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The Configuration of the Carvomenthols, Carveols, and Related Compounds

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The literature evidence for the configuration of the four diastereomeric carvomenthols is reviewed and combined with new deductions from n.m.r. data. The carvomenthols have the configurations shown in Scheme I in accordance with the original assignments of Johnston and Read and contrary to several recent opposing assertions. Adoption of a rational nomenclature for the carvomenthols is proposed. The configurations of the carveols, carvotanacetols, and other compounds related to the carvomenthols are discussed.

Whereas the configurations of the stereoisomeric menthols and menthylamines are very well established,[2] those of their positional isomers, the carvomenthols (**1–4**)[3] and carvomenthylamines **1a–4a**, and, consequently, the configurations of compounds that have been related to them are not.

Thus the "isocarvomenthol" of Johnston and Read[4] has subsequently been called both "iso"[5–8,15a] and "neoiso"[9–11] carvomenthol and has been assigned the *cis*[5,12–14,15a] and the *trans*[6–10,11b,14a,16] configuration of the hydroxyl and isopropyl groups. The "isocarvomenthylamine" of the same authors[4] has been assigned configuration **4a**[5] as well as configuration **1a**.[17] The carveols **5** and **9**, likewise prepared by Johnston and Read,[4b] have also been assigned opposing configurations.[4b,15b] Subsequently, the configurations of the carvotanacetols **6** and **10**, sobrerols **18** and **19**, dihydrocarveols **25–28**, and related compounds, whose configurations have been based[18] on those of the carveols and carvomenthols as given by Johnston and Read,[4] were inverted[15b] too. Because of the opposing configurational assignments of the carvomenthols, opposing configurations have also been assigned to the epimeric *p*-mentha-1(7), 8-dien-2-ols **7** and **11**.[8–10,11b,12–14,19]

It is the purpose of this paper to show that reconsideration of all the data now available from the literature, together with some newly presented herein, makes it possible to assign configurations to all the above compounds beyond doubt.

Nomenclature.—As in the case of the stereoisomeric menthols, the prefixes neo, iso, and neoiso have been applied to distinguish the carvomenthols. However, much confusion has arisen in the application of these prefixes to the carvomenthols, since two different ways of adapting the menthol system have been used.

The nomenclature used in this article and recommended for universal adoption is based on configuration, the prefix iso indicating that the alkyl substituents are *cis* to each other. The prefix neo indicates the configuration of the hydroxyl group as being *cis* to the alkyl substituent next to it. This corresponds to the same convention now invariably used in the case of the menthols.[2] To rule out any possible misunderstanding, we have added the melting points and optical rotations

(1) The Radiation Laboratory is operated under contract with the Atomic Energy Commission. This is AEC Document No. COD-38-354. Presented at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

(2) J. L. Simonsen, "The Terpenes," Vol. 1, Cambridge University Press, London, 1947.

(3) In all figures, R = OH, unless the index "a" is added, in which case R = NH_2; thus **3** = carvomenthol, **3a** = carvomenthylamine. All formulas in this paper represent correct absolute configurations [see A. J. Birch, *Ann. Rept. Progr. Chem.*, **47**, 192 (1950)].

(4) (a) J. Read and R. G. Johnston, *J. Chem. Soc.*, 226 (1934); (b) R. G. Johnston and J. Read, *ibid.*, 233 (1934); (c) R. G. Johnston and J. Read, *ibid.*, 1138 (1935).

(5) A. K. Bose, *Experientia*, **8**, 458 (1952).

(6) A. Blumann, E. W. Della, C. A. Henrick, J. Hodgkin, and P. R. Jefferies, *Australian J. Chem.*, **15**, 290 (1962).

(7) R. L. Kenney and G. S. Fisher, *J. Org. Chem.*, **28**, 3509 (1963).

(8) E. E. Royals and J. C. Leffingwell, *J. Am. Chem. Soc.*, **86**, 2067 (1964).

(9) S. H. Schroeter, Inaugural Dissertation, Göttingen, 1962.

(10) G. O. Schenck, K. Gollnick, G. Buchwald, S. H. Schroeter, and G. Ohloff, *Ann.*, **674**, 93 (1964).

(11) (a) Z. Chabudzinski, Z. Rykowski, and H. Kuczynski, *Roczniki Chem.*, **37**, 1517 (1963); (b) Z. Chabudzinski and H. Kuczynski, *Bull. acad. polon sci., ser. sci. chim.*, **12**, 91 (1964).

(12) Y.-R. Naves and A. V. Grampoloff, *Bull. soc. chim. France*, 37 (1960).

(13) M. Swaleh, B. Bhushan, and G. S. Sidhu, *Perfumery Essent. Oil Record*, 295 (1963).

(14) Y.-R. Naves, *Helv. Chim. Acta*, **47**, 308 (1964). See, however, ref. 14a.

(14a) NOTE ADDED IN PROOF (NOV. 7, 1964).—After the present paper was accepted, a publication appeared [Y.-R. Naves, *ibid.*, **47**, 1617 (1963)] in which the author substantially revises his earlier[12,14] conclusions.

(15) (a) A. Kergomard and M. Th. Geneix, *Bull. soc. chim. France*, 394, 397 (1958); (b) G. Farges and A. Kergomard, *ibid.*, 51 (1963).

