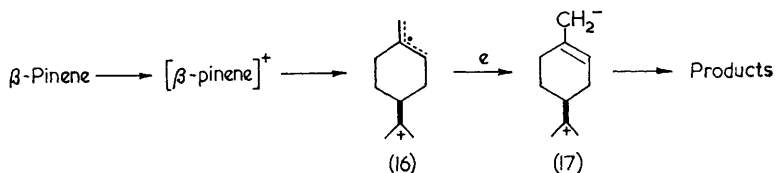
<sup>16</sup> L. A. Goldblatt and S. Palkin, *J. Amer. Chem. Soc.*, 1941, **63**, 3517; L. Steinbach, E. T. Theimer, and B. M. Mitzner, *Canad. J. Chem.*, 1964, **42**, 959; L. Steinbach and J. Walt, *J. Org. Chem.*, 1965, **30**, 646.

<sup>17</sup> B. D. Sully, *Chem. and Ind.*, 1964, 263.

tion of (14): it also requires any  $\beta$ -pinene re-formed from the biradical to be optically active, but this point remains unchecked.

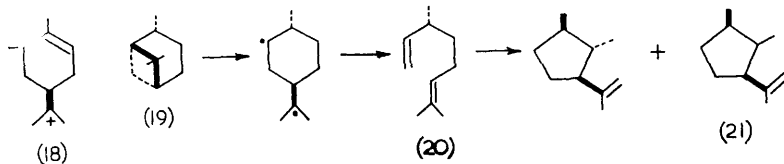


Interesting comparisons with the above are provided by decompositions induced by  $\gamma$ -irradiation.<sup>18</sup> (-)- $\beta$ -Pinene gives limonene (of unspecified optical purity) and polymers, and as formation of the latter was inhibited by traces of water, the whole reaction was considered to pass through a zwitterion (17) which cannot be attained under the less-forcing thermal



conditions. (+)- $\alpha$ -Pinene gives dipentene, ocimene, and unidentified hydrocarbon and polymers, and unchanged substrate is partially racemised. Despite this close resemblance to the corresponding thermal decomposition, a mechanism involving a zwitterion (18) was again suggested. The ocimene does not decompose further, probably owing to rapid quenching from its high-energy state of formation before the transition state for further reaction can be achieved. The mass spectra of  $\beta$ - and  $\alpha$ -pinene resemble those of myrcene and ocimene respectively,<sup>19</sup> and result from fragmentation of a molecular ion (16) and its analogue.

Few other thermal rearrangements have been studied. The isomerisation of (+)-pinane (19) (probably the *trans*-isomer from its method of preparation) is more sluggish than those of the pinenes, but probably involves a similar but less stable biradical.<sup>20</sup> Up to 90% yields of (20) are isolated at 400–700°, together with cyclopentyl compounds formed in



<sup>18</sup> T. H. Bates, J. V. F. Best, and T. F. Williams, *J. Chem. Soc.*, 1962, 1521, 1531.

<sup>19</sup> R. Ryhage and E. von Sydow, *Acta Chem. Scand.*, 1963, 17, 2025, 2504; A. F. Thomas and B. Willkalm, *Helv. Chim. Acta*, 1964, 47, 475.

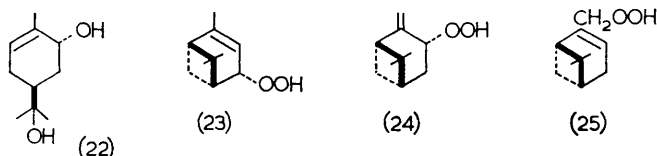
<sup>20</sup> V. N. Ipatieff, W. D. Huntsman, and H. Pines, *J. Amer. Chem. Soc.*, 1953, 75, 6222; H. Pines, N. E. Hoffmann, and V. N. Ipatieff, *J. Amer. Chem. Soc.*, 76, 4412.

secondary, probably radical, reactions.<sup>21</sup> High pressures and lower temperatures favour the formation of (21).

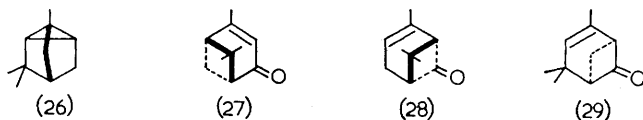
### 3. Photochemical Rearrangements

The few reported photochemically-induced rearrangements have only been briefly studied and it is not known whether excited states decompose directly into the isolated products or form transient intermediates.

