PARTIAL

# MECHANISM OF REARRANGEMENT OF LONGIFOLENE TO ISOLONGIFOLENE

# CHAPTER I

## ELUCIDATION OF TERPENE REARRANGEMENTS USING DEUTERIUM LABELS

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## Abstract

The elucidation of mechanism of terpene rearrangements has been reviewed in this chapter. Since a vast literature on terpene rearrangements is available, the discussion is limited to only those terpenes whose rearrangements have been studied using deuterium labels. The review covers thermal, photochemical, acid or base catalyzed rearrangements among terpenoids which include camphane derivatives, verbenone, 10-isobornyl sultone, thujene, humulene, caryophyllene, thujopsene, manool, friedlin etc. The application of deuterium labels in establishing the mechanism of rearrangements has been brought out.

# ELUCIDATION OF TERPENE REARRANGEMENTS USING DEUTERIUM LABELS

## 1. INTRODUCTION

The chemistry of terpenes abounds in bizarre and fascinating molecular rearrangements which occur under a variety of reaction conditions like acid or base catalysis, photoirradiations or heat. Similar rearrangements also occur *in vivo* under enzymatic conditions so that from a few common precursors, a large number of diverse carbon skeletons arise. Elucidation of mechanism of such rearrangements, apart from being intellectually stimulating, provides a clearer insight about the basic physico-chemical principles involved in organic reactions and can also serve as models for biosynthetic pathways occurring in nature. Alternatively, in cases where biosynthetic pathways have been elucidated in elaborate details, similar stereospecific rearrangements or cyclization have been attempted in the laboratory. As a result, regiospecific carbonium ion generation has been utilized[1-2] for the synthesis of naturally occurring polycyclic terpenes by the acid catalysed rearrangements of other olefinic terpenoids like caryophyllene, humulene, thujopsene, manool, citral etc.

It is often possible to rationalize a rearrangement in more than one ways. A number of methods are commonly used to ascertain the reaction mechanism[3]. These methods often involve identification of products[4] and intermediates[5], stereochemical evidence[5], kinetic evidence[5,6], isotope effect[7], nature of catalyst, and isotopic labelling[8]. The radioactive isotopes such as $^{14}C$, $^{3}H$ had been powerful tools for this purpose before the advent of new spectroscopic techniques, but in recent years, considerable efforts have been directed to the use of nonradioactive isotopes such as $^{13}C$, $^{2}H$, $^{18}O$, since these isotopes are free from radiation hazards and are safer to handle.

Deuterium labels have been introduced in rearranged products mainly by two methods;

(a) by effecting the rearrangements of terpene substrates with deuterated reagents

(b) by subjecting site-specifically labelled substrates to rearrangements under suitable reaction conditions.

The number, position and stereochemistry of the deuterium atoms incorporated in rearranged products are established by spectroscopic and chemical means and the data obtained are

often sufficient to unequivocally establish the reaction mechanisms.

A number of reagents and methods are available for the synthesis of deuterium-tagged substrates and have been reviewed recently[9-11]. In some cases very elaborate syntheses have been undertaken to prepare the required substrates[12] (see below). Since vast literature[13] is available on molecular rearrangements of terpenes, this discussion is limited to only those examples among monoterpenes, sesquiterpenes, diterpenes, and triterpenes, where mechanisms have been elucidated with the aid of deuterium labels.

## 2. MONOTERPENES

Monoterpenes have long been known to undergo very diverse and complicated rearrangements. Investigation of these rearrangements have significantly contributed towards better understanding of reaction mechanisms among terpenoids and have also led to the development of new theoretical concepts. For examples, the ideas of nonclassical bridged carbonium ion[14,15] developed through the study[16,17] of rearrangement of camphene hydrochloride to isobornyl chloride. Rearrangements among monoterpenes of bicyclo[2,2,1]heptane type have been extensively studied in the last few years and some of these are discussed below.

## 2.1. Rearrangements in Camphane Class

### 2.1.1. Classical vs Nonclassical Carbonium Ion

The formation of isobornyl chloride (2) from camphene hydrochloride (1) was proposed by Wilson et al[17] to proceed through rapidly equilibrating pair of ions which were represented by a cyclic intermediate 3 in preference to the carbonium ion 5 (Chart I). Later on, Winstein et al.[15] proposed a nonclassical carbonium ion intermediate 6 for such bicyclo[2,2,1]heptane system i.e. 2-norbornyl cation. The proposal for the bridged carbonium ion 6 involving $\sigma$-participation, in the solvolysis of 2-norbornyl derivative was based on the following observations:

(a) Abnormally fast rate of solvolysis of the exo-derivatives campared to that of t-butyl derivatives[18].

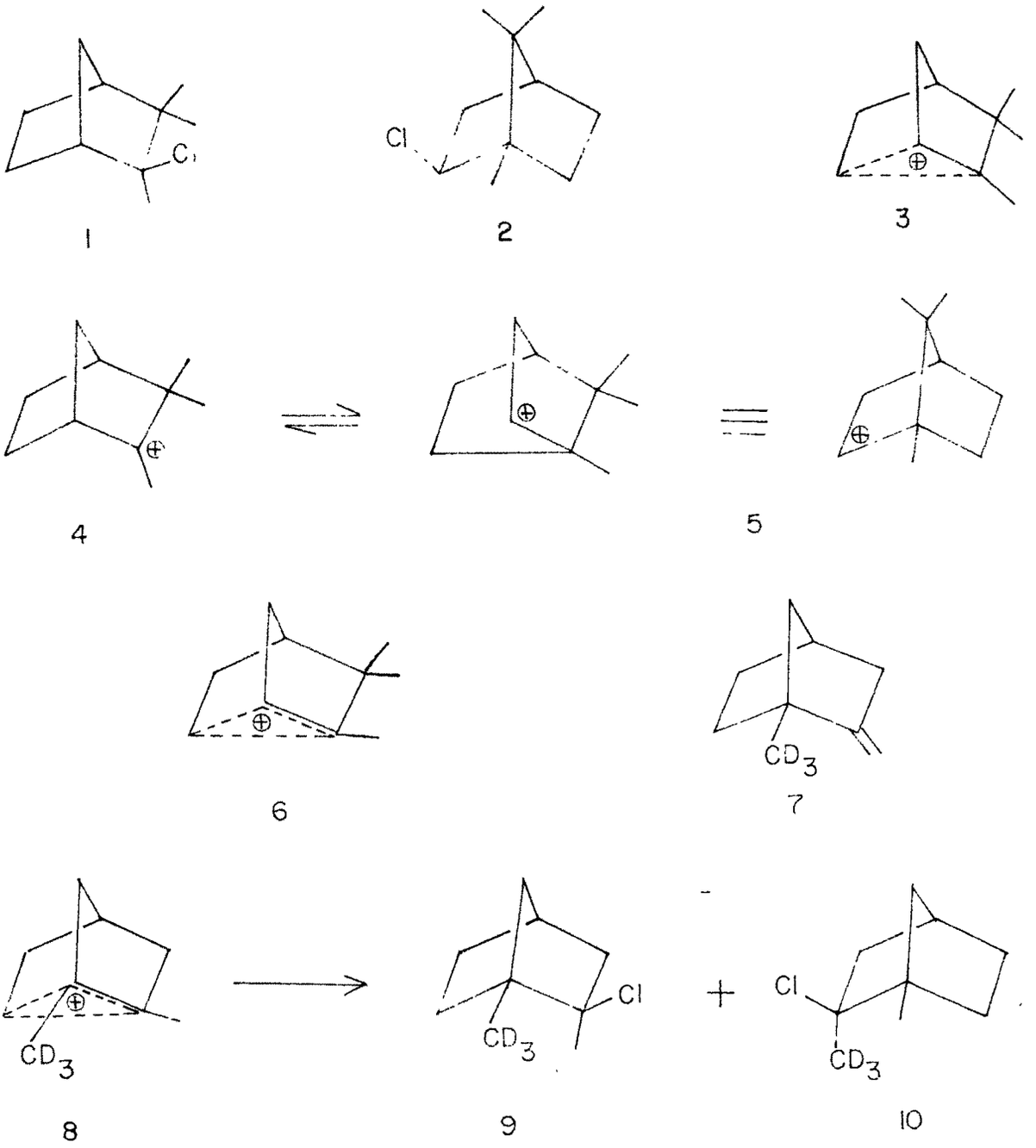
(b) High exo/endo rate ratio[15].

(c) Almost exclusive formation of exo-derivative in the solvolysis of both exo and endo derivatives[15,19].

Through the last decade controversy has raged over whether ions such as 6 have a finite existence or merely represent a transition state in the rapid interconversion of 4 and 5. The subject has been treated in a greater length elsewhere[13a,20-23]. It is still a matter of speculation if

nonclassical carbonium ions do indeed exist as reactive intermediates and the discussion of all the evidence in favour or against their existence is beyond the scope of this review. The present discussion will be confined to the examples where deuterium labelling has been utilized to resolve this issue.

(a) Rearrangement of 1-deuteriomethyl-2-methylene-norbornane: The hydrochlorination of 1-deuteriomethyl-2-methylenenorbornane (7) to 1-methyl-2-methyl-exo-norbornyl chloride (9) proceeds[24] only with 35-56% scrambling in contrast to 100% scrambling expected if the reaction goes through bridged carbonium ion intermediate (Chart I). Brown argued that these results are consistent with the intermediacy of a pair of rapidly equilibrating classical ions which react with chloride ion somewhat more rapidly than they interconvert. The data could however also be explained by postulating initial formation of a classical 1,2-dimethyl-2-norbornyl cation, which reacts with the chloride ion and rearranges to the bridged ion 8 at a comparable rate. Similar results have been obtained in the addition of DCl, AcOD and $CF_3COOD$ to 2-norbornene and addition of HCl, HBr and $PhOH/BF_3$ to 2,3-dideuterionorbornene[25-28]. It has been further demonstrated that initially formed classical carbonium ions also show high stereoselectivity for capture of nucleophile from exo-side.




1 2 3

4 5

6 7

8 9 10

CHART I. CLASSICAL vs NONCLASSICAL IONS

(b) Face-protonation vs edge-protonation in 6,2-hydride shifts: To explain the distribution of $^{14}C$ in 2-norbornyl acetate formed in the acetolysis of exo-2-norbornylbrosylate-2,3-$^{14}C_2$, Roberts et al.[29] proposed nortricyclonium ion 11 in which carbon atoms 1,2 and 6 are equivalent instead of less symmetrical bridged ion 12 proposed by Winstein et al.[15] earlier. Later Roberts et al.[30] agreed with Winstein that $^{14}C$ scrambling could also be interpreted as resulting from the interconversion of one bridged ion 12 to another bridged ion 13 by means of 6,2-hydride shift. Winstein et al[15,31] further suggested that an edge-protonated cyclopropane intermediate or transition state 14 might well be involved in the 6,2-hydride shift rather than the face-protonated cyclopropane species 11. The intermediacy of edge-protonated cyclopropane derivative 14 in preference to face protonated cyclopropane species 11 receives further support from the work of Berson et al[32] who have shown that lactone 16 formed from 15 by treatment with aqueous acid retains deuterium at C-2, consistent with the sequence of reactions depicted in Chart II. The intermediate cation 11 would not discriminate between exo and endo configurations for 6,2-hydride shift, whereas, intermediate 12 would allow only 6,2-endo-endo migration. The formation of 16 involves exclusive endo-endo intramolecular transannular hydride shift. Face-protonated cyclopropane intermediate 17 would not be expected to retain deuteriums at C-2 in lactone 16, and is therefore ruled out. Similar endo-endo 6,2-hydride shifts have been observed by Collins and Benjamin[33,34] in the solvolysis