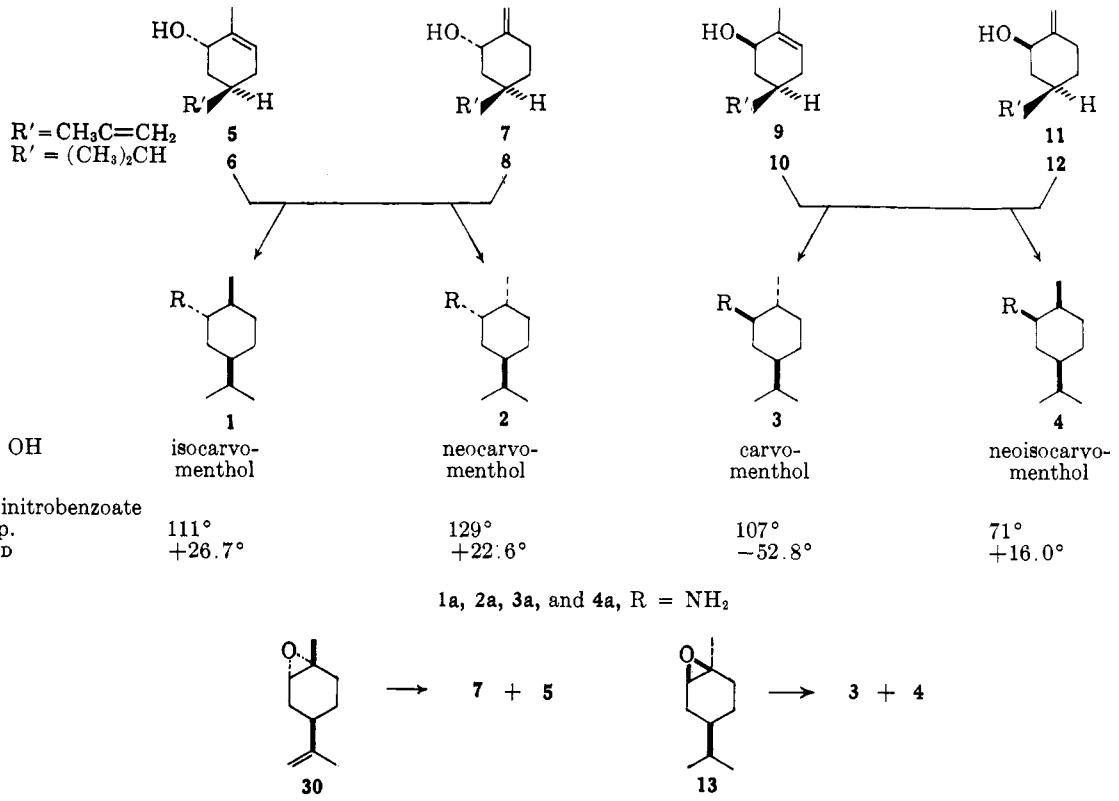
(16) D. K. Shumway and J. D. Barnhurst, *J. Org. Chem.*, **29**, 2320 (1964).

(17) S. Schroeter and E. L. Eliel, *J. Am. Chem. Soc.*, **86**, 2066 (1964).

(18) (a) H. Schmidt, *Ber.*, **83**, 193 (1950); (b) *ibid.*, **86**, 1437 (1953); (c) *ibid.*, **88**, 453 (1955); (d) *ibid.*, **88**, 459 (1955).

(19) Z. Chabudzinski, *Bull. acad. polon. sci., ser. sci. chim.*, **10**, 157 (1962).

SCHEME I



of the 3,5-dinitrobenzoates of the alcohols in Scheme I.[20]

A conflicting system of nomenclature was based on the analogy of the (assumed) conformations of the menthols and carvomenthols.[11b] Following this nomenclature, **1** was called neoiso- and **4** isocarvomenthol, respectively, assuming the conformations as shown.

isomenthol, R = OH; R′ = H
neoisomenthol, R = H; R′ = OH

4, R = OH; R′ = H
1, R = H; R′ = OH

This assumes an overriding tendency for the isopropyl group to be equatorial, an assumption now known to be wrong.[21] In fact, neither neoisomenthol nor **1** exist exclusively in the above conformation. Apart from that, since configurational nomenclature should be based on configuration rather than on conformation, the latter system is, as a matter of principle, to be rejected.

It so happens that, with the nomenclature used here, the old prefixes originally proposed by Johnston and Read[4] can be retained.

Chemical Evidence.—The four diastereoisomeric optically active carvomenthols have been prepared by Johnston and Read[4c] by the reduction of their parent ketones, by the reduction of the oximes of these ketones and reaction of the amines thus obtained with nitrous acid, and, further, by hydrogenation of the carveols **5** and **9**.

The Normal Series.—As already pointed by Ohrloff[22] the configurations of epimers **2** and **3** can be unambiguously deduced from the chemistry of these reductions and from that of the reduction products, as explained in the sequel.

Dihydrocarveol (**27**) is the major product of the reduction of carvone **16** with sodium and alcohol[4b] or with sodium in aqueous ammonia.[23] Neodihydrocarveol (**26**) is obtained from the sodium–alcohol reduction as a minor product in 5% yield.[4b] On oxidation both alcohols give the same ketone, dihydrocarvone (**29**),[4c,18a] from which, in turn, they can be obtained by Meerwein–Ponndorf reduction.[4b]

When hydrogenated, dihydrocarveol (**27**) gives carvomenthol (**3**),[4b,c] neodihydrocarveol (**26**) gives neocarvomenthol (**2**),[4b,c] and dihydrocarvone (**29**) gives carvomenthone (**14**).[4a] This ketone is also the predominant isomer in the sodium alkoxide catalyzed equilibration of the two *p*-menthan-2-ones[4,24] and thus must have the stable equatorial position of the methyl group (*i.e.*, the *trans* configuration of methyl and isopropyl) which is also in accord with the results of the application of the Auwers–Skita rule to the two

(20) The same nomenclature applies to the dihydrocarveols **25–28** and should also be used for the *p*-menthane-1,2-diols.

(21) N. L. Allinger and S.-E. Hu, *J. Org. Chem.*, **27**, 3417 (1962); A. H. Lewin and S. Winstein, *J. Am. Chem. Soc.*, **84**, 2464 (1962); E. L. Eliel and T. J. Brett, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 1963, p. 19Q; N. Mori and F. Suda, *Bull. Chem. Soc. Japan*, **36**, 227 (1963).

(22) H. D. Ohrloff, *Chem. Rev.*, **54**, 375 (1954).

(23) H. Ueda and S. Shimizu, *Bull. Agr. Chem. Soc. Japan*, **23**, 524 (1959); *Chem. Abstr.*, **54**, 9982 (1960).

(24) B. Rickborn, *J. Am. Chem. Soc.*, **84**, 2414 (1962).

ketones.[4c] The formation of the more stable ketone is also expected from its preparation by the sodium–alcohol reduction of **16** followed by oxidation.

For the same reason, dihydrocarveol and carvomenthol should have an equatorial hydroxyl group.[25,26] The neo compounds, which differ only in the position of the hydroxyl group, therefore must have the axial hydroxyl group.