The action of sunlight on an aqueous emulsion of (+)- $\alpha$ -pinene has long been recognised<sup>1</sup> to give mainly (+)-*trans*-sobrerol (22), which arises from decomposition of the epoxide formed by oxidation of unchanged substrate by the initially formed verbenyl hydroperoxide (23)<sup>22</sup> (see section 4d). A quite different reaction predominates in the presence of a photosensitiser, such as eosin or chlorophyll, and causes migration of the double



bond without skeletal rearrangement. Thus  $\alpha$ - and  $\beta$ -pinene give excellent yields of the hydroperoxides of *trans*-pinocarveol and myrtenol respectively (24 and 25). In the absence of oxygen, ultraviolet radiation of low energy readily epimerises pinylic compounds with negligible ring-opening;<sup>23</sup> but under more forcing conditions  $\alpha$ -pinene is cleaved to *p*-menthadienes, ocimene, and allo-ocimene together with polymers and a large yield of a cyclofenchane (26), not detected as a product of thermal or  $\gamma$ -irradiation-induced rearrangements.<sup>24</sup>



A solution of (+)-verbenone (27) in benzene readily rearranges to (+)-chrysanthenone (28) on ultraviolet irradiation at room temperature and there is no evidence for reversibility, for migration of the methylene bridge to form (29), or for the ring-opened products characteristic of the bi-radical mechanism.<sup>25</sup> In protic solvents, acyclic products are isolated that may result from capture of an intermediate ketene (30). Such a species

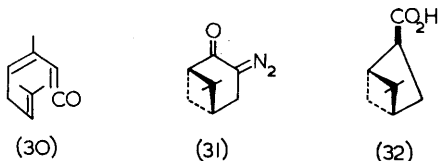
<sup>21</sup> R. Rienacker and G. Ohloff, *Angew. Chem.*, 1961, 73, 240; J. P. Bain, *Fr. P.* 1,349,980/1964.

<sup>22</sup> G. O. Schlenk, H. Eggert, and W. Denk, *Annalen*, 1953, 584, 177.

<sup>23</sup> A. J. N. Hope and S. Mitchell, *J. Chem. Soc.*, 1954, 4217.

<sup>24</sup> R. Mayer, E. Bochow, and K. Ziegler, *Z. Chem.*, 1964, 9, 348.

<sup>25</sup> J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 1960, 2864.



would have to cyclise almost stereospecifically in benzene to form chrysanthenone. Alternatively, the reaction in benzene may involve a concerted electronic reorganisation direct to product followed by the slow establishment of an equilibrium between (28) and (30). This would accommodate the observation that prolonged irradiation of verbenone in benzene produces racemic (28).

An interesting ring-contraction is the conversion of (31) into (32) under irradiation,<sup>26</sup> presumably *via* a carbene.

#### 4. Rearrangements of $\alpha$ - and $\beta$ -Pinene

(a) **Catalysis over Solids.**—The isomerisation of  $\alpha$ -pinene in both liquid and vapour phases over clays, minerals, and salts, typically at 20–80°, has been the subject of an immense patent literature. Camphene (36) and less extensively limonene are usually the main primary products, but both are absorbed on the catalyst as the substrate, which preferentially occupies the binding sites, is consumed, and both are racemised and limonene is converted into other *p*-menthadienes and polymers.<sup>27,28</sup>  $\beta$ -Pinene reacts similarly. Typical products of biradical mechanisms are not found from these reactions and carbonium ions bound to the surface or  $\pi$ -complexes are likely intermediates.

The stereochemistry of absorption was first realised to be important in studies of isomerisation over clays,<sup>27</sup> but the “hydrogen-switch” mechanism that was suggested (a concerted absorption and isomerisation) was only applicable to catalysis by protons. Some of the catalysts, *e.g.*, silica gel, titanate acid, and alumina, are proton carriers but silicate minerals and salts such as magnesium sulphate cannot thus act,<sup>29</sup> and the catalytic activity in these, and other, examples depends on the formation of a  $\pi$ -complex between the substrate and a metal ion in the lattice. Thus, very pure silica gel does not isomerise  $\alpha$ -pinene at 100°, although reaction occurs at much higher temperatures, but the addition of 0.1% w/w of neutral alumina increases the activity thousands-fold to the level characteristic of clays.<sup>30</sup> A greater proportion of alumina causes extensive polymerisation, no doubt owing to the multiplicity of active sites which cause

<sup>26</sup> J. Meinwald and P. G. Gassmann, *J. Amer. Chem. Soc.*, 1960, **82**, 5445.

<sup>27</sup> V. P. Wystrach, L. H. Barnum, and H. Garber, *J. Amer. Chem. Soc.*, 1957, **79**, 5786.

<sup>28</sup> G. A. Rudakov, Z. S. Khomenko, and M. M. Shestaeva, *Zhur. obshchei Khim.*, 1954, **24**, 549; V. M. Nikitin, *ibid.*, 1948, **18**, 209.

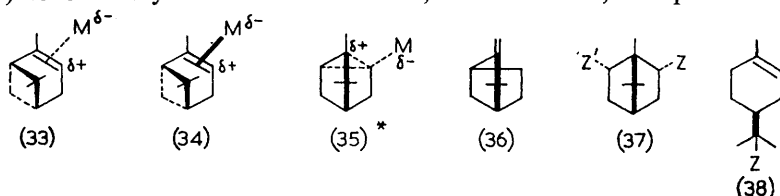
<sup>29</sup> G. Swann, *Ind. Chemist*, 1948, **24**, 141.

<sup>30</sup> G. A. Rudakov and M. M. Shestaeva, *Zhur. obshchei Khim.*, 1959, **29**, 2062.

an overlapping of adsorbed substrate on the surface. Catalysts can be treated with heat or acids to favour the formation of camphene or monocyclic compounds and the topology of the surface must differ for the two pathways, although the effect of pore size does not influence the products.<sup>31</sup>

Two factors, which may act separately or jointly depending on the conditions, probably govern the predominance of camphene formation over ring-opening.