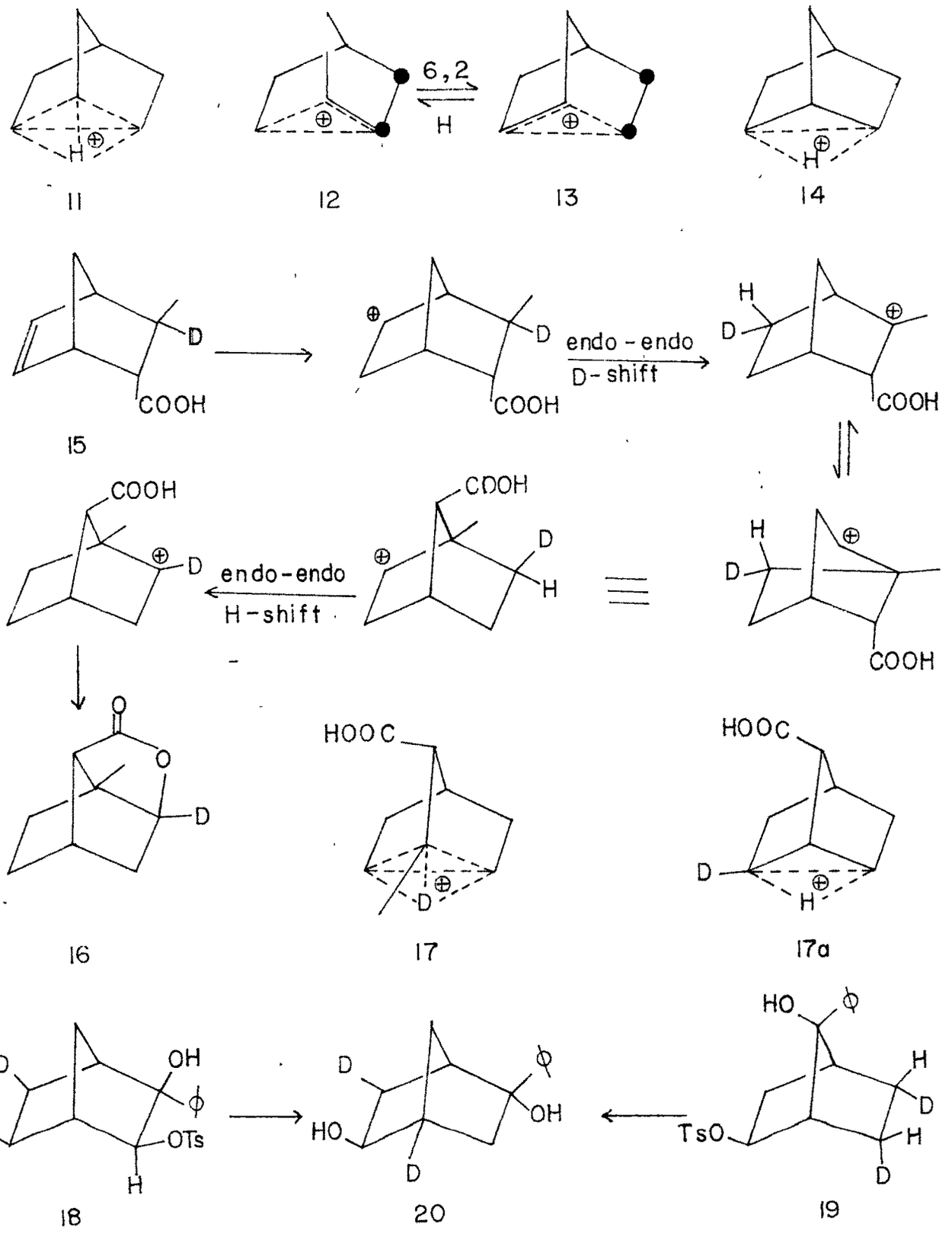



CHART II : endo, endo -6,2-HYDRIDE SHIFTS

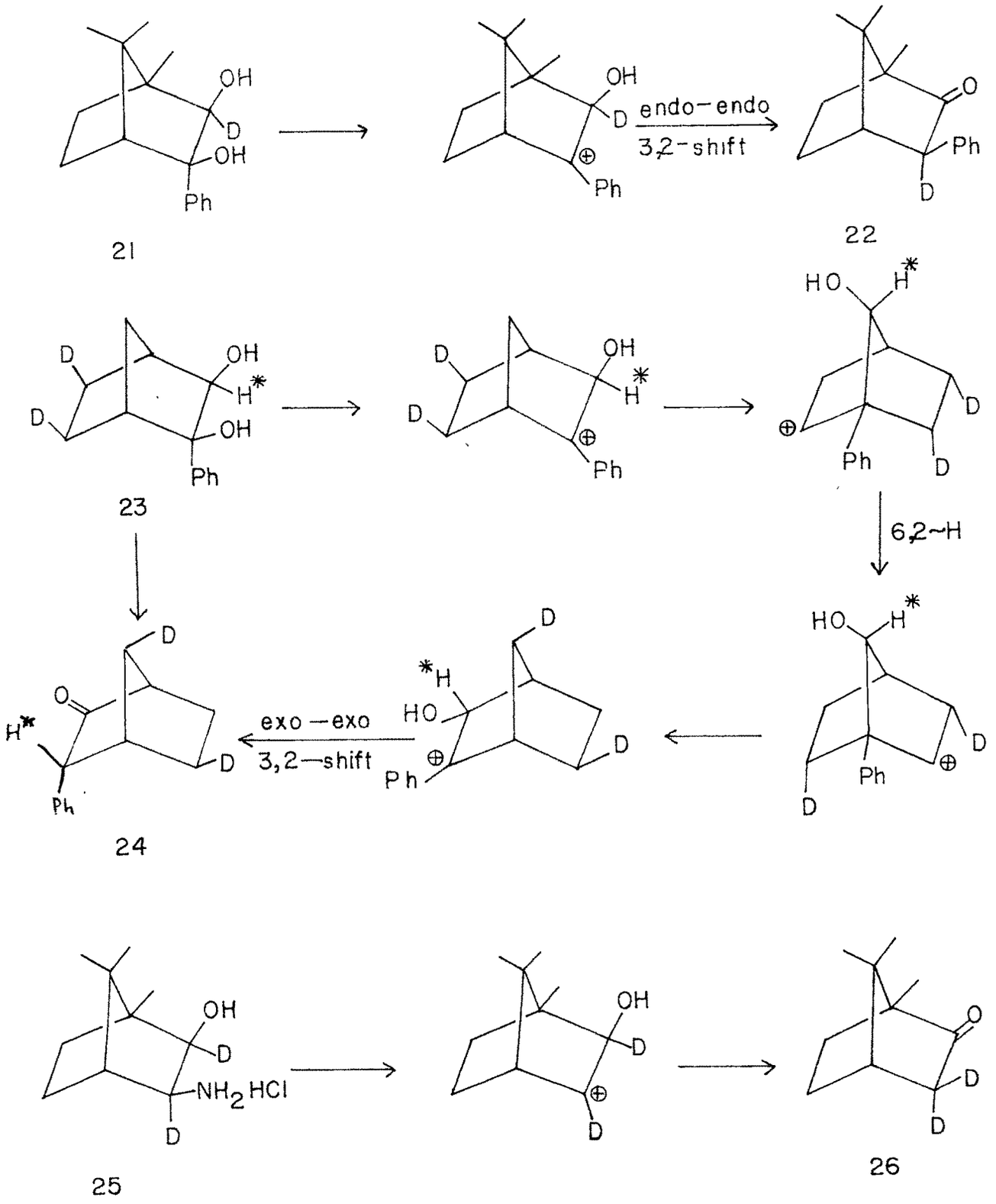
of norbornane diol tosylates 18 and 19 to 20.

2.1.2. 3,2-endo Migration in 2-norbornyl cations

endo-3-Phenyl-2,3-exo,cis-bornanediol (21) undergoes[35] pinacol rearrangement to exo-3-phenylcamphor (22) via endo-endo 3,2-hydride shift in contrast[34,36,37] to the rearrangement of analogous endo-3-phenyl-2,3-exo,cis-norbornanediol (23) to 24 which involves an exo-exo-2,3-hydride shift. Recently, it has also been shown[38] that deamination of exo-2-hydroxy-2-exo-aminobornane-2,3-$d_2$ (25) yields camphor-3,3-$d_2$ (26) which also involves endo-endo 3,2-hydride shift in the intermediate carbonium ion. In both 21 and 25 endo-endo-3,2-hydride migration provides relief to steric interaction between 7,7-gemdimethyl and hydroxyl group by making the hydroxyl bearing carbon planar, while there is no such interaction in 23 (see Chart III) and endo-endo-6,2-hydride transfer takes precedence over endo-endo 3,2-hydride shift.

2.1.3. Rearrangement of 10-Isobornyl Sultone

10-Isobornyl sultone (27) thermally rearranges first to endo-camphene sultone (28) and then slowly goes over to exo-camphene sultone (29)[39,40]. Two mechanisms have been proposed for this transformation. Path a postulates an exo-




21 22 23 24 25 26

CHART III : endo, endo –3,2-HYDRIDE SHIFTS

3,2-methyl shift among a number of other steps and path b involves an endo-3,2-methyl shift (Chart IV).

A nearly optically active sample of 27, when heated to its melting point gives optically inactive 29. However, it is not possible to decide whether racemization is a result of a 6,2-hydride shift or a nonselective methyl migration. Dimmel et al.[41] attempted to distinguish paths a and b by studying the rearrangement of site-specifically labelled sultone -9-$d_1$ 30. If 30 were to rearrange via an endo methyl migration the product should be 32; on the other hand, if an exo-methyl shift occurred, the product will be 31. However, a rapid 6,2-hydride shift in the carbonium ion from 30 renders these two methyl groups identical and path a and path b indistinguishable. To resolve the question, the same authors synthesized[41] sultone-3,3-$d_2$ 33 successfully taking all care to avoid scrambling of deuterium atoms. The expected positions of deuteriums in rearranged exo-camphene sultone-$d_2$ from 33 have been shown in Chart IV. Assuming that ion 34 undergoes rapid 6,2-hydride shift to 35, the intermediate 34 and 35 on rearrangement via path a or path b will lead to products 36a to 36d in which distribution of labels will be as shown in Chart IV. It can be inferred that an observation of 50% deuteriums at C-1 in exo-camphene sultone would establish an exo-methyl shift (path a) while no deuteriums at C-1 would

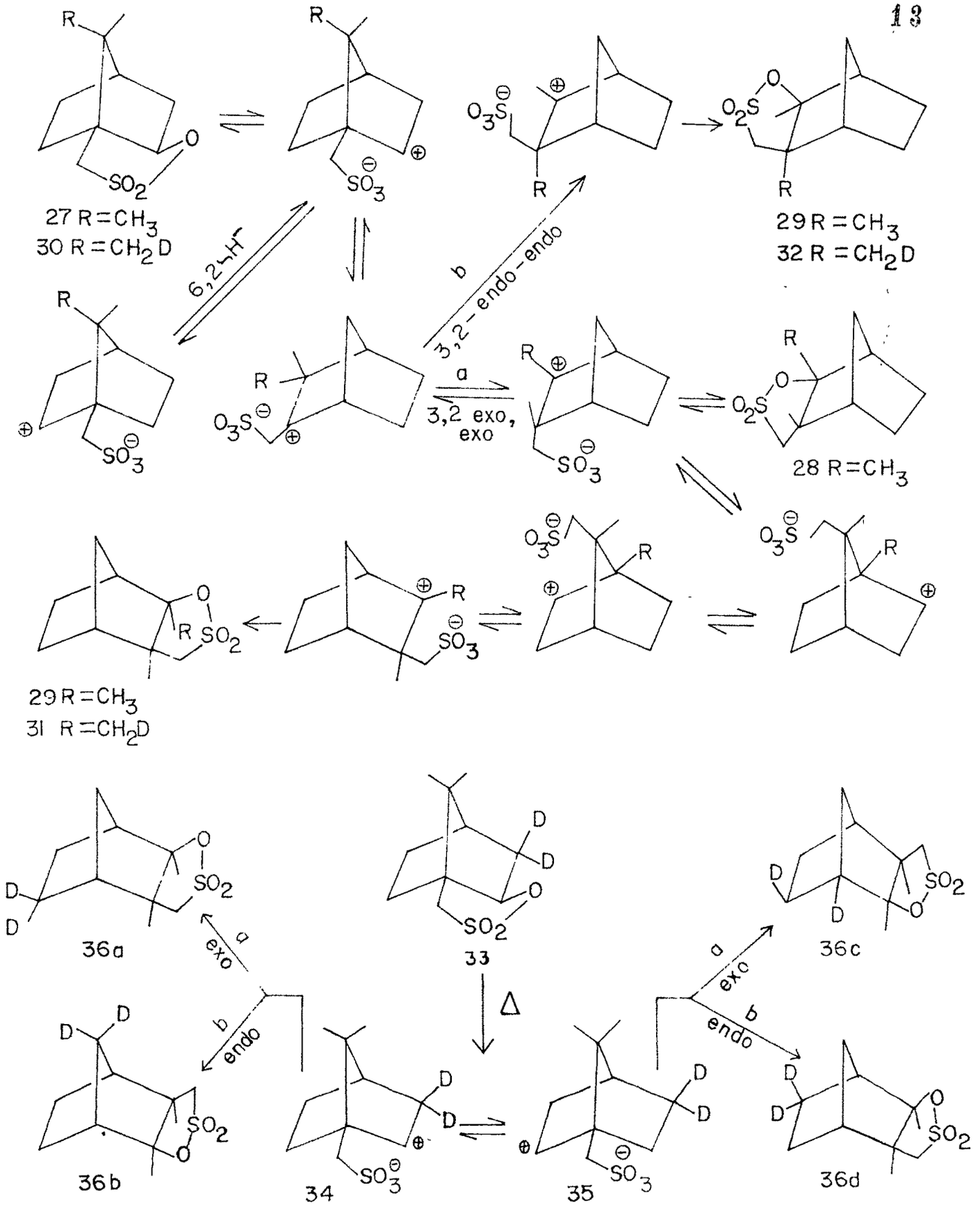



CHART IV: REARRANGEMENT OF 10-ISO-BORNYL SULTONE

favour the endo-methyl shift mechanism path b. Similarly, deuteriums at C-7 would also favour endo-methyl migration. In exo-camphene sultone, deuterium content at C-1 was determined to be 0.41 (slightly less than expected 0.5) and very little deuterium ( 0.04) was detected at C-7-syn. position. Based on these results, it has been concluded that an exo-3,2-methyl migration prevails over endo shift in the formation of exo-camphene sultone. Endo-Methyl migration, if at all taking place, must be only a minor pathway.

2.1.4 Homoenolization of Camphenilone, Fenchone and Camphor.

(+)-Camphenilone[42] (37) is completely racemized when heated with t-BuOK/t-BuOH at 200° for 4 hr. Racemization was believed to occur via the homoenolate ion 38 which on reopening can give two enantiomers 37 and 39 (Chart V). The contention was borne out when the racemization was carried out in presence of t-BuOK/t-BuOD and it was found that in a number of runs, the percentage of racemization corresponded closely with percentage of molecules having deuterium.

Fenchone[43,44] (40) under similar conditions not only gives the 6-monodeuterio and 6,6-dideuterio derivatives 41 and 42 but also undergoes skeltal rearrangement to 43 and 44 which are formed in the ratio of 3:1 upto the extent of about 6%.