Further evidence for the assigned configurations comes from relative rates of esterification and saponification. The acetate of dihydrocarveol (**27**) is saponified four times as fast as that of neodihydrocarveol (**26**).[18a] Carvomenthol (**3**) reacts faster with acid chlorides than neocarvomenthol (**2**).[4b,c]

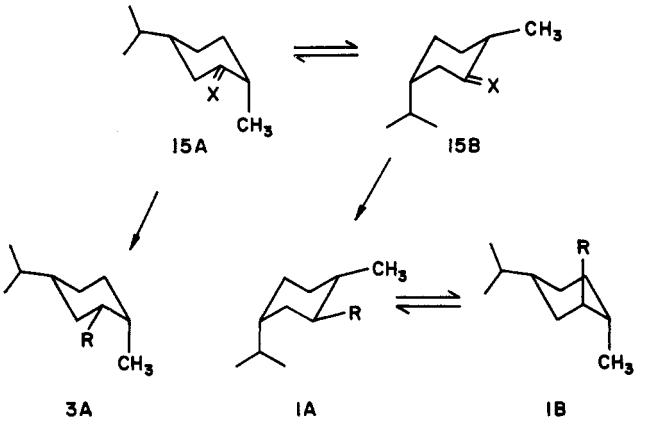
The configurations of the alcohols discussed are further supported by the results of the reduction of carvomenthone with lithium aluminum hydride which gives mainly the more stable (equatorial) carvomenthol (70%).[14] Further support comes from the reported[7,16] formation of carvomenthol by hydroboration of Δ^1-*p*-menthene (carvomenthene) which in analogy with the case of 1-methylcyclohexene[27] should lead to *cis* addition of the elements of water leaving the hydroxyl group *trans* to the adjacent methyl. Also, in a gas chromatogram, the axial neocarvomenthol shows a shorter retention time than its equatorial epimer, as expected from analogy.[28]

The same conclusions regarding the configurations of carvomenthol and neocarvomenthol are derived from the reactions of the isomeric carvomenthylamines.

Reduction of carvone oxime with sodium and alcohol gives dihydrocarvomenthylamine (**27a**) which can be hydrogenated to give carvomenthylamine (**3a**).[4a] The same amine **3a** can also be prepared directly by sodium–ethanol reduction of carvomenthone oxime.[4a] The amines **3a** and **27a** when treated with nitrous acid give the corresponding alcohols **3** and **27** in high yields.[4a,c] Now it is known that sodium–alcohol reduction of ketoximes leads to equatorial amines which react with nitrous acid with retention of configuration.[25,29,30] Since carvomenthone was shown to have configuration **14**, the results just discussed support configuration **3a** for carvomenthylamine,[31] and **3** for carvomenthol.

Besides carvomenthylamine, a little (7.5%) neocarvomenthylamine (**2a**) is obtained in the sodium–alcohol reduction of carvomenthone oxime.[4a,34] Amine **2a** is the major product from the platinum-catalyzed hydrogenation of the oxime in acetic acid.[35,36a] This

SCHEME II



reduction is known to produce more of the axial isomer[25] so that, on the basis of both ways of preparation, neocarvomenthylamine is concluded to be the isomer with the axial amino group. Consequently, only little carvomenthol together with some neocarvomenthol would be expected to be formed from the reaction of **2a** with nitrous acid, since axial amino groups in deamination give mainly elimination together with some inversion.[29,30] In full accord with this and with configuration **2a** proposed for neocarvomenthylamine, the compound gives 75% of *p*-menthenes and only 25% of **3** and **2** in a 4:1 ratio.[4a,34–36a]

The n.m.r. studies to be discussed below also support configurations **2** and **3** for neocarvomenthol and carvomenthol, respectively.

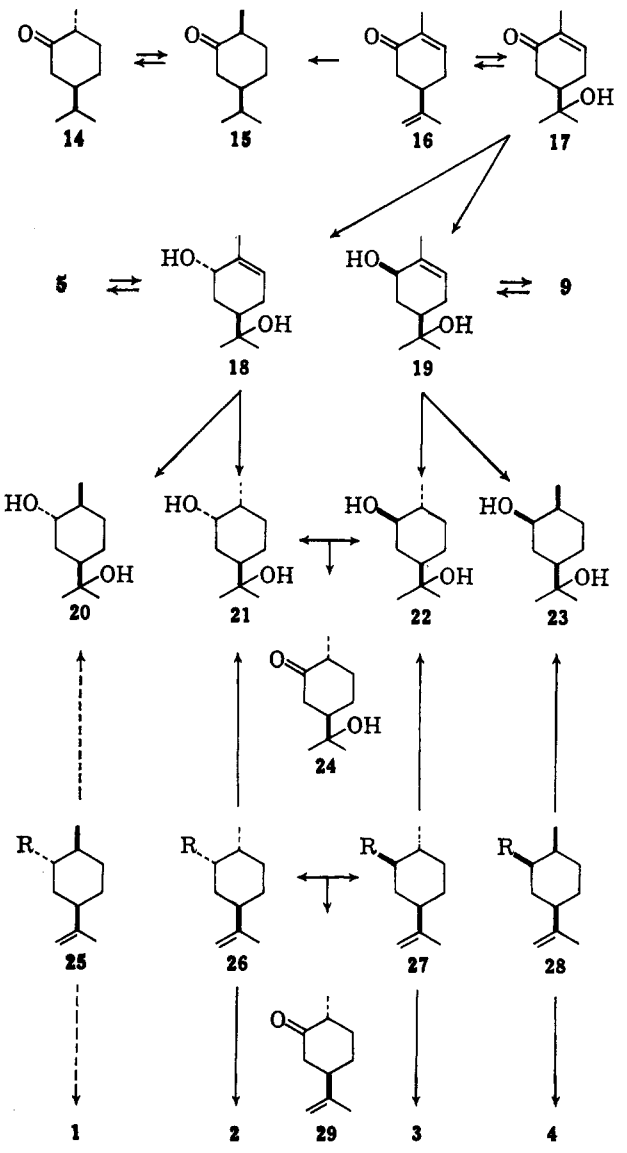
The Iso Series.—In contrast to the clear-cut assignment of configuration to carvomenthol and neocarvomenthol, the reactions by which the two carvomenthols of the iso series were obtained did not give an unambiguous picture, but led to contradictory assignments of configuration to these alcohols.

Johnston and Read[4c] had obtained isocarvomenthol (**1**) together with neocarvomenthol (**2**) by hydrogenation of *trans*-carveol (**5**) and, on the other hand, neoisocarvomenthol (**4**) together with carvomenthol (**3**) from *cis*-carveol (**9**). From this relationship and from the configurations established for **2** and **3**, it follows that the two alcohols **1** and **4** should have the configurations shown in Scheme I.