(i) For steric reasons the favoured orientation of absorption is (33) (where M is a Lewis acid site in the lattice) rather than (34). The conversion of (33) into (35) and (36) then proceeds smoothly through a non-classical ion, similar to that occurring in the well-known isobornyl chloride–camphene interconversion,<sup>2</sup> whilst an analogous conversion from (34) is sterically hindered. The latter, less favoured, complex either



probably cleaves directly or forms a classical ion and in either case leads to monocyclic products. Despite this restriction, (34) will be relatively favoured at high temperatures, and limonene is in fact the major product at above 300° over various clays.<sup>32</sup>

(ii) Typical isomerisations occur under non-nucleophilic conditions. Consequently, ions or  $\pi$ -complexes are not stabilised by solvation and simulate the high-energy species well established in deamination with nitrous acid,<sup>33</sup> which are known to undergo skeletal rearrangement rather than ring-opening. In more solvating conditions, *e.g.*, with aqueous titanous acid as catalyst, nucleophilic attack on the *gem*-dimethyl bridge of the stabilised ion or  $\pi$ -complex leads to monocyclic products.<sup>34</sup>

Special products can be obtained under unusual conditions. Treatment of  $\alpha$ -pinene with clay and mercuric oxide in acetic acid at low temperatures gives bornyl and  $\alpha$ -terpinyl acetates<sup>35</sup> (37, 38, Z' = H, Z = OAc), and Friedel–Crafts catalysts produce polymers in reactions that are of the first order in substrate.<sup>36</sup>  $\alpha$ -Pinene does not react with Ziegler catalysts, probably because of steric hindrance, but the  $\beta$ -isomer readily polymerises under similar conditions.<sup>37</sup>

<sup>31</sup> L. S. Ivanova and G. A. Rudakov, *Chem. Abs.*, 1965, **62**, 9176(f).

<sup>32</sup> H. Kosima, *J. Chem. Soc. Japan*, 1961, **82**, 115.

<sup>33</sup> J. H. Ridd, *Quart. Rev.*, 1961, **15**, 418.

<sup>34</sup> G. A. Rudakov, *Zhur. obshchei Khim.*, 1954, **24**, 1402.

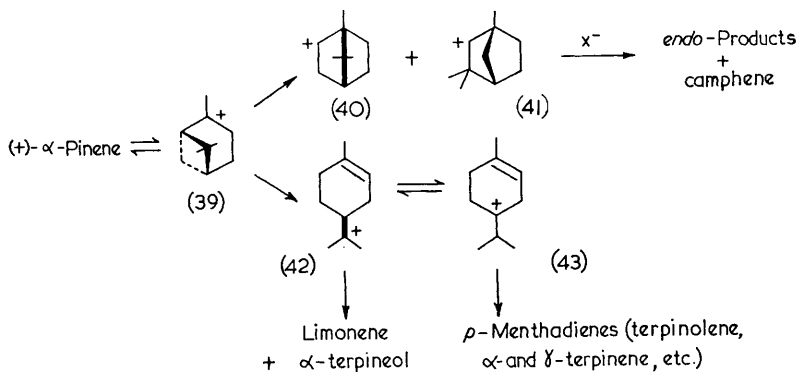
<sup>35</sup> H. Kuwata, *J. Soc. Chem. Ind. Japan*, 1936, **39**, 392.

<sup>36</sup> A. L. Rummelsburg, U.S.P., 2,386,063/1945; W. J. Roberst and A. R. Day, *J. Amer. Chem. Soc.*, 1950, **72**, 1226.

<sup>37</sup> C. S. Marvel, J. R. Hanley, and D. T. Longone, *J. Polymer Sci.*, 1959, **40**, 551.

The dotted line to M represents (from a stereochemical viewpoint) a full bond. The other dotted lines represent bonds in a mesomeric cation.

(b) **Action of Acids in the Liquid Phase.**—As with solid catalysts, these reactions can lead to either ring-expansion or ring-opening and the primary products can isomerise during the process, but now often solvent-stabilised, unadsorbed carbonium ions are intermediates. A recent quantitative study using  $\alpha$ -pinene<sup>38</sup> has delineated two pathways. One is Wagner rearrangement to bornyl and fenchyl ions (40, 41) by migration of bond electrons from the *gem*-dimethyl and methylene bridges respectively, and in the presence of a nucleophile this leads to *endo*-products (a stereoselectivity attributed to electronic and steric influences)<sup>2</sup> together with camphene. This route predominates typically under non-aqueous conditions such as on treatment with ethereal hydrogen chloride at low temperature [when bornyl chloride (37,  $Z' = H$ ,  $Z = Cl$ ) is the main<sup>2</sup> product], with phenol,<sup>39</sup> and certain organic acids.<sup>40</sup> The relative proportions of bornyl and fenchyl products are highly dependent on slight changes in reaction conditions.