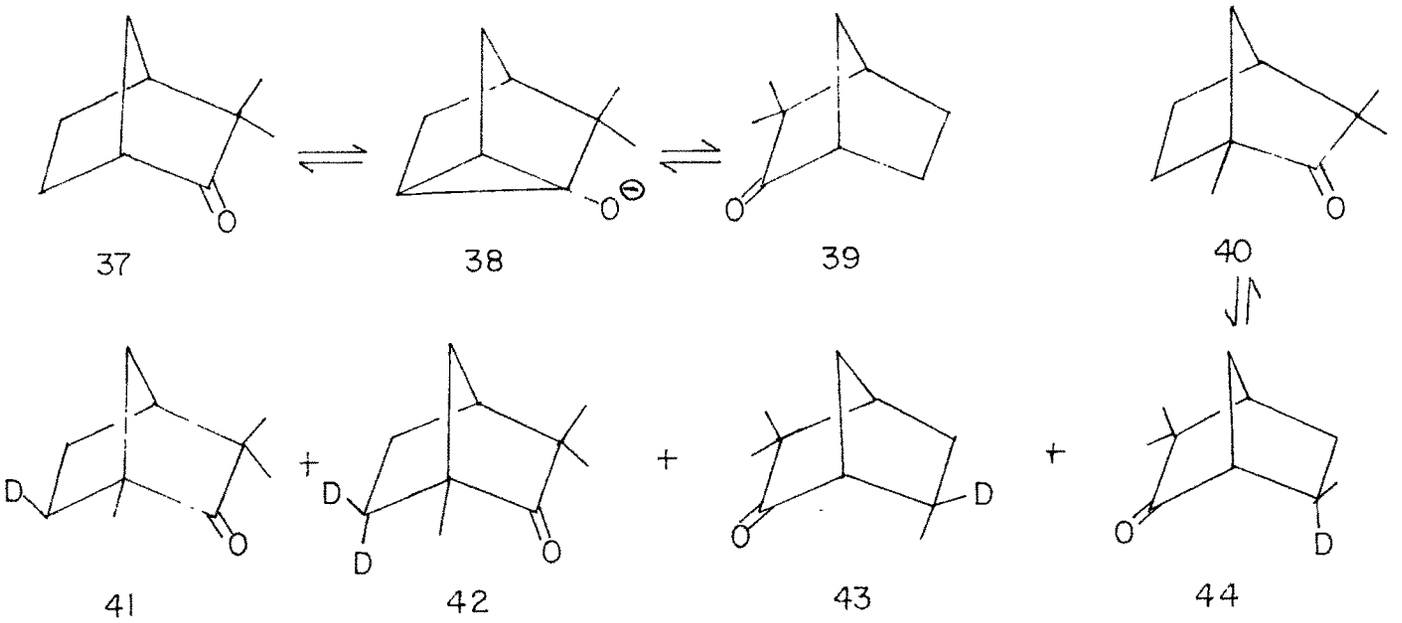



CHART V. HOMOENOLIZATION OF FENCHONE & CAMPHENILONE

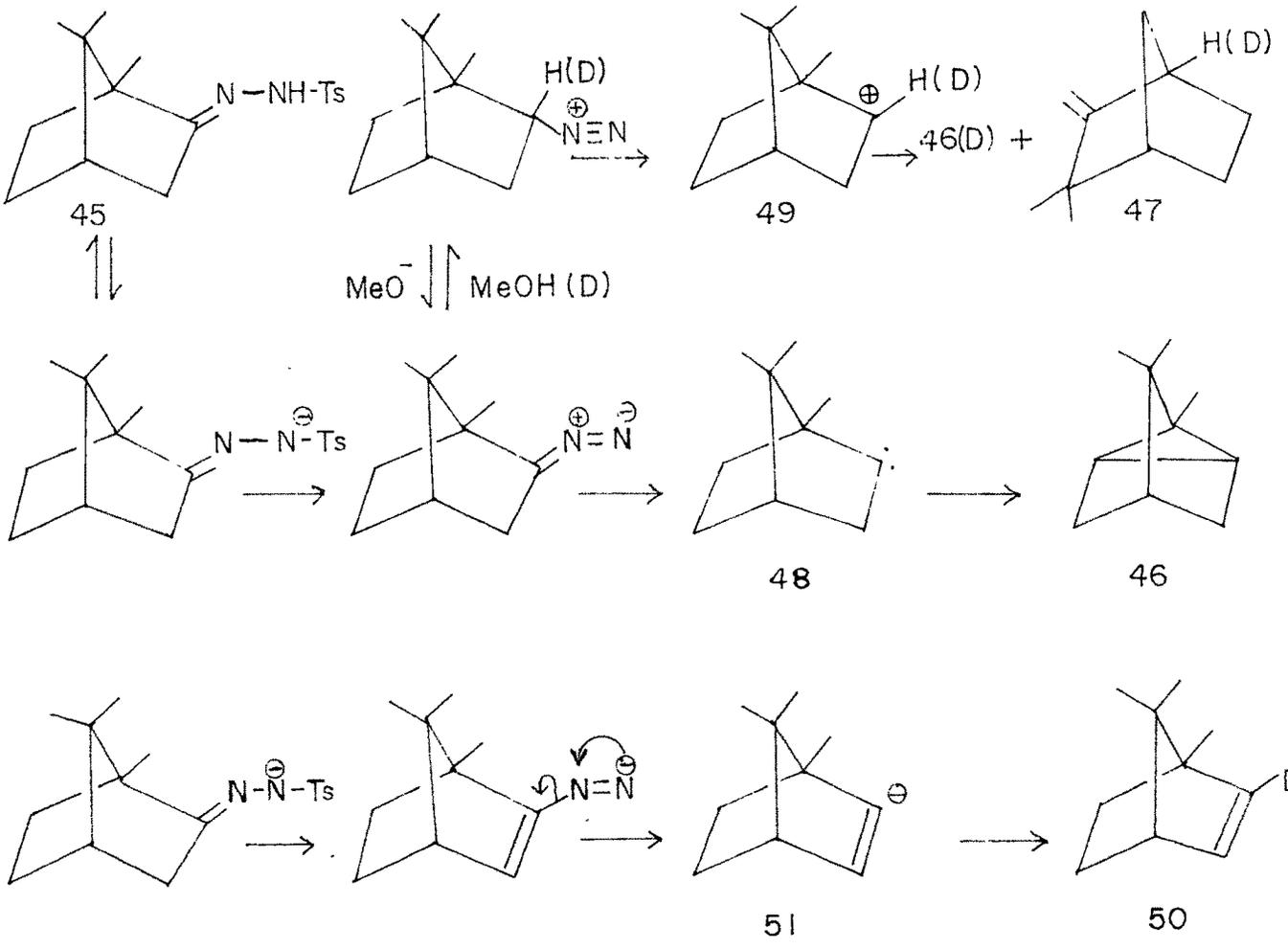



CHART VI : DECOMPOSITION OF CAMPHOR TOSYLHYDRAZONE

Similarly, it has been observed that camphor[45] and longicamphor[46] also incorporate deuteriums *via* homoenolizations.

2.1.5. Decomposition of Camphor tosylhydrazone

Camphor tosylhydrazone (45) decomposes[47,48] in the presence of a base in aprotic solvents to tricyclene (46) and camphene (47). The ratio of camphene to tricyclene decreases with increasing base concentration and decreasing solvent polarity[49,50]. The formation of tricyclene has been proposed to proceed through carbene 48 and carbonium ion 49, whereas camphene is presumed to arise only through carbonium ion intermediate 49 as shown in Chart VI. When the reaction is carried out in presence of sodium methoxide and deuterated methanol (MeOD), tricyclene and camphene forming *via* the carbonium ion should incorporate one deuterium each, whereas, tricyclene generated through carbene should not incorporate any deuteriums. It has been shown[50] that at higher concentrations of base, carbene formation predominates over carbonium ion formation and leads to the exclusive formation of tricyclene devoid of deuterium, whereas at lower concentrations of base tricyclene is formed in low yields and with the incorporation of deuterium in it. Similarly, carbene intermediate has been implicated in the oxidation of camphorhydrazone to tricyclene with mercuric oxide, as it

fails to incorporate deuterium in MeOD[51].

Decomposition of camphor tosylhydrazone, on treatment with alkyllithium followed by quenching with deuterium oxide gives 2-deuterio-2-bornene[52](50). These results have been accommodated by proposing a carbanion intermediate[52] (51) (Chart VI).

## 2.2. Rearrangement of α-Bromocamphoric Anhydride

A number of pathways had been proposed[53] for the formation of monocyclic laurolenic acid[54-56] (53) from α-bromocamphoric anhydride (52). Some of the routes proposed were discarded as they could not explain the formation of optically active laurolenic acid[53] (53); however, paths a, b and c could be expected to produce the same enantiomer as shown in Chart VII. D(-)α-Bromocamphoric anhydride-9,9,9-$d_3$ (52a) produced 53a without methyl scrambling[53]. Evidently, it is the 8-methyl group (indicated by heavy dot) trans to departing group bromine in 52b that migrates in a stereospecific manner in the rearrangement following path a-1 and/or a-2. However, which one of the carboxylic groups is lost during decarboxylation remains unresolved.