Unfortunately, there was conflicting evidence. Thus isocarvomenthol was obtained[4c,35,36] by the reaction of nitrous acid on "isocarvomenthylamine," isolated from the sodium–alcohol reduction of isocarvomenthone oxime. Assuming that the oxime would react in that conformation in which the isopropyl group is equatorial to give an equatorial amine, configuration **4a** was assigned[5] to the "isocarvomenthylamine," and, since this amine would furnish an equatorial alcohol upon nitrous acid deamination, configuration **4** was assumed[5] for isocarvomenthol.[37]

(25) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).
(26) A. V. Kamernitzky and A. A. Akhrem, *Tetrahedron*, **18**, 705 (1962).
(27) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).
(28) (a) R. Komers and K. Kochloefl, *Collection Czech. Chem. Commun.*, **28**, 46 (1963); (b) E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957).
(29) A. K. Bose, *Experientia*, **9**, 256 (1953).
(30) J. A. Mills, *J. Chem. Soc.*, 260 (1953).
(31) Further proof for configuration **3a** for carvomenthylamine comes from the pyrolysis of its trimethylammonium hydroxide which gives Δ^2-*p*-menthene of high optical purity.[32] As the pyrolysis proceeds *via trans* elimination[33] a large amount of Δ^1-*p*-menthene would be expected if the amino group were *trans* to the hydrogen at C-1 (*i.e.*, *cis* to the methyl group).
(32) N. L. McNiven and J. Read, *J. Chem. Soc.*, 159 (1952).
(33) M. L. Dhar, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Maw, and L. I. Woolf, *ibid.*, 2117 (1948).
(34) W. Hückel, *Ann.*, **533**, 1 (1938).
(35) W. Hückel and W. Doll, *ibid.*, **526**, 103 (1936).
(36) (a) W. Hückel and E. Wilip, *J. prakt. Chem.*, **158**, 21 (1941); (b) W. Hückel, H. Feltkamp, and S. Geiger, *Ann.*, **637**, 1 (1960).
(37) It was based on this assignment that the different nomenclature of the carvomenthols arose. When Bose[5] assigned structure **4** to isocarvomenthylamine and isocarvomenthol, respectively, he kept the old names for these compounds. Later investigators who corrected his assignment in some cases adopted his system of nomenclature[9–11,38–42] so that the isocarvomenthol of Johnston and Read was then called neoisocarvomenthol.[9–10,11b]
(38) P. R. Jeffries and B. Milligan, *J. Chem. Soc.*, 4384 (1956).
(39) A. R. H. Cole and P. R. Jefferies, *ibid.*, 4391 (1956).
(40) W. F. Newhall, *J. Org. Chem.*, **23**, 1274 (1958).
(41) H. Kuczynski and K. Piatkowski, *Roczniki Chem.*, **33**, 299 (1959); **33**, 311 (1959).
(42) H. Poksoon, *Ann. chim.* (Paris), **5**, 765 (1960).

SCHEME III



This contradiction was recently removed when it was shown[17] that "isocarvomenthylamine" does not have configuration **4a** but **1a**. Its deamination to give **1**, the reduction product of *trans*-carveol, can be adequately explained by the fact that the amine will exist to a considerable extent in conformation (**1A**, R = NH_2) (Scheme II). From the conformational equilibrium values[43] of the methyl (1.7 kcal./mole), isopropyl (2.1 kcal./mole), hydroxyl (0.7 kcal./mole), and amino (1.5 kcal./mole) group, it is clear that isocarvomenthol (**1**) and isocarvomenthylamine (**1a**) will exist in both conformations **1A** and **1B** (in contrast to the other isomers **2–4** which exist exclusively, or nearly so, in the conformation with equatorial isopropyl). This fact, already recognized by Hückel,[36b] explains adequately why deamination of **1a** gives principally **1**; the deamination proceeds to a considerable extent from the equatorial conformation of the amino group, and, therefore, with retention of configuration. For analogous reasons, isocarvomenthone oxime may react, in the sodium–alcohol reduction, in conformation **15B** (X = NOH) and, therefore, give isocarvomenthylamine (**1A**, R = NH_2).

The stereochemical relationship of the epimers **1–4** as derived from the hydrogenation experiments of Johnston and Read[4] has recently been confirmed by a number of investigators.

Thus isocarvomenthol (**1**) has been obtained together with neocarvomenthol (**2**) from *trans*-carveol (**5**),[8] *trans*-carvotanacetol (**6**),[6–8] *p*-mentha-1(7),8-dien-*trans*-2-ol (**7**),[8] and *p*-menth-1(7)-en-*trans*-2-ol (**8**).[7] On the other hand, neoisocarvomenthol (**4**) was obtained together with carvomenthol (**3**) from the corresponding epimers **9**,[8] **10**,[8] **11**,[9,10] and **12**,[7] and from *trans*-*p*-menthadiene oxide (**13a**, isopropenyl instead of isopropyl in **13**).[11]

The connection of the carveols with the carvomenthols has further been achieved[18] through the sobrerols **18** and **19**, the dihydrosobrerols **20–23**, and the dihydrocarveols **25–28** as shown in Scheme III.

In contradiction to all this were some experiments of Naves[14] who had claimed the isolation of both isocarvomenthol (**1**) and carvomenthol (**3**)[44] from the same *p*-mentha-1(7), 8-dien-2-ol (**7**). More recently, however, Naves' conclusions have been revised.[14a]

Recently the *p*-menthadienol (**7**) has been obtained together with *trans*-carveol (**5**) from the epoxide **30** by two independent syntheses[8,45] (Scheme I). This confirms the *trans* configuration of hydroxyl and isopropenyl in **7**. Furthermore, epoxide **30** was also converted into *trans*-carvotanacetol (**6**) and *p*-menth-1(7)-en-*trans*-2-ol,[45] whereas the epimeric Δ^1-*p*-menthene oxide **13** was transformed into *p*-menth-1(7)-en-*cis*-2-ol (**12**).[46] As already mentioned, both **12** and **13a** have been independently correlated with carvomenthol (**3**) and neoisocarvomenthol (**4**) by hydrogenation.[7,11] The n.m.r. spectra of compounds **5–12** (see below) confirm configuration **7**, *i.e.*, the *trans* configuration of the hydroxyl and the isopropenyl group, for the *p*-mentha-1(7),8-dien-2-ol.[47] Recently Chabudzinski and Kuczynski[11b] in correction of the earlier assignment[12,14,19] have also proposed configuration **7** for the *p*-menthadienol. It is quite clear that this compound may well give isocarvomenthol (**1**) but cannot give carvomenthol (**3**) upon hydrogenation. Configurations **1–4** for the carvomenthols are further supported by Brewster's interpretation of their optical rotation. The values from Brewster's work[48] have been included in Table I.