The other route is generally favoured when dilute (0.1—1.0N) aqueous acids are used, and typically limonene and  $\alpha$ -terpineol (38,  $Z = OH$ ) and isomerisation and dehydration products resulting from the ions (42) and (43) are formed together with traces of  $\beta$ -pinene and terpene ethers (cincoles).<sup>38,41,42</sup> Similar ring-opening sometimes results from treatment with organic acids<sup>43</sup> when esters are isolated<sup>41</sup> unless amides, which stimulate the formation of limonene, are added. In the two-phase aqueous conditions, hydrocarbons separate into the organic layer and tend to accumulate at the expense of the more water-soluble products.

$\beta$ -Pinene gives the same products as  $\alpha$ -pinene under the same conditions,

<sup>38</sup> G. Valkanas and N. Iconomou, *Helv. Chim. Acta*, 1963, **46**, 1089.

<sup>39</sup> M. Delepine, *Compt. rend.*, 1924, **178**, 2087.

<sup>40</sup> M. Delepine, J. Reisman, and E. Suau, *Bull. Soc. chim. France*, 1930, **47**, 966; M. S. Kharasch and W. R. Reynolds, *J. Org. Chem.*, 1944, **9**, 148.

<sup>41</sup> W. Zubyk and A. Z. Conner, *Analyt. Chem.*, 1960, **30**, 912.

<sup>42</sup> J. Reisman, *Bull. Soc. chim. France*, 1927, **41**, 94.

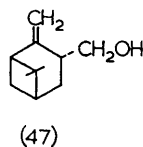
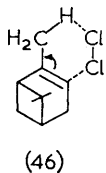
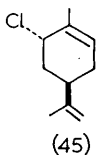
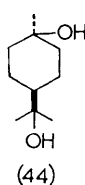
<sup>43</sup> W. Mosher, *J. Amer. Chem. Soc.*, 1947, **69**, 2139; J. Verghese, *J. Sci. Ind. Res., India*, 1959, **18B**, 270; I. I. Bardyshev and V. I. Efimenko, *Chem. Abs.*, 1955, **55**, 15534 (i).



as is expected if a common carbonium ion (39) is generated by Markownikoff addition of a proton to either substrate, but there are quantitative differences. These are probably due to differing solubilities of substrates and products in the aqueous acidic media usually employed, causing different reaction and contact times; and also, perhaps, to slight differences in the geometries of the two (formally identical) ions leading to different proportions of bornyl- and fenchyl-producing rearrangements (cf. section 5).

Quite different products are formed with more concentrated aqueous acids. At low temperatures terpin hydrate (44) and its derivatives and *p*-cymene have been isolated,<sup>1</sup> and the yield of the former products is spectacularly increased by the use of resin acid as an emulsifier.<sup>44</sup> On refluxing with 20% aqueous mineral acids, *p*-menthadienes predominate,<sup>45</sup> whilst more concentrated acids initiate polymerisation,<sup>46</sup> perhaps by a radical-anion mechanism.

(c) **Other Additions.**—Reactions with halogens differ from the above in that the pinene skeleton is often preserved. Thus, chlorination of  $\alpha$ -pinene under basic conditions<sup>47</sup> gives pinocarvyl, myrtenyl, and carvyl chlorides [see (24), (25), and (45)], the second being formed during the working-up from the first.  $\beta$ -Pinene gives myrtenyl chloride and 2,6-*endo*-dichlorobornane (37,  $Z' = Z = \text{Cl}$ ) directly in excellent yield. Early workers also isolated bornyl chloride (37,  $Z' = \text{H}$ ,  $Z = \text{Cl}$ ), but this probably results from the reactions of adventitious hydrogen chloride and unchanged substrate. Where characterised, the halides are invariably *endo*-isomers, such as result from addition of acids.



The primary products presumably derive from either (i) concerted *cis*-addition and elimination of hydrogen chloride; (ii) electrophilic addition to form a carbonium ion that is stabilised against skeletal rearrangement by overlap of the *p* orbitals of chlorine with the positive centre to form a pseudo-allylic system (cf. section 6); or (iii) a concerted 1,4-addition-elimination as illustrated for addition to  $\alpha$ -pinene in (46).

Reaction with bromine at low temperatures is similar, but iodine,

<sup>44</sup> R. G. Koy, U.S.P., 2,481,845/1944.

<sup>45</sup> K. K. Sugathan and J. Verghese, *Current Sci.*, 1964, 33, 711; J. Verghese, *J. Indian Chem. Soc.*, 1959, 36, 157.

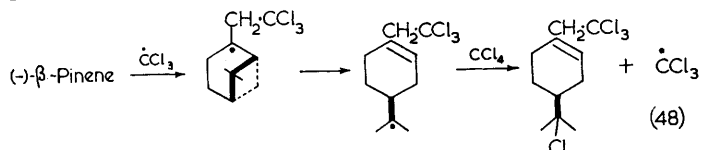
<sup>46</sup> J. J. Ritter and V. Bogert, *J. Amer. Chem. Soc.*, 1940, 62, 1509.