## 2.3. Photochemical Reaction of Carvonecamphor.

Carvonecamphor (55) a photoproduct of carvone (54) when

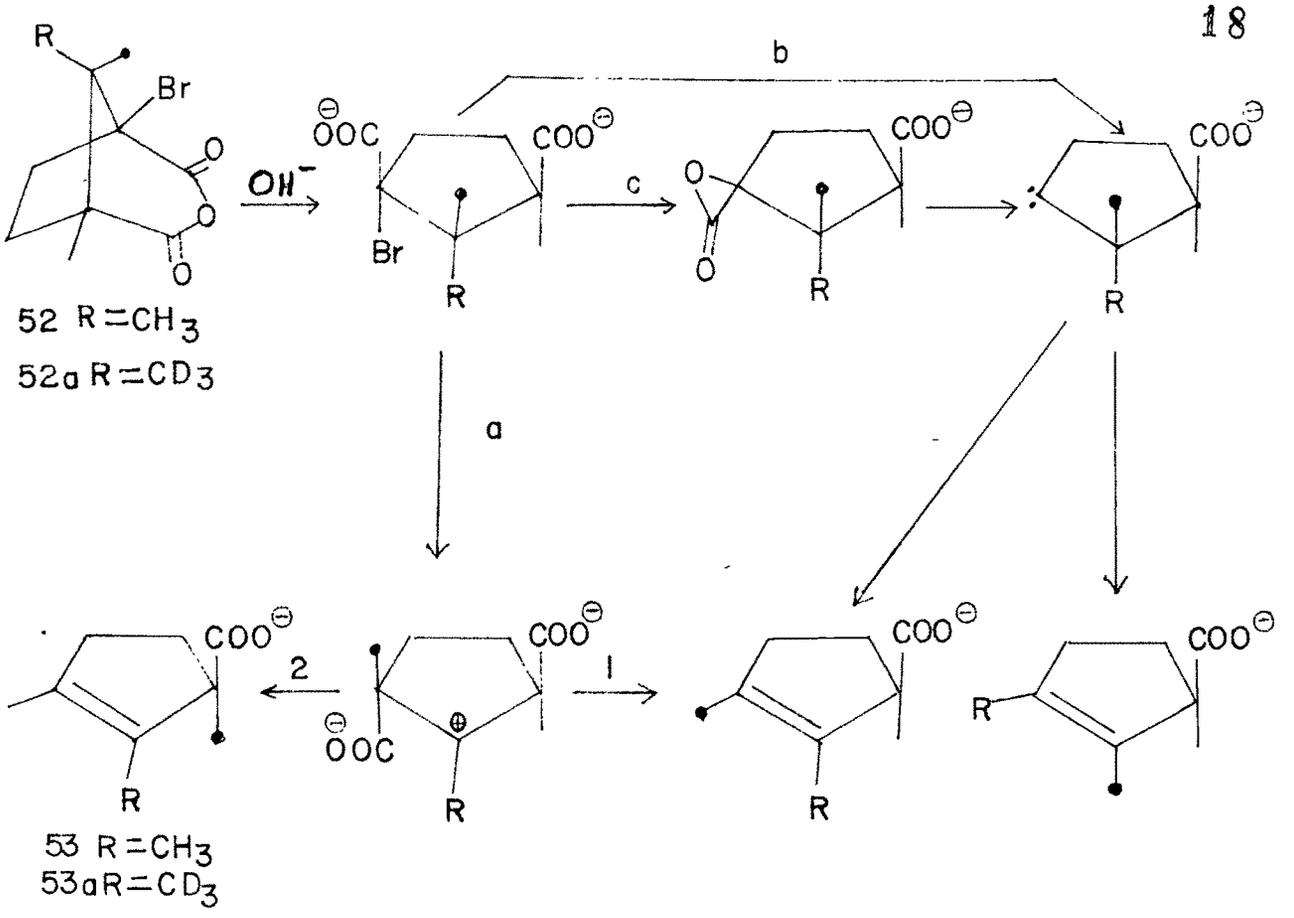



CHART VII: REARRANGEMENT OF α-BROMOCAMPHORIC ANHYDRIDE

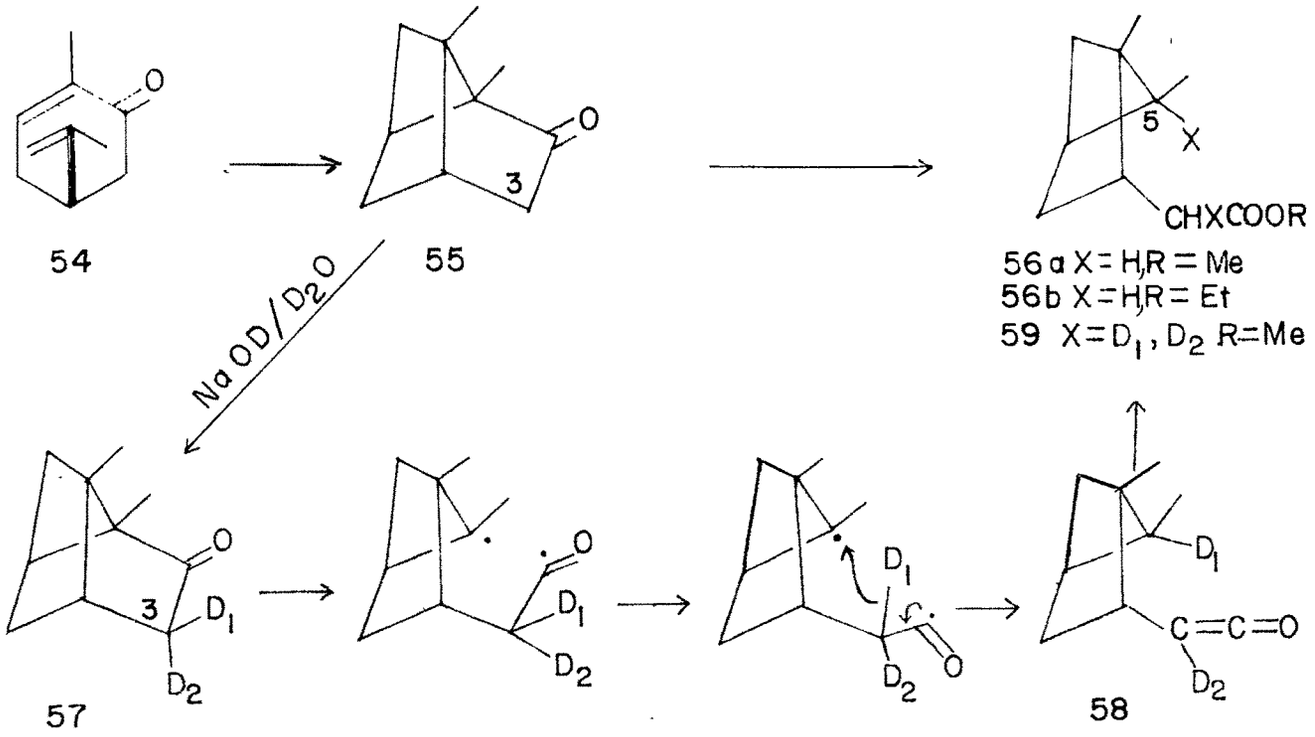



CHART VIII: PHOTOLYSIS OF CARVONECAMPHOR

irradiated to high pressure mercury lamp in aqueous or alcoholic dioxane undergoes photolytic cleavage to an acid 56a or an ester[57,58] (56b). The proposed mechanism involves a homolytic cleavage of the bond between carbonyl group and more substituted carbon atom followed by intramolecular hydrogen transfer to the tertiary radical site leading to the formation of saturated ketone 58 (Chart VIII). The validity of this mechanism has been checked[58] by irradiation of carvonecamphor-3,3-$d_2$ (57), which gave the expected product 59 with deuterium at C-5. When irradiation of 55 was carried out in $D_2O$/dioxane, one deuterium was incorporated at position $\alpha$ to carboxylic group and no deuterium was incorporated at C-5. It has been further verified[59] that only exo-hydrogen at C-3 in 55 is transferred to tertiary carbon. Intramolecular hydrogen transfer from the carbon atom $\alpha$ to the carbonyl group to the tertiary carbon is in sharp contrast to the usual hydrogen abstraction from the solvent in cyclic ketones[60].

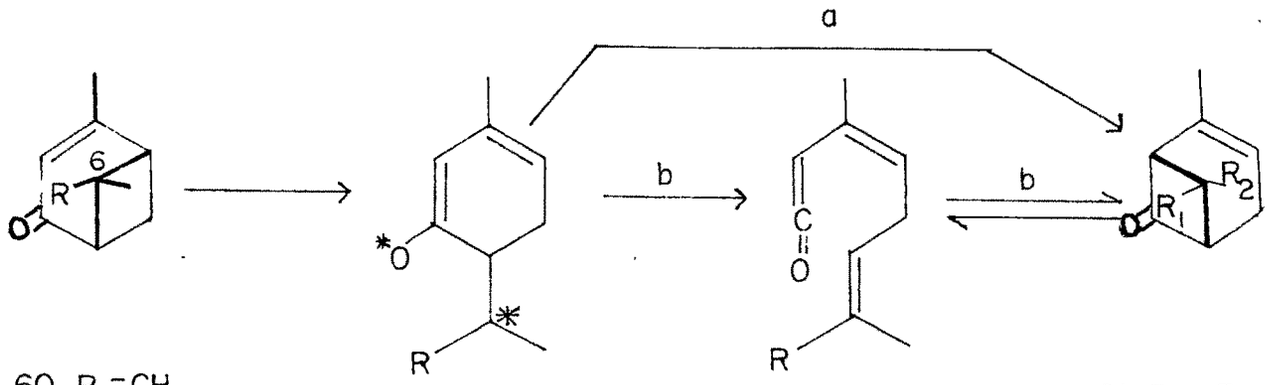
## 2.4. Photoisomerization of Verbenone

The mechanism of photoisomerization of verbenone 60 to chrysanthenone 61 has been investigated[61-63]. A number of mechanisms e.g. 1,3-sigmatropic rearrangement, path a and path b have been proposed for the isomerication. The stereochemical fate of the migrating carbon atom C-6, the nature of transient species 62 and other mechanistic aspects of rearrangement have been established using specifically labelled methyl at

C-9 in 60a[63]. Verbenone-9,9,9-$d_3$ (60a) on irradiation either in cyclohexane or in acetic acid gives 61a and 61b in a ratio of 1:1. The complete scrambling of methyl groups during formation of 61a and 61b indicates that transition state 62a is best represented as a discrete intermediate of diradical or dipolar nature which recyclizes to the racemized product 61a and 61b which can arise from path a and/or path b (Chart IX) Although no distinction is provided between path a and path b, a photochemical concerted 1,3-sigmatropic rearrangement of 60a controlled by local symmetry is clearly ruled out as the latter would occur with retention of stereochemistry at C-6 to give chrysanthenone-8,8,8-$d_3$[61](61a) as the only product. Further, verbenone-$d_3$ recovered after irradiation gave PMR identical with that of verbenone before irradiation. Therefore, species 62 does not close to verbenone to cause the scrambling of methyls.

## 2.5. Ene Reaction[64] with β-Pinene

Four possible transition states have been proposed[65-67] for the ene reaction between β-pinene (64) and maleic anhydride (65) based on four different ways in which the enophile 65 can approach β-pinene as shown in Chart X. In order to distinguish between the four possible intermediates A-D it is



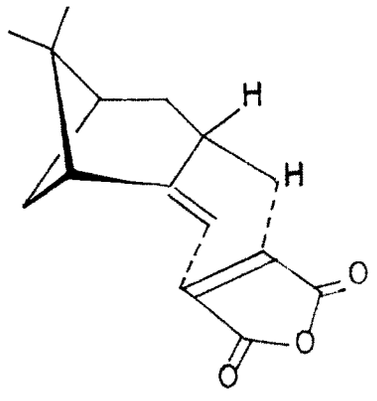

60 R = $CH_3$
60a R = $CD_3$

62 R = $CH_3$
62a R = $CD_3$

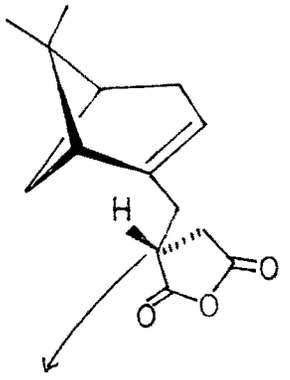
63 R = $CH_3$
63a R = $CD_3$

61 $R_1 = R_2 = CH_3$
61a $R_1 = CD_3$ $R_2 = CH_3$
61b $R_1 = CH_3$ $R_2 = CD_3$

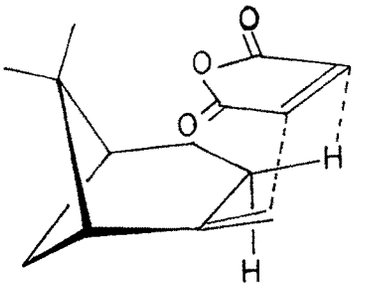
CHART IX: PHOTOISOMERIZATION OF VERBENONE



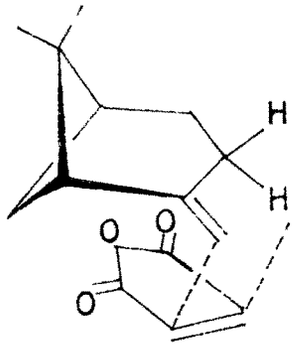

'A' exo – ORIENTATION



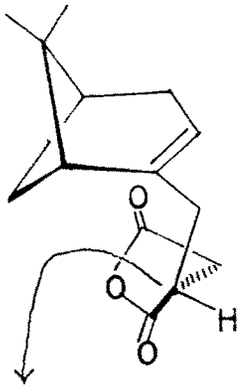

'S' CONFIGURATION



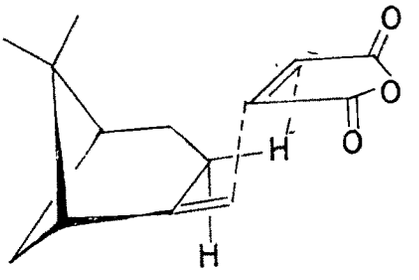

'B' endo – ORIENTATION



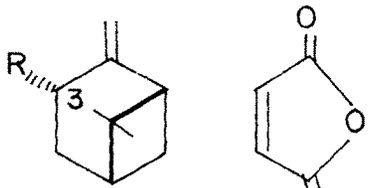

'C' endo – ORIENTATION




'R' – CONFIGURATION



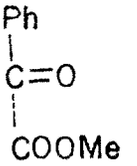

'D' exo – ORIENTATON



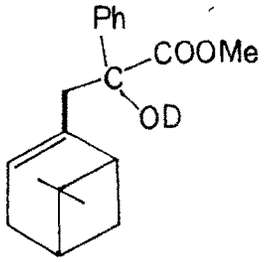

64 R = H
64a R = D



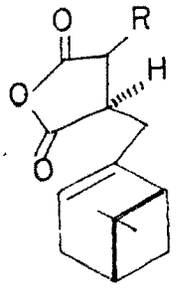

65




66




66a



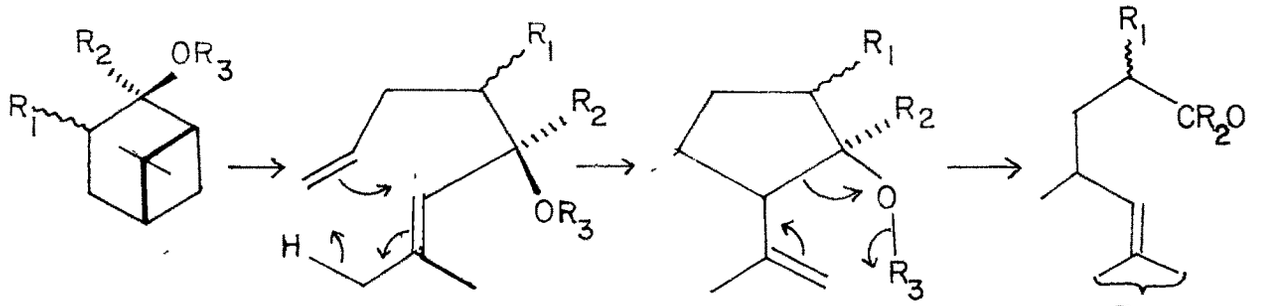

67 R = H
67a R = D

CHART X: ENE REACTION OF $\beta$-PINENE

important to know which of the allylic hydrogens (equitorial or axial) at C-3 in 64 is transferred to 65 and the absolute configuration at the new asymmetric centre generated in the adduct. When stereospecifically labelled β-pinene endo-3-$d_1$ 64a was subjected to the ene reaction with maleic anhydride, 94 ± 6% of the deuterium was transferred to the enophile in adduct which is expected only in the transition state A or C[66,67]. The configuration at new asymmetric centre in the adduct has been shown[66] 'R' by degradation to a product of known stereochemistry. Thus, the ene reaction proceeds almost entirely through the transition state 'C'. Arnold et al.[67] have also studied the ene reaction of β-pinene (64) with methylphenyl-glyoxylate (66). Since the reaction is reversible, the adduct 66a on equillibration with $D_2O$ followed by thermolysis gives β-pinene stereospecifically labelled at endo-3-$d_1$, 64a.

## 2.6. Pyrolysis of Nopinol

Pyrolysis of nopinol (68) at 580° produces an aldehyde 69 besides other normal products[68,69]. The mechanism proposed for its isomerization is given in Chart XI. Pyrolysis of three samples of monodeuterated nopinol 68a, 68b and 68c gives three monodeuterated aldehydes 69a, 69b and 69c respectively which is consistent with the proposed route. Thermal rearrangement of 2-deutereonorpinene has been proposed via