Further direct chemical evidence for the configuration of isocarvomenthol comes from the combined work of Schenck[49] and of Blumann, *et al.*[6] (Scheme IV). Blumann and co-workers have converted the diol **34**, one of the hydrogenation products of **33**, into isomenthol (**36**) and isocarvomenthol (**1**). It follows that **1**

(43) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Interscience Division, John Wiley and Sons, Inc., New York, N. Y., 1965.

(44) The exclusive isolation of (−)-carvomenthol from (−)-*p*-mentha-1(7),8-dien-2-ol has been claimed.[14] The significance of this claim is obscure. (−)-Carvomenthol and (−)-*p*-menthadienol belong to series of opposite absolute configuration at the ring carbon next to the isopropyl group.

(45) H. Kuczynski and A. Zabza, *Roczniki Chem.*, **37**, 773 (1963).

(46) H. Kuczynski and M. Walkowicz, *ibid.*, **37**, 955 (1963).

(47) For a preliminary report regarding the configuration of this compound, see E. Klein and G. Ohloff, *Tetrahedron*, **19**, 1091 (1963).

(48) (a) J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5483 (1959); (b) *ibid.*, **81**, 5493 (1959).

(49) (a) G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957); (b) G. O. Schenck and K. Ziegler, *Festschr. Arthur Stoll*, 620 (1957); (c) see also R. D. Stolow, *J. Am. Chem. Soc.*, **86**, 2170 (1964).

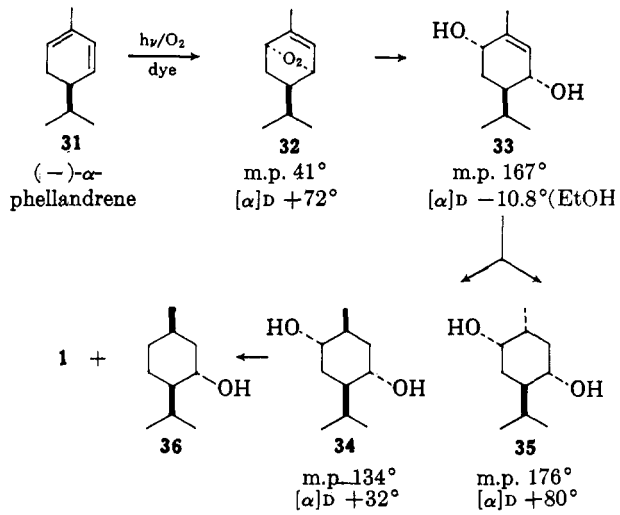
TABLE I

Compd.	Chemical shift[a] Calcd.	Found	Lit.[b]	W[c]	MD, deg. Calcd.[d]	Lit.[d]	Found
3	−180	−179.5	−179	16.0	−50	−43	−39[e]
2	−226.5	−226.5	−229	8.5	+50	+65	+68
4[f]	−219.5	−217	223	18.0	+50	+55	+59
1A	−189[g]	−207[h]	−210	12.0	+50	+28[i]	+30
1B	−219.5				±0		

[a] In c.p.s. at 60 Mc./sec., downfield from TMS. [b] Ref. 14a. [c] Half-width of the bands in c.p.s. [d] Ref. 48. [e] Calculated from rotation of a sample containing 95% **3** and 5% **4**. [f] Unfortunately the values for **1** and **4** were inverted in E. L. Eliel and S. H. Schroeter, Abstracts, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 47S. [g] This value is subject to the uncertainty of the shift parameter of axial isopropyl; ref. 52. [h] If one assumes $A_{i\text{-}Pr}$ = 2.1 kcal./mole, A_{Me} = 1.7 kcal./mole, and a Me–OH *gauche* interaction of 0.4 kcal./mole,[43] **1** should exist equally in conformations **1A** and **1B** and the calculated shift is 204 c.p.s. (see, however, *g*). [i] The calculated molecular rotation for a 1:1 ratio is +25°.

has the same relative configuration of the alkyl groups as **36**, namely *cis*. Moreover, since the diol **33** was also obtained from the *endo*-peroxide **32** by Schenck, the hydroxyl groups in **33** (and therefore, also **34**) must be *cis* to each other. Since the hydroxyl group in isomenthol (**36**) is known to be *trans* to the alkyl groups,[2] the same follows for isocarvomenthol (**1**).

SCHEME IV



The configuration of isocarvomenthol also follows from the fact that, along with carvomenthol, it is obtained[16] in the hydroboration of Δ^1-*p*-menthene (*cis* addition[27]).

N.m.r. Spectra.—Recently it has become possible to calculate the chemical shift of the carbinol protons of substituted cyclohexanols of known conformation by using basic shift values for equatorial and axial protons and additive parameters for various alkyl substituents on the ring.[50] We have now applied this method to the carvomenthols.

As might be expected from the corresponding values of the 3-methyl and the 3-*t*-butyl groups,[50] the chemical shift parameters for equatorial isopropyl groups in both equatorial and axial cyclohexanols are small. From the observed[51] carbinol proton shifts in *cis,cis*-3-methyl-5-isopropylcyclohexanol (210.0 c.p.s.) and *trans,trans*-3-methyl-5-isopropylcyclohexanol (243.0 c.p.s.), and of *cis*-3-isopropylcyclohexanol (208.0 c.p.s.), shift parameters for equatorial isopropyl of 2 c.p.s. (relating to equatorial OH) and 1.5 c.p.s. (relating to axial OH) have been found. The value for an axial 3-isopropyl group in an equatorial cyclohexanol has been calculated[51] from the shift (242.0 c.p.s.) in *trans*-3-isopropylcyclohexanol to be 11 c.p.s.[52] which thus turns out to be the same as that for an axial 3-methyl group.

With the parameters given earlier[50] and those derived for the isopropyl group the shifts of the carbinol protons for **1–4** have been calculated. Experimental data were obtained in carbon tetrachloride solution with tetramethylsilane as internal standard. The carvomenthols were prepared according to Johnston and Read[4] from the appropriate carveols, obtained, in turn, from commercially available (−)-carvone. Lithium aluminum hydride reduction of carvone gave *cis*-carveol (**9**) whose hydrogenation led to a mixture of carvomenthol (**3**) and neoisocarvomenthol (**4**). Aluminum isopropoxide reduction of carvone gave a mixture from which *trans*-carveol (**5**) was isolated through its 3,5-dinitrobenzoate. Hydrogenation of **5** gave a mixture of neocarvomenthol (**2**) and isocarvomenthol (**1**). Preparative gas chromatography readily separated **1** from **2** and **3** from **4**. Calculated and observed chemical shifts for compounds **1–4** are given in Table I.