<sup>47</sup> A. Kergomard, *Ann. Chim. (France)*, 1953, 8, 153; D. V. Tischenko and B. Matveev, *Zhur. obshchei Khim.*, 1950, 20, 896.

fluorine, and certain halogenating agents cause aromatisation to *o*- and *p*-cymenes under vigorous conditions.<sup>48</sup> Bromination of 3-keto-pinanes gives  $\alpha$ -substitution without skeletal rearrangement, but on heating a rapid isomerisation to 3,6-*endo*-dibromocamphor results.<sup>4</sup>

Hydroboration of either pinene followed by heating causes the boron group to migrate without skeletal rearrangement,<sup>49</sup> but most other additions have led to bornyl or monocyclic products, e.g., with phosphorus halides<sup>50</sup> and *t*-butyl hypochlorite.<sup>51</sup> However, addition of thionyl chloride in pyridine preserves the pinane skeleton<sup>52</sup> and nitryl chloride forms an unrearranged nitroschloride dimer.<sup>53</sup> Reaction of either pinene with formaldehyde causes double-bond migration: thus (47), for example, is formed from  $\alpha$ -pinene, probably by means of a cyclic transition state analogous to (46).<sup>54</sup>

Radicals generally show little tendency to rearrange, but examples are the peroxide-induced additions of carbon tetrachloride and chloral to  $\beta$ -pinene<sup>55</sup> (cf. 48). Addition followed by ring-opening, rather than a concerted reaction, seems likely as unrearranged products result if the lifetime of the pinyl radical is reduced by the presence of a more reactive scavenger.<sup>56</sup>



**(d) Oxidations.**—Tracer and stereochemical evidence for several pathways of oxidation have recently been reviewed.<sup>57</sup> Reaction with mercuric acetate forms a mesomeric ion (49) which is stabilised in water and ring-cleaves, but in less solvating media the pinane skeleton is retained. Lead tetra-acetate generates a similar ion but forms different products: in benzene solution *cis*-pin-3-en-2-yl acetate (50) accumulates, but this rapidly rearranges into *trans*-verbenyl acetate (51) on addition of acetic acid.<sup>58\*</sup> Skeletal rearrangement is absent from the allylic intermediates

<sup>48</sup> K. K. Sugathan and J. Verghese, *Indian J. Chem.*, 1964, 2, 497.

<sup>49</sup> H. C. Brown and M. V. Bhatt, *J. Amer. Chem. Soc.*, 1960, 82, 2074.

<sup>50</sup> L. Bert, *Bull. Soc. chim. France*, 1923, 33, 787.

<sup>51</sup> J. J. Ritter and D. Ginsberg, *J. Amer. Chem. Soc.*, 1950, 72, 2381.

<sup>52</sup> M. Malenovski and V. F. Yaravaskoya, *Ukrain. khim. Zhur.*, 1955, 25, 107.

<sup>53</sup> Ref. 1, vol. II, p. 132, 178.

<sup>54</sup> A. T. Blomquist, J. Verdol, C. L. Adami, J. Wolinsky, and D. D. Phillips, *J. Amer. Chem. Soc.*, 1957, 79, 3493.

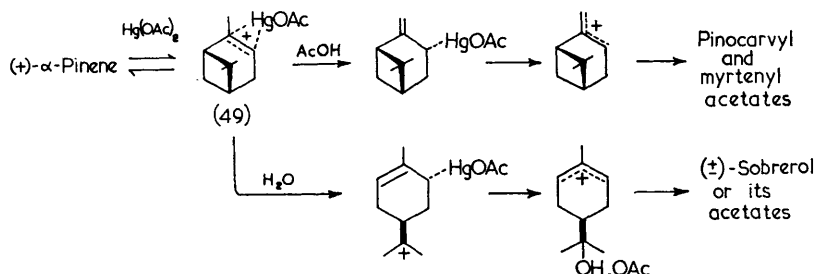
<sup>55</sup> D. M. Olroyd, G. S. Fisher, and L. A. Goldblatt, *J. Amer. Chem. Soc.*, 1950, 72, 2407.

<sup>56</sup> F. E. Bordwell and W. A. Hewett, *J. Amer. Chem. Soc.*, 1957, 79, 3493.

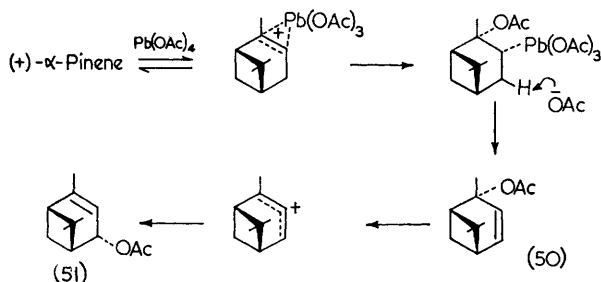
<sup>57</sup> K. B. Wiberg and S. D. Nielsen, *J. Org. Chem.*, 1964, 29, 3353.

<sup>58</sup> G. H. Whitham, *J. Chem. Soc.*, 1961, 2232.

\* The accepted nomenclature can be confusing. For saturated pinanes and pin-3-ene derivatives the terms *cis* and *trans* refer to the relative orientations of the *gem*-dimethyl bridge and the 2-methyl group. In pin-2-ene derivatives, the terms describe the orientations of the same bridge and any ring substituent at C(4) or C(7).