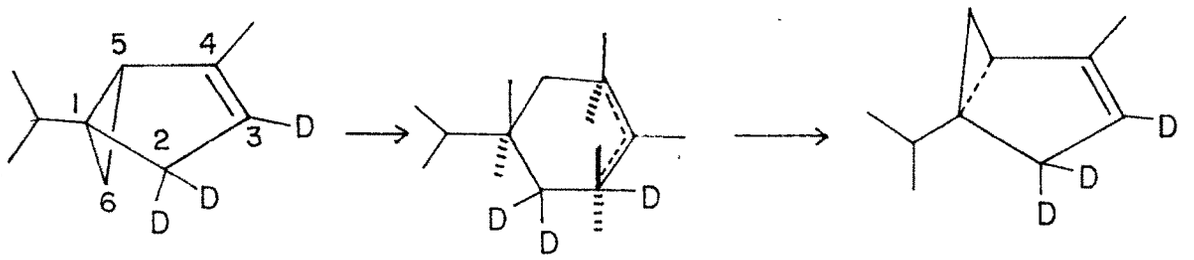


68 $R_1 = R_2 = R_3 = H$ b $R_1 = R_3 = H, R_2 = D$

a $R_1 = R_2 = H, R_3 = D$ c $R_1 = D, R_2 = R_3 = H$ 69

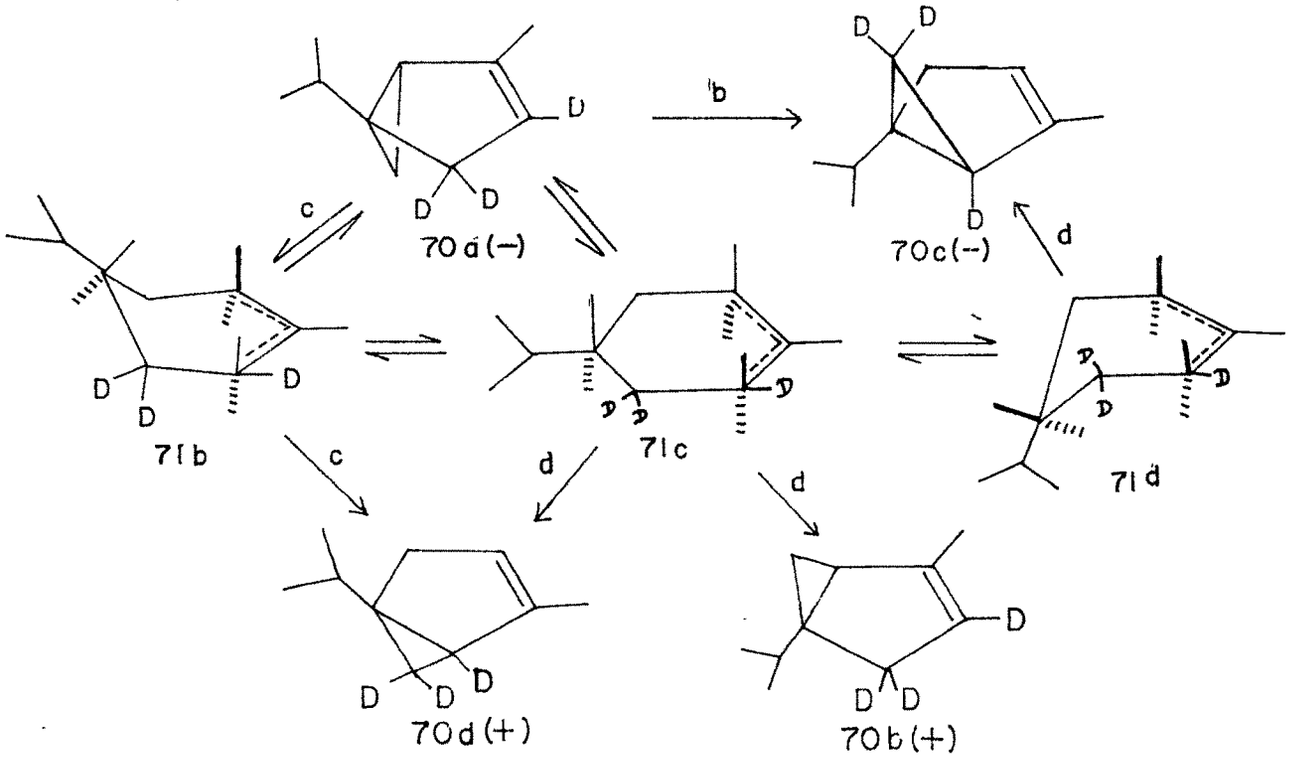
CHART XI: PYROLYSIS OF NOPINOL

Path a : CONCERTED & SYMMETRY ALLOWED



70a(−) 71a 70b(+)

Paths b, c and d : NONCONCERTED: HYPOTHETICALLY STEREOSPECIFIC



70d(+) 70b(+)

CHART XII : RACEMIZATION OF $\mathcal{L}$-THUJENE

concerted mechanism and has also been experimentally verified[70].

## 2.7. Thermal Isomerization of α-Thujene

(-) α-Thujene (70a) racemizes[71] slowly on being heated at 200° and rapidly at 255°C. Doering and Schmidt[73] considered four different mechanisms for this isomerization (Chart XII). Path a involves a concerted symmetry-allowed process and should lead to enantiomerization without transmutation of deuteriums which is not found to be true. Path b involves rearrangement by a hypothetically stereospecific vinylcyclopropane rearrangement with retention of original chirality. This pathway should cause rearrangement of deuterium labels without racemization. There is no theoretical justification for path b to operate and this can, at best, be only a minor pathway. Both paths c and d, involve symmetry-disallowed nonconcerted vinylcyclopropane rearrangements[72], but differ from each other in the following respects.

In path c the transition state is isoconformational with the starting material, whereas, in path d conformational inversion takes place at a small extra cost of 1.2 K cal/mol of energy. The stereochemical outcome of isomerization according to path c and path d is shown in Table 1. Table 1 also shows the observed product composition of the reaction when it is

interrupted short of complete racemization followed by isolation of the enantiomers and proportions of isotopically distinguishable thujenes established by PMR. It is clear from the results that the major path followed is path c. However, the result can be better explained by a statistical combination of major path c and minor path d.

Table 1. Theoretical distribution of products for rearrangement of (-)α-thujene-2,2,3-$d_3$ 70a

| Path | (-)α-thujene-2,2,3-$d_3$ 70a | (+)α-thujene-2,2,3-$d_3$ 70b | (-)α-thujene-5,6,6-$d_3$ 70c | (+)α-thujene-5,6,6-$d_3$ 70d |
|---|---|---|---|---|
| a | - | 100% | - | - |
| b | - | - | 100% | - |
| c | 50% | - | - | 50% |
| d | 25% | 25% | 25% | 25% |
| observed | 65.5% | 7.0% | 8.1% | 19.4% |

## 3. SESQUETERPENES

### 3.1. Cyclization of Humulene

The acid catalysed rearrangement of humulene (72) with aqueous acids yields a secondary alcohol* 73 besides other products consisting of hydrocarbons 74, 75 and 76 possessing the same skeleton as the tertiary alcohol 77[74,78] (see Chart XIII)

3.1.1. Mechanism of Formations of Alcohol 73 : The mechanism of genesis of 73 is not known but the most plausible route proposed is depicted in Chart XIII, and has been verified by conducting the cyclization of 72 in $D_2SO_4/D_2O$ followed by location of deuteriums in appolan-11-ol[81] (73).

3.1.2. Mechanism of Formation of Hydrocarbon 74

The formation of 74 requires ring closure to a 6,7-bicyclic system followed by ring contraction of six membered

---

*This alcohol was originally isolated when caryophyllene (containing 10-15%) humulene) was treated with sulfuric acid and a trivial name viz α-caryophyllene alcohol was given to it[79]. Sukh Dev[80] obtained the same alcohol by hydration of humulene. This seems to be the first report of cyclization of humulene to alcohol 73. Nickon and coworkers[77] have finally shown that α-caryophyllene alcohol is derived only from humulene present in caryophyllene and suggested a new name, appolan-11-ol for it.

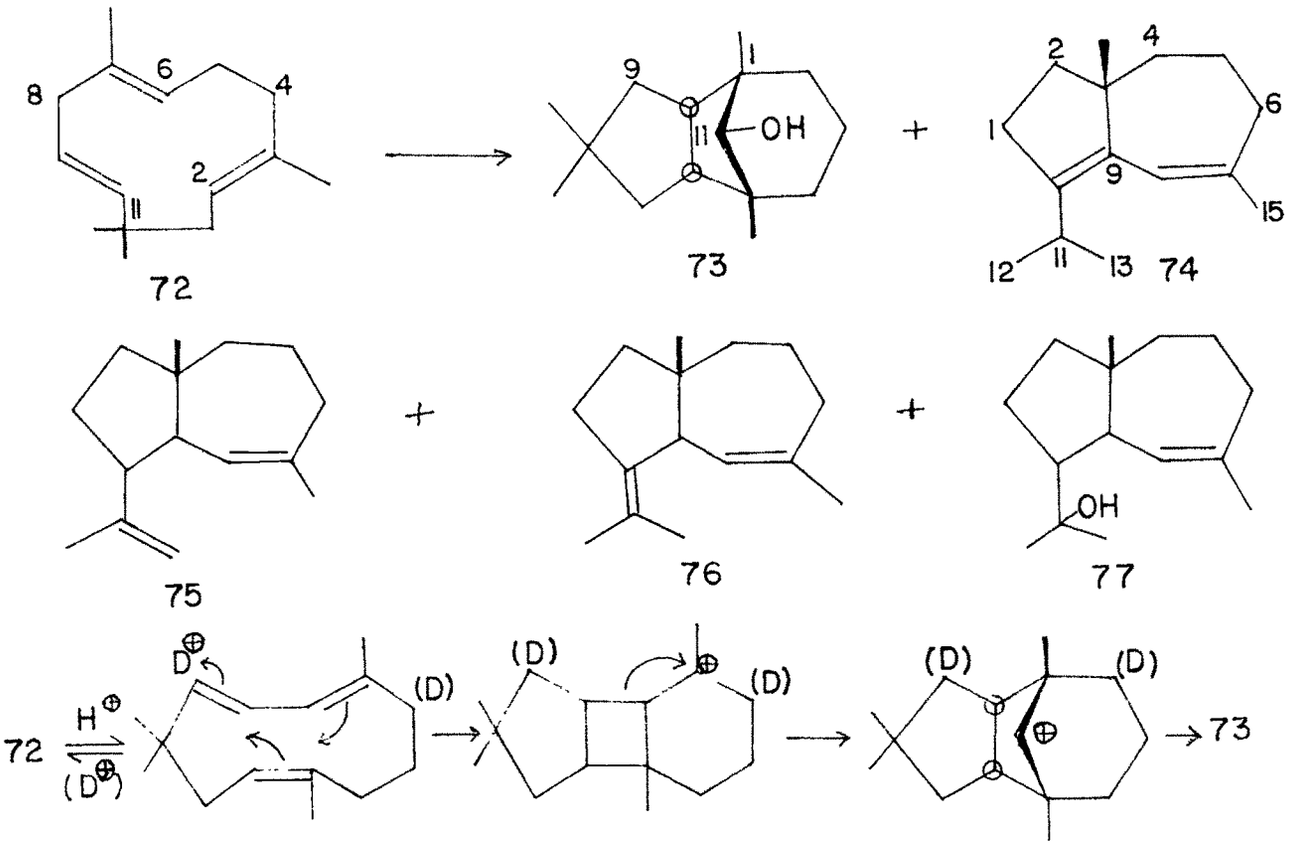



CHART XIII: FORMATION OF APPOLAN-11-OL (73)

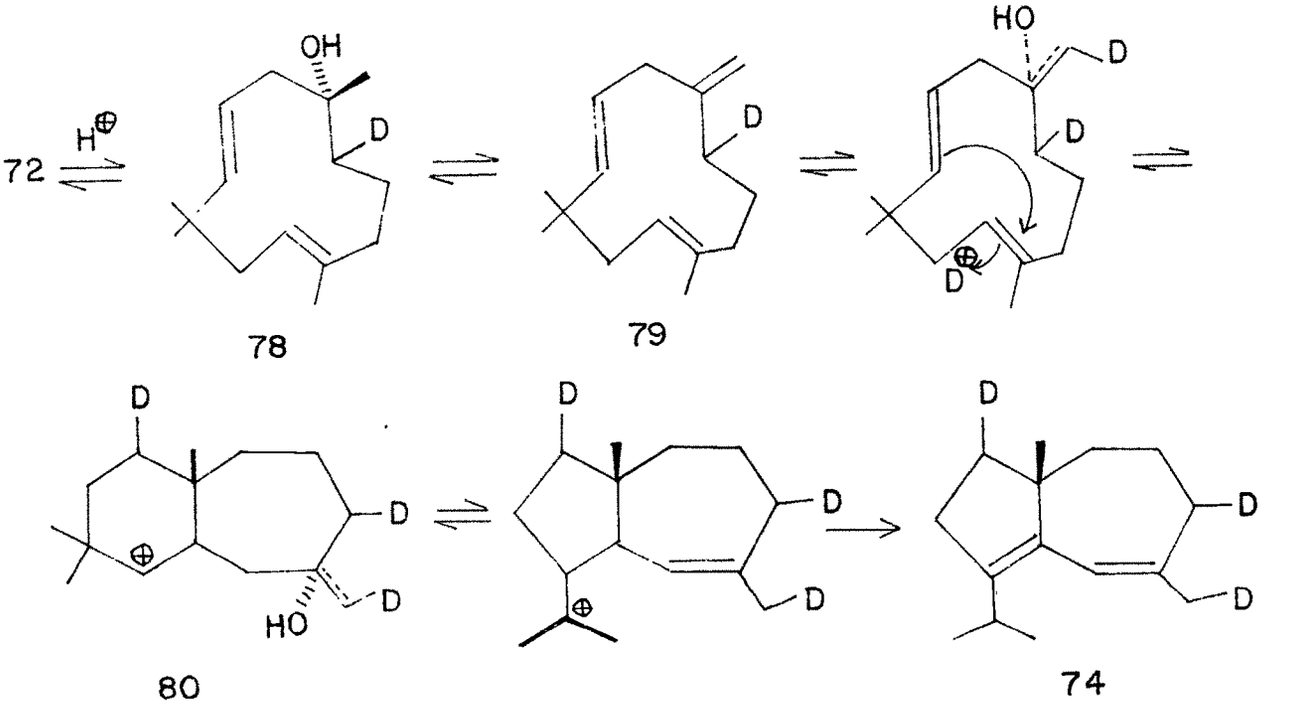



CHART XIV : CYCLIZATION OF HUMULENE

ring with extrusion of isopropyl group[74,76]. A detailed study of the reaction by Dauben et al.[74] reveals that $\alpha$-humulene (72), $\beta$-humulene (79) and humulol (78) are rapidly interconvertible under the reaction conditions (see Chart XIV). Humulol (78) appears to be a suitable intermediate for the formation of 74 because it blocks $C_6$-$C_7$ double bond in 72 and allows the protonation of $C_2$-$C_3$ double bond, which leads to bicyclic system 80 and then to products as delineated in Chart XIV. Analysis of products of cyclization of humulene with $D_2SO_4$ shows[74,75] major deuterium concentration at carbon C-2, C-6 and C-15 and very little amount at C-11, C-12 and C-13 in 74. A small amount of deuterium (~10%) incorporated at C-11 indicates that product 74 arose via 1,2-hydride shift from C-10 to C-11 as setforth in the postulated mechanism.