The good agreement of the calculated and the observed data confirms the assignments of configuration (**3**) for carvomenthol and (**2**) for neocarvomenthol given earlier[22] on the basis of chemical considerations. It also firmly supports configuration (**1**) for iso- and (**4**) for neoisocarvomenthol.

It was claimed by Naves[14] that isocarvomenthol (**1**) shows a broad "axial" carbinol proton signal rather than a narrow equatorial one, and, therefore, has configuration **4**. It must be considered, however, that in **1** conformations **1A** and **1B** (R = OH) will both participate so that **1** will not show a typical equatorial proton signal (as does **2**) but a broadened signal somewhere between that of an axial and that of an equatorial proton.[52b] In trifluoroacetic acid (which was used by Naves as a solvent in the determination of the spin–spin coupling constants) conformation **1A** may even be more favored than in a nonbonding solvent and therefore the conformationally heterogeneous carbinol proton would superficially resemble an axial proton. However, neoisocarvomenthol (**4**) whose carbinol proton is truly axial shows a much broader carbinol proton signal than does isocarvomenthol, in agreement with the assigned configurations and conformations.

Unsaturated Alcohols.—The configuration of the unsaturated alcohols **5–12** is established by that of their hydrogenation products **1–4**. The stereochemistry of **5–12** can also be deduced from the width of the car-

(50) E. L. Eliel, M. H. Gianni, T. H. Williams, and J. B. Stothers, *Tetrahedron Letters*, **No. 17**, 741 (1962).

(51) E. L. Eliel and F. Biros, unpublished results; F. Biros, Ph.D. Thesis, University of Notre Dame, Notre Dame, Ind., 1964.

(52) (a) Assuming this compound to exist to the extent of 93% in the conformation with equatorial isopropyl and axial carbinol proton (calculated shift: 244 c.p.s.) and 7% in the conformation with axial isopropyl and equatorial hydroxyl. The calculated value is evidently not very accurate, but its similarity to that of a 3-methyl group indicates that it is probably of the right order of magnitude. (b) H. Booth, *Tetrahedron*, **20**, 2211 (1964).

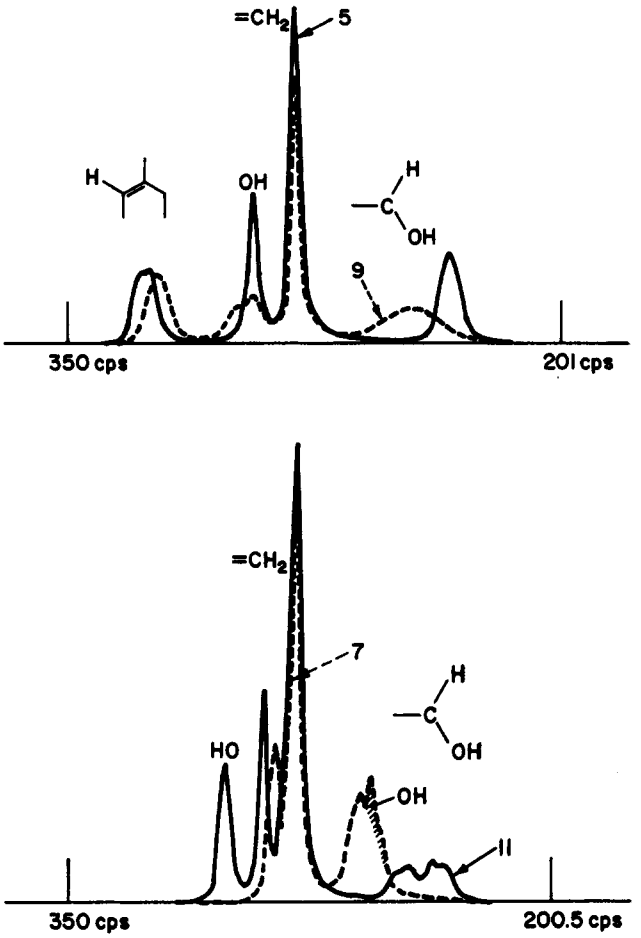


Figure 1.—N.m.r. spectra of allylic alcohols **5**, **9**, **7**, and **11** (neat samples).

binol proton signal in their n.m.r. spectra (Figure 1). The spectra of **5**–**8** are consistent with the postulated *trans* configuration assuming those chair conformations in which the isopropyl groups are equatorial, and the carbinol protons therefore pseudo-equatorial. On the other hand, the much broader carbinol proton signals observed for compounds **9**–**12** show the carbinol protons being pseudo-axial, indicating an equatorial position of the isopropyl and the hydroxyl group.

The configurations of epimers **5** and **9**, **7** and **11**, **6** and **10**, and **8** and **12** are further confirmed by their optical rotation[48b] and by the relative retention times of the epimers in a gas chromatogram (a′ < e′)[7,9,10] as well as by the fact that *cis*-carveol (**9**) is obtained in great preponderance from the reduction of carvone with lithium aluminum hydride[53] and diphenyltin hydride.[54] The photosensitized oxygenation (a reaction which has been shown to give mostly axial alcohols in other cases[10]) of limonene and carvomenthene gives mostly **5** and **6**.[7,9,10] The Meerwein–Ponndorf reduction of carvone produces more of the quasi-axial isomer, *i.e.*, *trans*-carveol (**5**), 50–58% of the *trans* compound having been reported.[4b,53a,d,e] (−)-*trans*-Carvontanacetol (**6**) was further obtained by dehydration of one of the four optically active diastereoisomeric *p*-menthane-1,2-diols (m.p. 88–89°)[6] for which the *trans* configuration of the hydroxyl and isopropyl groups has been independently established.[38–42]

The configurations of the carveols and carvomenthols thus turn out to be as originally proposed by Johnston and Read[4] (as derived from their hydrogenation data).[55] Recent suggestions based on the application of the Auwers–Skita rule that the configurations of all these compounds must be reversed[15b] therefore must be rejected. Although the unsaturated epimers shown in Scheme I all show an inversion of the Auwers–Skita rule[56] it is now known to be unsafe to base assignments simply on this rule, from which other exceptions are known.[57]

Epimers **7** and **11** and **8** and **12** still follow the rule observed among saturated cyclohexanols in that the n.m.r. signal (see Table II) for equatorial alcohols is observed at higher field than that for their axial isomers.[58] This rule does not hold for the epimers **5** and **9** and **6** and **10**, however. While **5** and **6** absorb at nearly the same field (232 c.p.s. in CCl_4, with TMS as internal standard) as the saturated alcohol **2** (227 c.p.s., Table 1), the signal for the axial protons in **9** and **10** (243 c.p.s.) shows a large paramagnetic shift compared with that of **3** (180 c.p.s., Table 1).