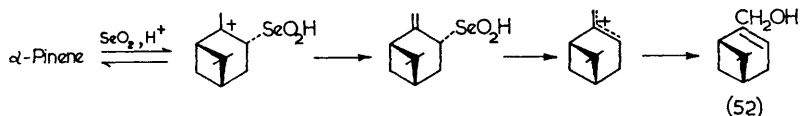


(see section 6) and  $\beta$ -pinene behaves similarly.<sup>59</sup> Treatment with the reagent in acetic acid leads to predominant ring-opening as found with aqueous mercuric acetate.



Autoxidation of  $\alpha$ -pinene in non-aqueous conditions and reduction of the resulting hydroperoxides leads mainly to *cis*-pin-3-en-2-ol and verbenols:<sup>60</sup> these are probably derived from the formation of an epoxide and abstraction of a hydrogen atom from C(4) respectively. Verbenols also result from treatment with chromium oxide and on microbiological oxidation.<sup>61</sup> Ring-opening is unimportant in these conditions, but on photolytic oxidation in water (cf. section 3) much sobrerol is formed.

Use of selenium oxide typically gives large yields of myrtenol (52),<sup>62</sup> although the co-addition of cobalt salts promotes radical pathways to verbenols. Addition of  $\text{HSeO}_2^+$  is believed to form an open carbonium ion that eliminates before rearrangement: with excess of reagent the alcohol is further oxidised. Thallium oxides behave similarly.<sup>63</sup>



<sup>59</sup> M. P. Hartshorn and A. F. A. Wallis, *J. Chem. Soc.*, 1964, 5254; L. E. Gruenewald and D. C. Johnson, *J. Org. Chem.*, 1965, 30, 1673.

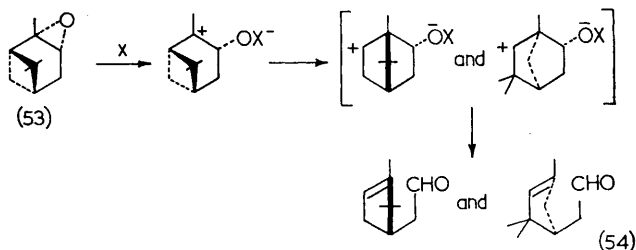
<sup>60</sup> J. P. Bain, U.S.P., 2,863,882/1958; 2,911,442/1959.

<sup>61</sup> P. K. Bhattacharyya, B. R. Prema, B. D. Kulkarni, and S. K. Pradhan, *Nature*, 1960, 187, 689.

<sup>62</sup> A. Kergomard, *Ann. Chim. (France)*, 1953, 8, 158.

<sup>63</sup> J. B. Lee and M. J. Price, *Tetrahedron Letters*, 1962, 1159.

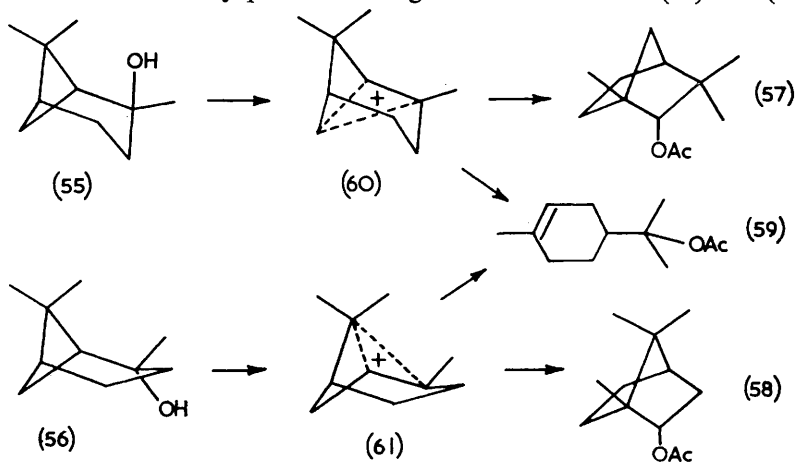
*cis*- $\alpha$ -Pinene oxide (53) which is formed in some of these oxidations, undergoes unique rearrangement and fission to aldehydes (54) in large yield.<sup>64</sup> On treatment with sodium acetate in acetic acid, or with aqueous acids or bases,<sup>57,65</sup> the initial carbonium ion is stabilised and ring-opening to carvyl compounds and *p*-cymene predominates. An analogous ring-opening takes place for  $\beta$ -pinene under all the investigated conditions.<sup>66</sup>



X =  $\text{H}^+$ ,  $\text{BF}_3$ ,  $\text{ZnCl}_2$ ,  $\text{MgI}_2$ ,  $\text{LiAlH}_4$  in non-aqueous media

### 5. Rearrangements of Pinanols and their Derivatives

Both *trans*- and *cis*-methylpinanols (55, 56) readily isomerise when heated with acetic anhydride and form fenchyl acetate and bornyl acetate together with some terpinyl acetate, respectively (57, 58, 59).<sup>67</sup> As addition of pyridine has no effect on the rates, these reactions apparently do not involve the acetate esters as intermediates and these and other isomerisations almost certainly proceed through non-classical ions (60) and (61).