## 3.2. Acid Catalysed Cyclization of Caryophyllene

Caryophyllene (81) with a highly reactive double bond, is prone to undergo transannular ring closure in contact with mild acid to yield caryolanol (82), clovene (83) and neoclovene[82,83] (84). Since caryophyllene is a flexible molecule containing a nine membered ring which is able to take up a number of conformations separated by small energy barriers, it behaves like acyclic diene. The products 82 and 83

belonging to two different stereochemical families, may be derived from two different conformers A and B of 82 or from tertiary cations C and D after protonation of endocyclic double bond as depicted in Chart XV. Conformation A in which olefinic methyl group projects upward (syn. to hydrogen at C-5) will close to 82, while conformation B with olefinic methyl group anti to C-5 proton will cyclize to 83. However, cations C and D formed after the protonation of the endocyclic double bond may be interconvertible by conformational flipping. Furthermore, the addition of proton on the endocyclic double bond may occur from either side giving rise to net cis or trans addition. Thus six stereochemically distinct pathways are possible[84]. The actual pathways operating in the cyclization could be decided by determining the configuration of deuterium at C-9 in product 82 and 83 derived from $D^+$ catalysed cyclization of 81. It has been found[84,85] that $D^+$ catalysed cyclization of 81 produces caryolanol-9,$\beta$ —$d_1$ (82a) and clovene-9,$\alpha$-$d_1$ (83a). The results are compatible with trans addition of proton to endocyclic double bond in conformation A and B without intervening flipping of C and D.

### 3.3. Rearrangement of Thujopsene

When thujopsene (85) a tricyclic sesquiterpene is allowed to react with an aqueous acid, a bicyclic sesquiterpenic alcohol,

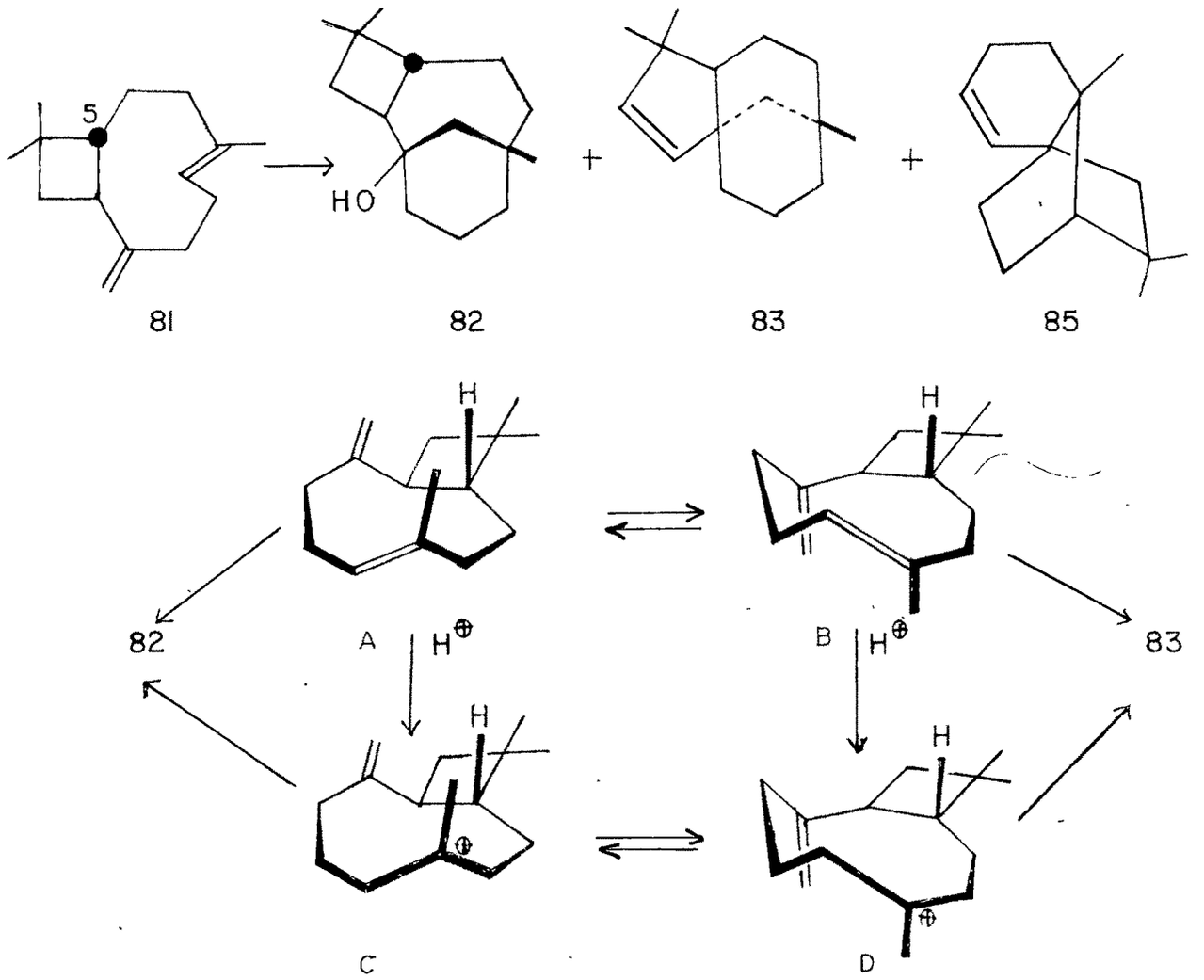



CHART XV: CYCLIZATION OF CARYOPHYLLENE

widdrol (86), along with other products, is formed, whereas prolonged heating affords a nonconjugated diene 87.

### 3.3.1. Mechanism of Formation of Widdrol 86

Enzell[86] has proposed the formation of 86 from 85 via hydration of double bond, followed by cyclopropane opening after protonation as shown in Chart XVI, path a. Later Douben et al.[87] proposed one of the less probable mechanisms (path b) via homoallylic cation 89 to a homoannular diene 90 followed by its hydration to widdrol (86). These mechanisms are electronically improbable and were proved[87-89] erroneous. Another proposed mechanism involves[87,88] cyclopropylcarbinyl-cyclopropylcarbinyl-type rearrangement[90,91]. The first step is protonation of double bond to cyclopropylcarbinyl cation 88 which rearranges to another cyclopropylcarbinyl cation 92. 92 collapses to a homoallylic cation 93 which on quenching gives widdrol (86) as shown in Chart XVI, path c. This route was shown to be correct by using a labelled substrate. Thujopsene-6,6-$d_2$ (85a), on rearrangement afforded widdrol-7,7-$d_2$ (86a) as expected from path c; paths a and b would have produced widdrol-6-$d_1$[88] (86c).

Stereospecifically labelled widdrol-7,$\beta$-$d_1$ (86b) produces thujopsene-6,$\beta$-$d_1$ (85b) with retention of configuration of

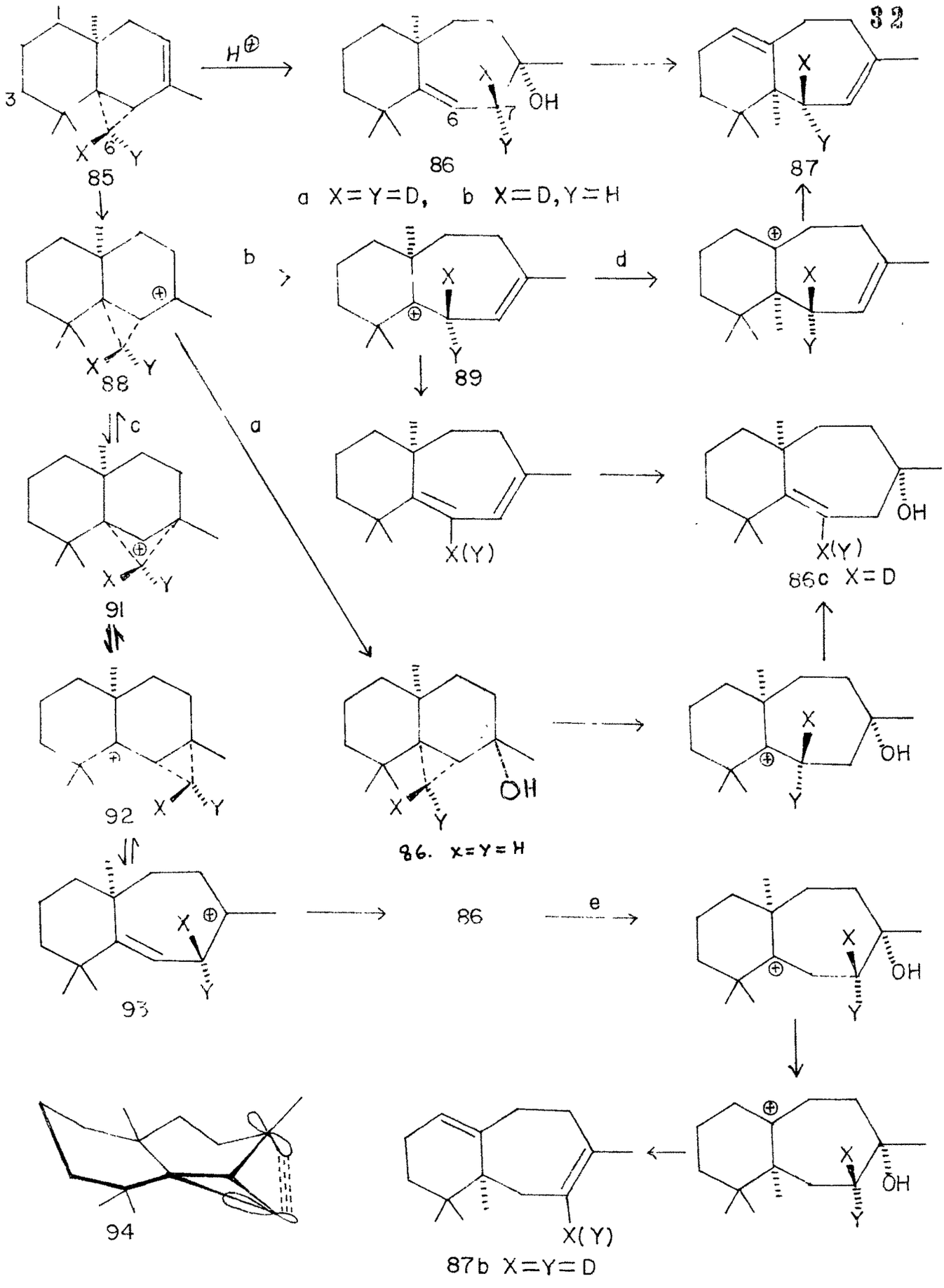



CHART XVI: REARRANGEMENT OF THUJOPSENE

deuterium in it[91,92]. This result suggests that cyclopropyl-carbinyl-cyclopropylcarbinyl rearrangement has occured either by the participation of backside (small lobe) of the orbital of bond C5-C6 of cyclopropyl ring with the orbital at the cationic centre at C-8 as shown in 94 or via puckered cyclo-butonium ion 91; the latter appears more probable as an activated complex by molecular orbital calculations carried out on less complicated systems[90,93-97].

### 3.3.2. Formation of Diene 87

When thujopsene was allowed to react for longer time with acid, the initially formed products including widdrol disappear and a nonconjugated diene 87 is obtained[88]. The mechanism proposed for the formation of diene 87 from widdrol (86) is given in Chart XVI, path e. However, diene 87a obtained from thujopsene-6,6-$d_2$ (85a) retained both deuteriums in it, which is expected through path d in contrast to path[88] e. It has been concluded that cations 88, 91, 92 and 93 are interconvertible under the reaction condition. And once the cation 89 is formed from them, it undergoes elimination to the stable diene 87.

## 3.4. Photorearrangement of Santonene Derivatives

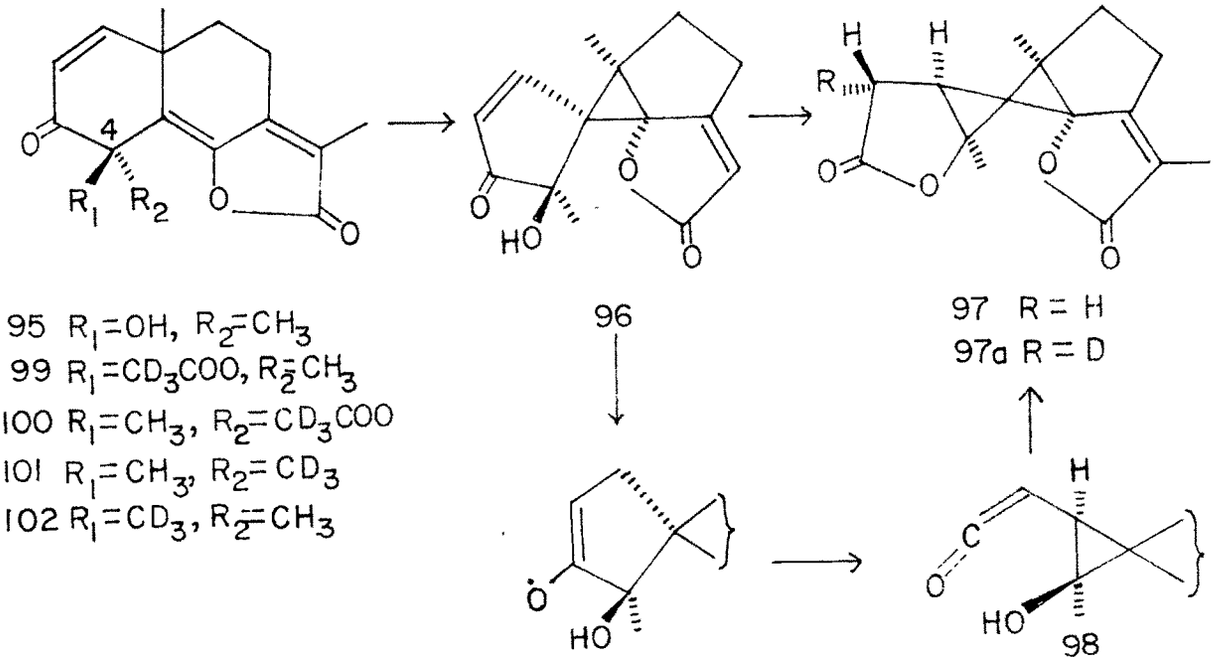
Photolysis of 4,$\beta$-hydroxysantonene (95) in presence of

triplet quencher affords a normal photoproduct[98-102], 96 which under the reaction conditions rearranges to dilactone[103] 97. When photolysis was carried out in MeOD, the resulting dilactone 97a incorporated one deuterium at the position and stereochemistry as shown in 97a. Similar results have been obtained when 4,α-hydroxysantonene was likewise irradiated[103]. A number of routes via concerted pathways have been proposed for this transformation but the stereochemistry and position of deuterium incorporated in the product can be best explained, if the reaction proceeds through a ketene intermediate 98, which recyclizes to the dilactone[103] 97. When 4,β or α-deuterioacetoxysantonene, 99 or 100 was irradiated under the same reaction conditions, the reaction follows a different route and either of the two gives 101 and 102 in the ratio of 3:1 (see Chart XVII).