TABLE II

Compd.[a]	Carbinol proton[b]	Olefinic proton[b]
5, a′	−232	−281, −328
9, e′	−244	−280, −325
6, a′	−231	−326
10, e′	−242	−320
7, a′	−253	−278, −283
11, e′	−236	−278, −296
8, a′	−252	−277, −282
12, e′	−236	−279, −295

[a] a′, pseudo-axial alcohol; e′, pseudo-equatorial alcohol. [b] In c.p.s., downfield from TMS.

The same shift has been observed in other allylic compounds and will be discussed in more detail elsewhere.

Experimental[59]

Preparation of Pure Alcohols.—(−)-*trans*-**Carveol** (**5**) was obtained from its 3,5-dinitrobenzoate, m.p. 113°, $[\alpha]^{21}D$ −230° (lit.[4b] m.p. 111.5°, $[\alpha]^{16}D$ −232.0°) prepared from the alcohol mixture of **5** and **9** (56:44 by v.p.c.) resulting from aluminum triisopropylate reduction of (−)-carvone. The alcohol, $n^{20}D$ 1.4961, d^{20}_4 0.9510, $[\alpha]^{22}D$ −213.8° (lit.[4b] $n^{18}D$ 1.4964, d^{25}_4 0.9484, $[\alpha]^{25}D$ −213.1°) was shown to be pure by v.p.c.

(−)-*cis*-**Carveol** (**9**) was prepared by lithium aluminum hydride reduction of (−)-carvone[53] and recrystallization of the crude alcohol (92% of **9** by v.p.c.) from Skellysolve F. The pure compound (v.p.c.) had m.p. 24–25° (lit.[4b] m.p. 24–25°).

(−)-**Carvomenthol** (**3**) **and** (+)-**Neoisocarvomenthol** (**4**).—Two successive hydrogenations of (−)-*cis*-carveol (**9**) with Adams

(53) (a) R. H. Reitsema, *J. Am. Chem. Soc.*, **75**, 1996 (1953). (b) D Lloyd and J. Read, *Chem. Ind.* (London), 436 (1953). From their data 96% of *cis*-carveol can be calculated. (c) A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *J. Chem. Soc.*, 1969 (1957). (d) S. H. Schroeter, *Ann.*, **674**, 118 (1964). (e) See also Experimental.

(54) H. G. Kuivila and O. F. Beumel, Jr., *J. Am. Chem. Soc.*, **80**, 3798 (1958).

(55) Similar conclusions have very recently been reached elsewhere.[8,10,11b,14a,16]

(56) All *trans* compounds **5**–**8** show lower boiling points, refractive indices, and densities than their *cis* epimers **9**–**12**.

(57) A review is given by H. van Bekkum, A. van Veen, P. E. Verkade, and B. M. Wepster, *Rec. trav. chim.*, **80**, 1310 (1961).

(58) See citations in ref. 50.

(59) All melting points are corrected. The optical rotations were measured with a Universal high precision polarimeter (Rudolph and Sons) in 2-dm. tubes and are taken in $CHCl_3$ unless otherwise stated. Gas chromatographic (v.p.c.) analyses were performed with an Aerograph Model A-90-P instrument on a 11-ft. Carbowax 20M (20% on Chromosorb W 60/80) or a 10-ft. Carbowax 20M (20%, + 5% KOH on Chromosorb W 60/80) column. Preparative gas chromatography was carried out on a Wilkens Aerograph Model A-700.

catalyst in methanol at room temperature and a pressure of 50 p.s.i. gave a mixture [n^{20}D 1.4660, [α]D +2.15° (*c* 10.0, MeOH); lit.[4c,10] n^{20}D 1.4665, [α]D −4.32°] of **3** and **4** in the ratio 3:7 (v.p.c.). The two alcohols were separated by preparative gas chromatography, using a 20-ft. Carbowax column (30% on Chromosorb W 60/80) and a temperature of 180°. Compound **4** showed n^{20}D 1.4675, [α]^{29}D +38.0° (*c* 6.4 MeOH); lit.[4c,7] n^{20}D 1.4676, [α]^{17}D +34.7°. Compound **3** was obtained 95% pure (v.p.c.), n^{20}D 1.4623, [α]^{29}D −22.0°; lit.[4c,7,16] n^{20}D 1.4617, [α]^{15}D −26.35°. The 3,5-dinitrobenzoate of **3** showed m.p. 105–107°, [α]D −51.6°; lit.[4c,10,14] m.p. 107°, [α]^{13}D −52.8°. The 3,5-dinitrobenzoate of **4** gave m.p. 71°, [α]D +15.5°; lit.[4c,10,11,18a] m.p. 71°, [α]D +16°. When obtained from its 3,5-dinitrobenzoate, **4** had n^{20}D 1.4675, [α]^{25}D +39.2° (*c* 9.2, MeOH).

(+)-**Isocarvomenthol** (**1**) **and** (+)-**Neocarvomenthol** (**2**).—Hydrogenation of (−)-*trans*-carveol (**5**) similar to that described above for (−)-*cis*-carveol (**9**) gave a mixture [n^{20}D 1.4658, [α]D +33.6° (*c* 7.2, MeOH); lit.[4c] n^{19}D 1.4658, [α]D +12.25°] of **1** and **2** in the ratio 28:72. (v.p.c.). The two alcohols were separated by preparative gas chromatography. Compound **1** showed n^{20}D 1.4660, [α]^{29}D +19.5° (*c* 2.8, MeOH); lit.[4c,7,25] n^{20}D 1.4662, [α]^{16}D +17.72°. Compound **2** gave n^{20}D 1.4641, [α]^{29}D +43.7° (*c* 6.1, MeOH); lit.[4c,7] n^{20}D 1.4632, [α]^{21}D +41.7°. The 3,5-dinitrobenzoate of **1** showed m.p. 111°, [α]^{25}D +28°; lit.[4c,6,10,14] m.p. 111°, [α]D +26.7°.