<sup>64</sup> L. C. King and H. Farber, *J. Org. Chem.*, 1961, **26**, 326; M. P. Hartshorn, D. N. Kirk, and A. F. A. Wallis, *J. Chem. Soc.*, 1964, 5494; B. Arbuzov, *Ber.*, 1935, **68**, 1430; Y. Chretien-Bessiere, *Bull. Soc. chim. France*, 1963, 2546.

<sup>65</sup> E. C. Royals and J. C. Seffergwell, *J. Org. Chem.*, 1964, **29**, 2098.

<sup>66</sup> A. Kergomard and J. Philibert-Bijou, *Bull. Soc. chim. France*, 1958, 393.

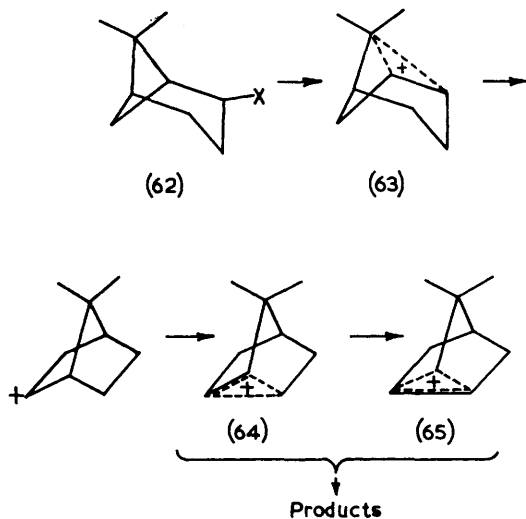
<sup>67</sup> W. D. Burrows and R. H. Eastman, *J. Amer. Chem. Soc.*, 1959, **81**, 245.

The reactions are stereospecific because of the necessity for the ions to be formed with inversion at the ionising centre, and so the products depend on the most stable conformation of the substrates.

Treatment of these alcohols with hydrogen chloride gives a more complex mixture of primary and secondary products. The alcohol (55) forms limonene hydrochloride and a tertiary chloropinane (probably a mixture of two isomers) which subsequently rearrange to bornyl and fenchyl chlorides, whilst (56) forms these, together with  $\alpha$ - and  $\beta$ -pinene.<sup>68</sup> With hydrogen fluoride both isomers yield only limonene hydrofluoride.<sup>69</sup>

The ions (60) and (61) would be expected to be formed in synretically accelerated reactions and at first sight it is surprising that they apparently do not participate in the solvolyses of methylpinyl *p*-nitrobenzoates in aqueous acetone.<sup>70</sup> Thus the *cis*-isomer gives mainly  $\alpha$ -pinene and the *trans*-isomer forms the less stable  $\beta$ -pinene. Such products are consistent with the necessity for an *anti*-periplanar orientation of the leaving groups (a requirement often found for *E1* as well as for *E2* mechanisms<sup>71</sup>) within transition states closely resembling a bridged-chair and a bridged-half chair respectively. However, the formation of these products does not rule out the initial formation of these non-classical ions: elimination of a proton from the latter may not be easy, and elimination to form camphene may require non-nucleophilic conditions and the formation of a "hot" ion.

Nopinyl compounds also isomerise in reactions controlled by the conformations of the ground state.<sup>72</sup>  $\beta$ -Nopinyl brosylate (62) solvolyses 10<sup>6</sup>



<sup>68</sup> W. Hückel and H. Gelchsheimer, *Annalen*, 1959, **625**, 12.

<sup>69</sup> M. Hanack, *Chem. Ber.*, 1960, **93**, 844.

<sup>70</sup> N. A. Abraham and M. Vilkas, *Bull. Soc. chim. France*, 1960, 1450; N. A. Abraham and M. Vilkas, *Ann. Chim. (France)*, 1960, **5**, 961.

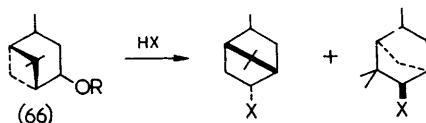
<sup>71</sup> Cf. D. V. Banthorpe, "Elimination Reactions", Elsevier, Amsterdam, 1963, p. 13.

<sup>72</sup> S. Winstein and E. C. Friedrich, *J. Amer. Chem. Soc.*, 1964, **86**, 2720.

times more rapidly than the corresponding unaccelerated apobornyl derivative in a complicated mechanism in which most of the ester undergoes internal return. The part of the reaction proceeding directly gives partially racemic products interpreted as arising from three non-classical ions (63), (64), and (65), linked by a classical ion. A peculiarity of these reactions is the formation of *exo*-rather than *endo*-products.

The solvolysis of isopinocampyl tosylate (*cis*-pinan-*endo*-2-yl tosylate) gives camphene and limonene in addition to  $\alpha$ -pinene, whereas the three isomeric pinocampyl tosylates give only  $\alpha$ - and  $\delta$ -pinene (pin-3-ene).<sup>73</sup> The former products must be derived from an ion formed by a hydride shift from C(2) to C(3). As there is no evidence of synartetic acceleration of the reaction of the iso-compound,<sup>4,74</sup> the difference may be due to steric hindrance in the derived ion uniquely permitting a normally insignificant reaction to compete with the usual unrearranged eliminations.