## 4. DITERPENENES

### 4.1. Rearrangement of Erythroxylol-A-Epoxide (103)

Epoxide 103 undergoes, a hibaene-type rearrangement[106-108] with dilute formic acid but with concentrated formic acid, a more deep seated molecular rearrangement takes place to give[105-107] 104. The mechanism proposed for the formation of 104 involves opening of epoxide ring in 103 followed by protonation of the developing carbonium ion at C-15, a hydride shift from C-11 to C-15 which then undergoes a number of Wagner-Meerwein



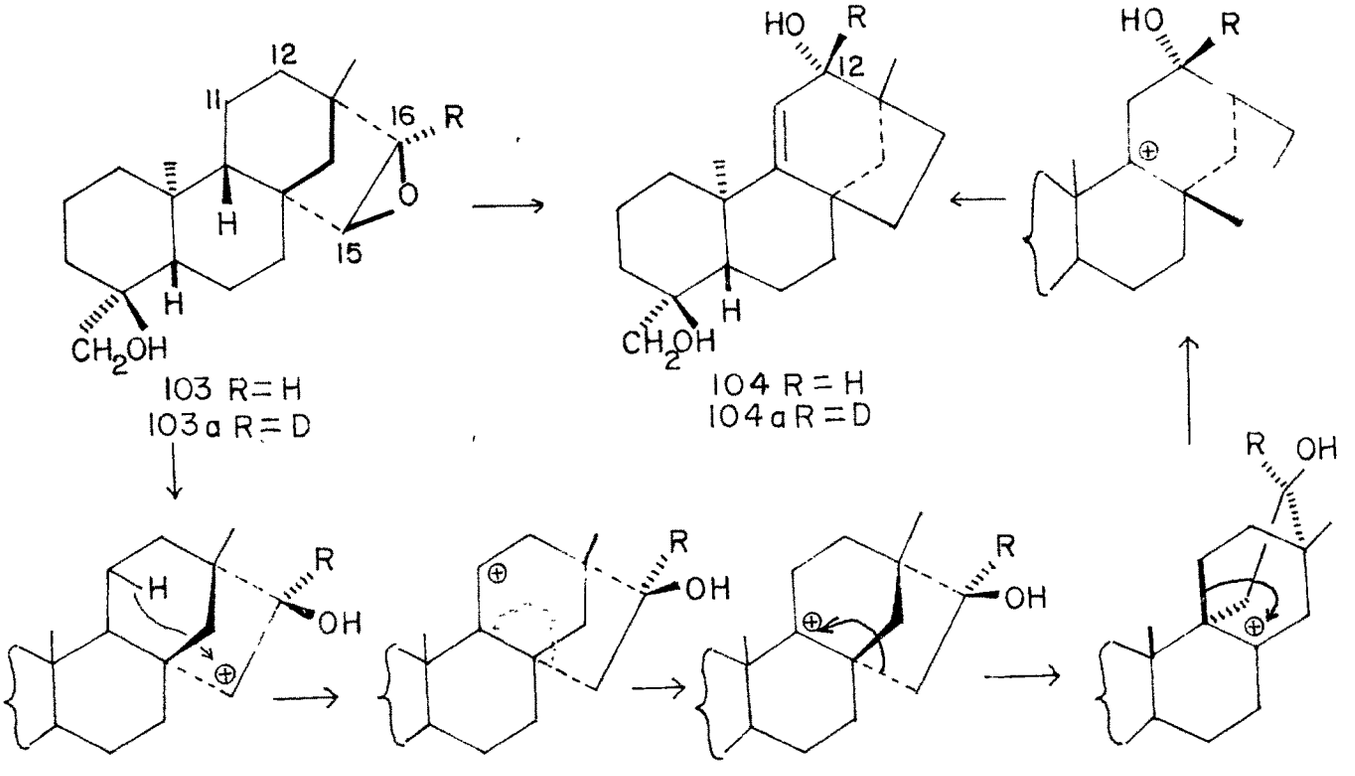
95 $R_1$=OH, $R_2$=$CH_3$
99 $R_1$=$CD_3COO$, $R_2$=$CH_3$
100 $R_1$=$CH_3$, $R_2$=$CD_3COO$
101 $R_1$=$CH_3$, $R_2$=$CD_3$
102 $R_1$=$CD_3$, $R_2$=$CH_3$

96

97 R = H
97a R = D

98

CHART XVII : PHOTO REARRANGEMENT OF SANTONENE DERIVATIVES



103 R=H
103a R=D

104 R=H
104a R=D

CHART XVIII : REARRANGEMENT OF ERYTHROXYLOL-A-EPOXIDE

rearrangements to yield[108] 104 as depicted in Chart XVIII. This mechanism was supported[108] by subjecting the epoxide-14-$d_1$ 103a to rearrangement to produce 104a in which the deuterium appeared α-to formate ester at C-12 position in conformity with the above suggested mechanism.

4.2. Acid-Catalysed Cyclization of Manool

Formolysis of manool (108) and isomanool (105) with formic acid in chloroform produces tricyclic dienes 106 and 107 and tetracyclic formate 109 or corresponding alcohol[109-112] 110. Manool (108) has been suggested as a biogenetic precursor for pimarane group of diterpenes viz. 106 which further rearranges to rimuene group of terpenes represented[112-114] by 107. For the unusual acid catalysed double cyclization of manool to tetracyclic alcohol, 14,α-hibol (110) two mechanisms have been advanced[110-111]; path a based on biogenetic considerations and path b an intuitively preferable but chemically less precedented route as given in Chart XIX. In order to differentiate between these two mechanisms, Edward et al.[115] carried out rearrangement of manool-7,7,10,17,17-$d_5$ (108a) and ascertained the position of deuterium in the product as shown in 110b. These results corroborate path b, whereas, path a would have produced 110c. Wenkert et al.[111] also obtained the same results by using isomanool-14-$^{14}C_1$.

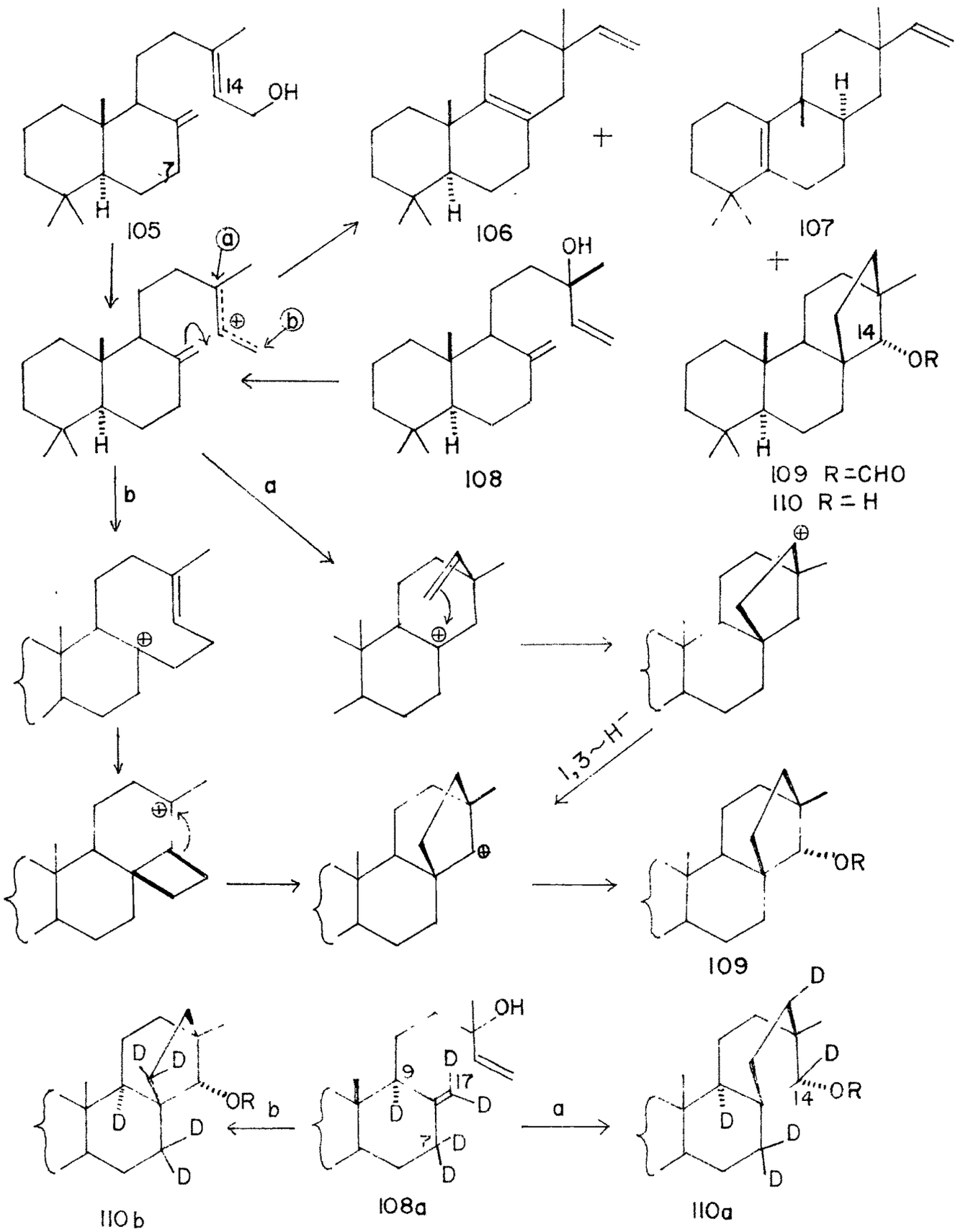



CHART XIX: CYCLIZATION OF MANOOL

## 5. TRITERPENES

### 5.1. Photoreaction of friedlin

Friedlin (111) on irradiation with a high pressure mercury lamp in hexane or ether undergoes an unusual photo-transformation by the loss of one carbon to aldehyde[117] 112. The proposed mechanism for this transformation involves a homolytic cleavage of $C_4$-$C_5$ bond to diradical 113 followed by usual hydrogen transfer to form ketene[118] 114. Ketene 114 forms an adduct with oxygen which decomposes to $CO_2$ and aldehyde 112 as shown in Chart XX. Photolysis of deuterated substrate 111a furnished the photoproduct 112a in which all the deuteriums were intact; furthermore friedlin-$^{18}O$ after irradiation had shown the total disappearance of $^{18}O$. Both these results support the proposed mechanism[118].

### 5.2. Friedelene-Oleanene Rearrangement

It has been shown[119] that acid catalysed rearrangement of $\Delta^3$-friedelene (115) into $\Delta^{18(18)}$-oleanene (116) proceeds via intermediate $\Delta^{5(10)}$-glutenene (117) and $\Delta^{12}$-oleanene and is a reversal of biogenetic route[120,121]. With the aid of deutereoacetic acid ($AcOD/ZnCl_2$), it has been possible to determine that $\Delta^{5(10)}$-glutenene (117) $\Delta^{12}$-oleanene (118) reaction is essentially irreversible. It has been demonstrated[115] that in