V.p.c. analysis of mixtures of all four isomers was effected at 140°. The order of the alcohols in terms of increasing retention times was **2**, **3**, **1**, and **4**. Compounds **3** and **1** were not completely separated.

Allylic alcohols **5–12** were obtained in pure form (as indicated by v.p.c.) from saponification of the following esters[9,10,53d,60] on a small scale. Their properties are reported elsewhere.[9,10,53d]

(−)-*trans*-**Carvotanacetol** (**6**).—The 3,5-dinitrobenzoate gave m.p. 117°, [α]^{23}D −188.5°; lit.[6] m.p. 115–116° [α]D −201°. The *p*-nitrobenzoate gave m.p. 86°, [α]^{23}D −228°; lit.[6] m.p. 86–87°, [α]D −226°. The *p*-nitrobenzoate described in ref. 45 is not the ester of pure (−)-*trans*-carvotanacetol.[53d]

(+)-*p*-**Mentha-1**(**7**),**8-dien**-*trans*-**2-ol** (**7**).—The 3,5-dinitrobenzoate showed m.p. 70–71°, [α]D +33°; lit.[12,45] m.p. 69–71°. The *p*-nitrobenzoate gave m.p. 114–115°, [α]D +49.3°. The phenylurethane showed m.p. 80°, [α]D +21.4°; lit.[12,13,45] m.p. 80°, [α]D +21°.

(+)-*p*-**Menth-1**(**7**)-**en**-*trans*-**2-ol** (**8**).—The *p*-nitrobenzoate gave m.p. 110°, [α]D +74.0° (lit.[45] m.p. 107–108°, [α]D +155.8°), the rotation probably being twice the true value.

(−)-*cis*-**Carvotanacetol** (**10**).—The 3,5-dinitrobenzoate showed m.p. 91°, [α]D +33.2°; lit.[61,62] m.p. 88.5–90°, [α]D +33.3°.

(+)-*p*-**Mentha-1**(**7**),**8-dien**-*cis*-**2-ol** (**11**).—The 3,5-dinitrobenzoate gave m.p. 76°, [α]D −60°.

(+)-*p*-**Menth-1**(**7**)-**en**-*cis*-**2-ol** (**12**).—The 3,5-dinitrobenzoate showed m.p. 118°, [α]D −59.4°; lit.[46] m.p. 116.5°, [α]^{20}D −54.3°. The *p*-nitrobenzoate gave m.p. 84°, [α]D −55.1°; lit.[46] m.p. 83.5°, [α]D −51.5°.

N.m.r. Spectra.—The n.m.r. spectra were measured on a Varian HR-60 instrument at 60 Mc./sec. in 5–20% CCl_4 solutions with TMS as internal standard. The chemical shifts (in c.p.s.) were averaged from repeated up- and downfield scans and are reproducible to at least ±2 c.p.s. Chemical shifts for the carbinol proton in the saturated alcohols are given in Table I; those in the unsaturated alcohols are given in Table II (along with the shifts for the olefinic protons).

(60) We are indebted to Professor Dr. G. O. Schenck, Mülheim, Ruhr, Germany, for samples.

(61) J. Read and G. Swann, *J. Chem. Soc.*, 239 (1937).

(62) J. A. Mills, *ibid.*, 4976 (1952).

Photodecomposition of 1,2,3-Triazolines. A New Entry into the Aziridine Series

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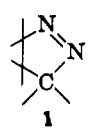
Photolysis of solutions of 1,2,3-triazolines results in loss of nitrogen and the formation of aziridines. A variety of triazoline structures have been found to undergo photodecomposition. The specificity of reaction path in the photolysis contrasts strikingly with the thermal decomposition of triazolines.

The chemical and structural similarity of 1-pyrazolines (**1**) and 1,2,3-Δ^2-triazolines (**2**), *e.g.*, thermal decomposition with loss of nitrogen and isoelectronic



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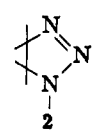
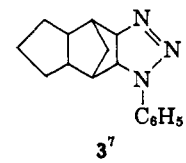


2

structures, prompted an investigation of the light-induced decomposition of triazolines. Van Auken and Rinehart have recently reported this mode of reaction in the 1-pyrazoline series.[2] It has been found that 1,2,3-triazolines readily decompose under the influence of ultraviolet light.

To determine the scope of the photodecomposition reaction, a variety of triazoline structures were prepared and irradiated. In all instances a quantitative evolution of nitrogen (1 mole/mole of triazoline) was observed. The diversity of substrates employed indicates that the photodecomposition of 1,2,3-triazolines, resulting in the loss of nitrogen, is a general reaction for this class of compounds. Compounds **3–8** are typical of those that have been photolytically decomposed.[3]



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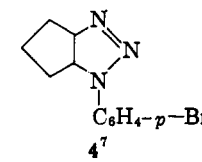

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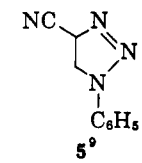
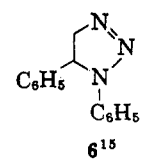


5[9]



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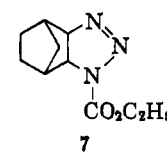

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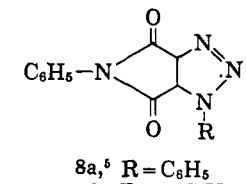

8a,[5] R = C_6H_5
b, R = *n*-C_4H_9

Although the thermal decomposition of certain 1-aryl-1,2,3-triazolines has been reported to produce the corresponding aziridines,[4–6] Alder and Stein's comprehensive study has shown that aziridine formation is

(1) Socony Mobil Oil Co., Princeton, N. J.

(2) T. V. Van Auken and K. L. Rinehart, *J. Am. Chem. Soc.*, **84**, 3736 (1962); **82**, 5251 (1960).

(3) Thiatriazolinethione has also been photolyzed in acetone solvent. The decomposition products are nitrogen, sulfur, and thiocyanic acid; *cf.* E. Lieber, E. Oftedahl; and C. N. R. Rao, *J. Org. Chem.*, **28**, 194 (1963).

(4) F. D. Chattaway and G. D. Parkes, *J. Chem. Soc.*, **127**, 1307 (1925).

(5) A. Mustafa, S. M. A. D. Zayed, and S. Khattab, *J. Am. Chem. Soc.*, **78**, 145 (1958).

(6) P. Scheiner and W. R. Vaughan, *J. Org. Chem.*, **26**, 1923 (1961).