Few other pinanols have been studied. The verbanols (66) would be expected to rearrange readily, by analogy with the nopinols, but no results are available.



## 6. Rearrangements of Pinenols and their Derivatives

Pinenols provide an important contrast with their saturated analogues as the creation of a positive centre at C(2) does not now usually lead to skeletal shifts. Addition of hydrogen chloride to verbenene (67) gives 2-chloropin-3-ene which on hydrolysis forms *cis*-pin-3-en-2-ol (see 50).<sup>75</sup> This alcohol on further treatment gives *trans*-verbenyl chloride,<sup>76</sup> which in alkaline methanol yields methyl verbenyl ether and 2-methoxypin-3-ene.<sup>77</sup> Both *cis*- and *trans*-pin-3-en-2-ols readily rearrange in aqueous acid to form exclusively *trans*-verbenol, the *cis*-isomer the more readily;<sup>78</sup> the *trans*-acetates behave similarly (see section 4d).<sup>58</sup> Failure to isolate *cis*-verbenyl compounds may be the result of their ready elimination to form verbenene.<sup>78</sup>

These reactions probably proceed through some type of allylic ion, in which expansion of the bridge to C(2) is inhibited by dispersion of the positive charge. It has not yet been established whether *trans*-verbenyl products are formed under thermodynamic or kinetic control; the former

<sup>73</sup> H. Schmidt, *Chem. Ber.*, 1947, **80**, 520.

<sup>74</sup> W. Hückel and D. S. Nag, *Annalen*, 1961, **645**, 101.

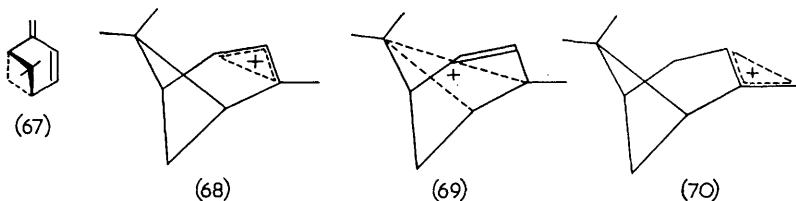
<sup>75</sup> G. Ohloff and E. Klein, *Tetrahedron*, 1962, **18**, 37.

<sup>76</sup> J. P. Bain and A. B. Booth, U.S.P., 2,972,631/1961.

<sup>77</sup> J. P. Bain, W. Y. Gary, and A. B. Booth, U.S.P., 2,834,814/1958; J. P. Bain and W. Y. Gary, U.S.P., 2,818,427/1957.

<sup>78</sup> L. Shulz and W. Doll, *Ber. Schimmel A.G.*, 1942—1943, 50.

situation can be accommodated by the conventional allylic ion, but the latter requires a modified ion, such as (68), which would favour formation and decomposition of *cis*-pin-3-en-2-yl or *trans*-verbenyl derivatives. It is worth noting, however, that although pinene hydrochloride rearranges very readily through an ion which is the saturated analogue of (68), 2-chloropin-3-ene does not form (69) but reacts by an alternative route through (68). Since 2-chloropin-3-ene is considerably more stable than its saturated analogue, clearly this route is energetically favourable only because the formation of an ion such as (69) is inhibited by the presence of a double bond; this effect could arise from partial electron transfer from the latter to C(6) and C(7) which prevents the tendency for migration of the bonds from these atoms, and from repulsion between the  $\pi$ -electrons and those of any developing C(6)-C(2) or C(7)-C(2) bond.



A bridged ion (70) similar to that just discussed is probably intermediary for certain pinocarvyl to myrtenyl interconversions, *e.g.*, the formation of myrtenyl chloride from pinocarvyl chloride<sup>47</sup> and the analogous reaction of the acetates.<sup>59</sup> The treatment of *cis*- and *trans*-pinocarveol with hydrogen bromide gives bornyl and fenchyl derivatives respectively,<sup>59</sup> but these proceed by addition to the double bond and ions such as (70) cannot be formed.

## 7. Rearrangements *in Vivo*

Nothing is known concerning the interconversions of pinane derivatives in plants. Attractive schemes have been suggested<sup>79</sup> whereby  $\alpha$ -pinene plays a central rôle in monoterpene synthesis, being converted into bornyl and camphyl compounds and undergoing oxidation and reduction to a variety of products; but recent tracer work<sup>80</sup> has shown that this compound is not biosynthesised from the expected monocyclic intermediates. Although a zwitterion (18) has been suggested as a precursor, various bicyclic systems may be generated from acyclic terpenes by a concerted bicyclisation on an enzyme surface.<sup>81</sup>  $\alpha$ -Pinene labelled with carbon-14, is converted *in vivo* into at least five other terpenoids, but these remain unidentified.<sup>82</sup>

<sup>79</sup> L. Ruzicka, *Experientia*, 1953, 317.

<sup>80</sup> W. Sandermann, *Tetrahedron Letters*, 1962, 257.

<sup>81</sup> R. M. Gascoigne, *J. Chem. Soc.*, 1958, 876.

<sup>82</sup> R. H. Reitsema, F. J. Cramer, N. J. Scully, and W. Chorney, *J. Pharm. Sci.*, 1961, 50, 18.