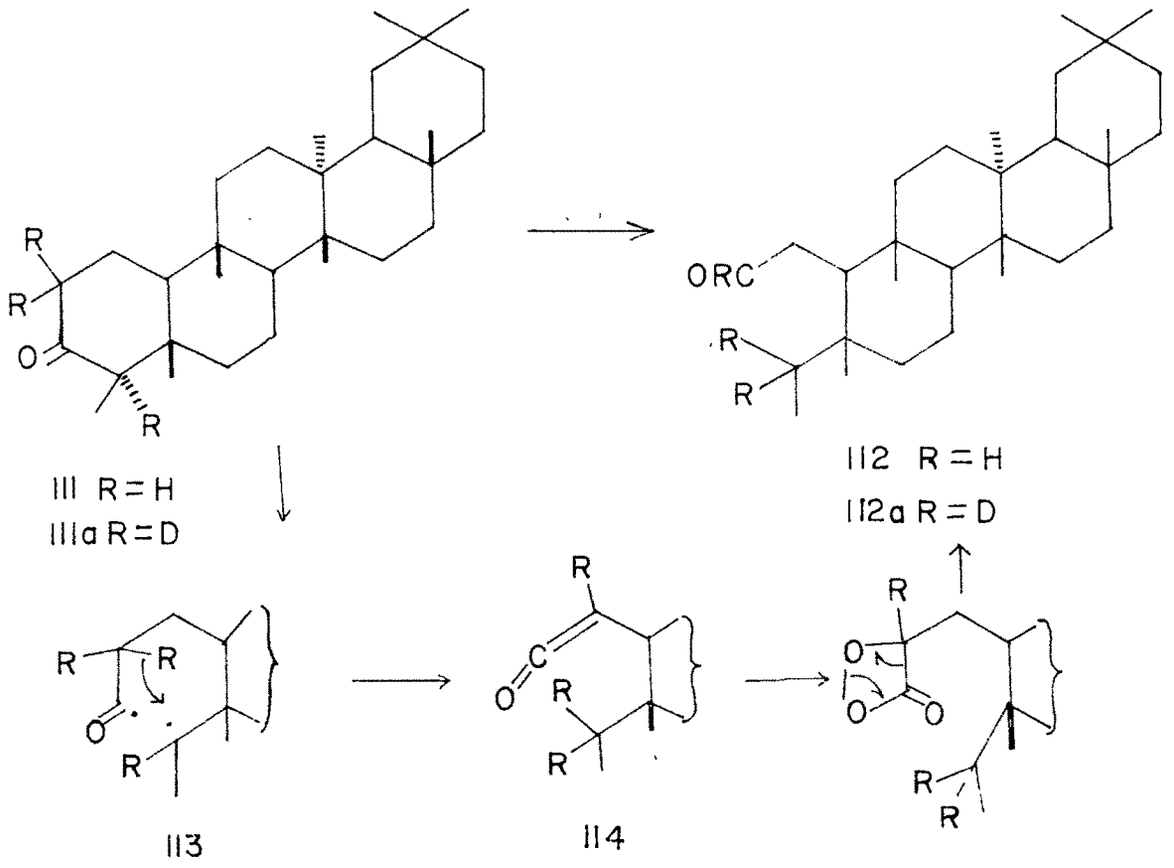



CHART XX: PHOTOREACTION OF FRIEDLIN

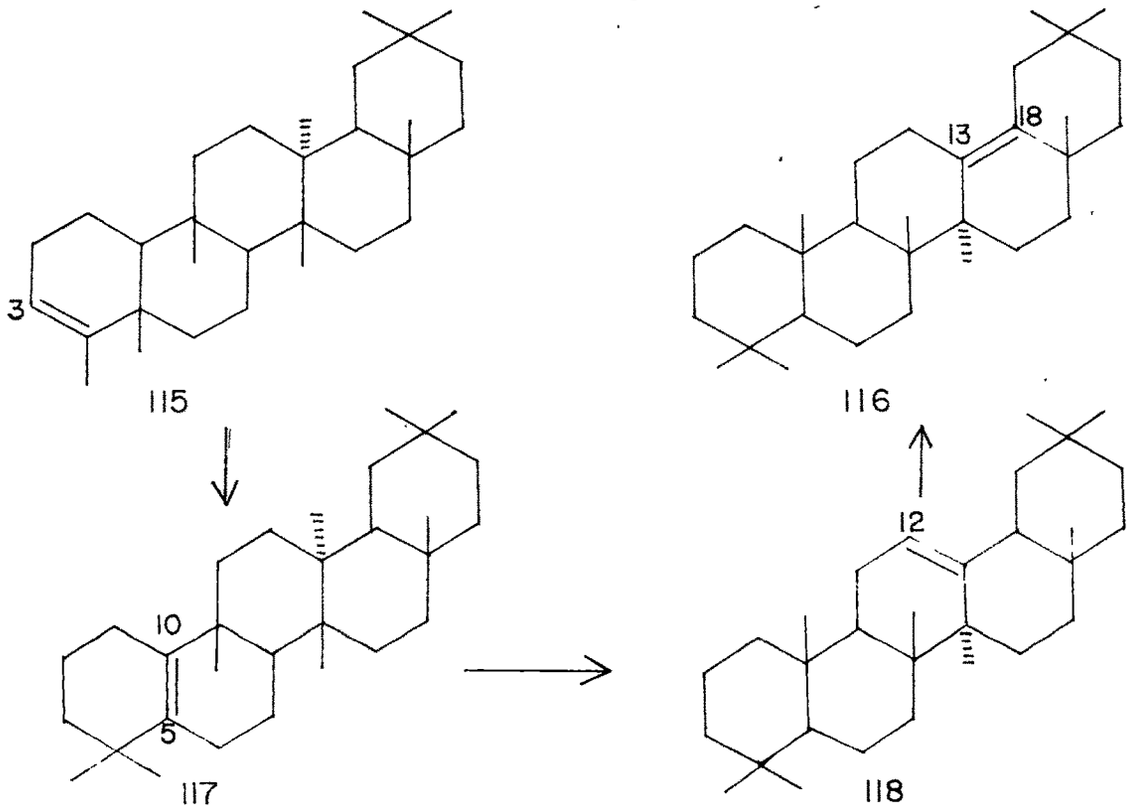



CHART XXI: FRIEDELENE — OLEANENE REARRANGEMENT

the formation of friedlin and $\Delta^5$-glutinone, the enzyme system involved must be able to compensate for energy deficit apparent in reverse rearrangement; $\Delta^{12}$-oleanene (118) $\longrightarrow$ $\Delta^{5(10)}$-glutinene[120-121] (117), (shown in Chart XXI).

REFERENCES


1. W.S. Johnson, Accounts Chem. Res. 1, 1 (1968)

2. For examples see:

   (a) G.L. Hodgson, D.F. MacSweeney and T. Money, J.C.S. Perkin I, 2113 (1973)

   (b) J.M. Greenwood, M.D. Solomon, J.D. Suther and T. Torre, J. Chem. Soc. 'C', 3004 (1968)

   (c) W.G. Dauben, J. Agr. Food. Chem. 22, 156 (1974)

   (d) A.P.S. Narula, J. Sc. Ind. Res. 35, 362 (1976).

3. E.S. Lewis, Technique of Chemistry, Wiley Interscience Publishers, Inc., New York (1974), Vol. VI, part 1.

4. S.L. Friess, E.S. Lewis and A. Weissberger in Technique of organic chemistry (Ed. A. Weissberger), Wiley Interscience Publishers Inc., New York (1961) Vol. VIII, Part 2 pp. 1407-1426.

5. V. Gold and D.P.N. Satchell, Quart. Rev. 9, 51 (1955).

6. A.A. Frost and R.G. Pearson, Kinetics & Mechanisms, 2nd Ed., Wiley Interscience Publishers Inc., New York (1961).

7. For examples see:

   (a) F.H. Westheimer, Chem. Rev. 61, 265 (1961)

   (b) K.B. Wiberg, Chem. Rev. 55, 713 (1955)

   (c) P. Lazzlo and Z. Welvart, Bull. Soc. Chim. Fr. 2412 (1966)

8. For Examples see:

   (a) C.J. Collins in Advances in Physical Organic Chemistry (Ed. V. Gold), Academic Press, London, (1964) vol. 2 pp. 3-91.

   (b) Ref. 4 pp. 1519-1548.

9. H. Budzikiewicz, C. Djerassi and D.H. William, Structure Elucidation of Natural Products by Mass spectroscopy, Holden-Day, San Franscisco (1964), Vol. I, pp 17-40

10. M. Fetizon and J.C. Gramain, Bull. Soc. Chim. Fr. 651 (1969).

11. L. Tokes and L.J. Throop in Organic Reactions in Steroid Chemistry (Eds. J. Fried and J.A. Edward), Van Nostrand Reinhold Co., New York (1972), vol. I, pp. 145-221.

12. For Examples see:

    (a) R.N. McCarty, Diss. Abstr. Ind. B33, 3558 (1973); Chem. Abstr. 78, 159889d (1973).

    (b) D.H. Bowen, C. Cloke and J. McMillan, J. Chem. Soc. Perkin I, 378 (1975).

    (c) C.G. Joshi and E.W. Warnhaff, J. Org. Chem. 37, 2383 (1972)

13. For examples see:

    (a) J.A. Berson in Molecular Rearrangements (Ed. P. de Mayo), Wiley Interscience Publishers, New York (1963), Part I, pp 111-233.

    (b) J.F. King and P. de. Mayo, Molecular Rearrangement, Wiley Interscience Publishers, New York (1964), part 2 pp 771-841.

    (c) A. Chatterjee, A.K. Dey and T. Chakroborthy, J. Sci. Ind. Res. (India), 33, 493 (1974).

14. J.D. Roberts and R.H. Mazur, J. Am. Chem. Soc. 73, 3542 (1951).

15. S. Winstein and D. Trifan, J. Am. Chem. Soc. 74, 1147, 1154 (1952).

16. H. Meerwein and K.V. Emster, Chem. Ber. 55, 2500 (1922).

17. T.P. Newell, E. de Salas and C.L. Wilson, J. Chem. Soc. 1188 (1939).

18. F. Brown, E.D. Hughes, C.K. Ingold and J.F. Smith, Nature 168, 65 (1951)

19. S. Winstein et al. J. Am. Chem. Soc. 87, 376, 378, 379 (1965).

20. a. H.C. Brown, Tetrahedron 32, 179 (1976) and ref. cited therein.

b. G.A. Olah, Accounts Chem. Res. 9, 41 (1976)

21. P.D. Bartlett, Nonclassical Ions, W.A. Benzamin Press, New York (1965).

22. G.D. Sargent, Quart. Rev. 20, 301 (1966).

23. H.C. Brown, The Transition States, Spec. Publs. Chem. Soc. London (1962) pp 140-158 and 174-178.

24. H.C. Brown and K.T. Liu, J. Am. Chem. Soc. 89, 466 (1967).

25. H.C. Brown and K.T. Liu J. Am. Chem. Soc. 97, 600 (1975)

26. H.C. Brown and K.T. Liu, J. Am. Chem. Soc. 97 2469 (1975).

27. H.C. Brown and J.H. Kawakami, J. Am. Chem. Soc. 97, 5521 (1975).

28. J.K. Stille and R.D. Hughes, J. Org. Chem. 36, 340 (1971).

29. J.D. Roberts and C.C. Lee, J. Am. Chem. Soc. 73, 5009 (1951).

30. J.D. Roberts, C.C. Lee and W.H. Saunders, J. Am. Chem. Soc. 76, 4501 (1954).

31. A. Colter, E.C. Friedrich, N.J. Holness and S. Winstein, J. Am. Chem. Soc. 87, 378 (1965).

32. J.A. Berson and P.W. Grub, J. Am. Chem. Soc. 87, 4017 (1965).

33. C.J. Collins and B.M. Benjamin, J. Am. Chem. Soc. 89, 1652 (1967).

34. C.J. Collins and B.M. Benjamin, J. Am. Chem. Soc. 88, 1556, 1558 (1966).

35. A.W. Bushell and P. Wilder Jr. J. Am. Chem. Soc. 89, 5721 (1967).

36. C.J. Collins, Z.K. Cheema, R.G. Werth and B.M. Benjamin J. Am. Chem. Soc. 86, 4913 (1964).

37. D.C. Kleinfelter and T.E. Dye, J. Am. Chem. Soc. 88, 3174 (1966).

38. P. Wilder Jr. and W.C. Hsieh, J. Org. Chem. 36, 2552 (1971).

39. J. Wolinsky, D.R. Dimmel and T.W. Gibson, J. Org. Chem. 32, 2087 (1967).

40. D.R. Dimmel and W.Y. Fu, J. Org. Chem. 38, 3778 (1973).

41. D.R. Dimmel and W.Y. Fu, J. Org. Chem. 38, 3782 (1973).

42. A. Nickon and J.L. Lambert, J. Am. Chem. Soc. 84, 4604 (1962).

43. D.H. Hunter, A.L. Johnson, J.B. Stothers, A. Nickon, J.L. Lambert and D.F. Corey, J. Am. Chem. Soc. 94, 8582 (1972).

44. A.L. Johnson, J.B. Stothers and C.J. Tan, Can. J. Chem. 53, 212 (1975).

45. A. Nickon, J.L. Lambert, J.E. Oliver, D.F. Corey and J. Morgan, J. Am. Chem. Soc. 98, 2593 (1976).

46. K.W. Turnbull, J.J. Gould and D. Arigoni, Chem. Commn. 597 (1972).

47. W.R. Bamford and T.S. Stevens, J. Chem. Soc., 4735 (1952).

48. J.W. Powell and M.C. Whiting, Tetrahedron 7, 305 (1959).

49. R.H. Shapiro, Tetrahedron Lett., 3407 (1966).

50. R.H. Shapiro, J.H. Duncan and J.C. Clopton, J. Am. Chem. Soc. 89, 1442 (1967); preliminary commn. J. Am. Chem. Soc. 89, 471 (1967)

51. W. Reusch, M.W. Carlo and L. Traynor, J. Org. Chem. 26, 1711 (1961).

52. R.H. Shapiro and M.J. Heath, J. Am. Chem. Soc. 89, 5735 (1967).

53. W.L. Meyer, A.P. Lobo and R.N. McCarty, J. Org. Chem. 32, 1754 (1967).

54. R.F. Hig and L. Woringer, Annalen 227, 1 (1885).

55. A. Lapworth and W.H. Leuton, J. Chem. Soc. 79, 1284 (1901).

56. W.L. Meyer, A.P. Lobo and E.T. Marguis, J. Org. Chem. 30, 181 (1965).

57. G. Buchi and I.M. Goldman, J. Am. Chem. Soc. 79, 4741 (1957).

58. J. Meinwald and R.A. Schneider, J. Am. Chem. Soc. 87, 5218 (1965).

59. J. Meinwald, R.A. Schneider, and A.F. Thomas, J. Am. Chem. Soc. 89, 70 (1967).

60. G. Quinkert, Angew. Chem. 77, 229 (1965).

61. J.J. Hurst and Whitham, J. Chem. Soc., 2864 (1964).

62. W. F. Erman, J. Am. Chem. Soc. 89, 3828 (1967).

63. G.W. Shaffer and M. Pesaro, J. Org. Chem. 39, 2489 (1974).

64. For review see (a) H.M.R. Hoffman, Angew. Chem. Int. Ed. 8, 556 (1969), (b) E.C. Keung and H. Alper, J. Chem. Ed. 49, 97 (1972).

65. R.T. Arnold and J.S. Showell, J. Am. Chem. Soc. 79, 419 (1957).

66. R.K. Hill, J.W. Morgan, R.V. Shetty and M.E. Synerhold, J. Am. Chem. Soc. 96, 4201 (1974).

67. V. Garsky, D.F. Koster and R.T. Arnold, J. Am. Chem. Soc. 96, 4209 (1974).

68. J.M. Coxon, R.P. Garland and M.P. Hartshorn, Chem. Comm. 1709 (1970).

69. J.M. Coxon, R.P. Garland and M.P. Hartshorn, Aust. J. Chem. 25, 947 (1972).

70. K. Dietrich and H. Musso, Ber. 107, 731 (1974).

71. W. von E. Doering and J.B. Lambert, Tetrahedron 19, 1989 (1963).

72. W. von E. Doering and W.R. Roth, Angew. Chem. Int. Ed. 2, 115 (1963).

73. W. von. E. Doering and E.K.G. Schmidt, Tetrahedron 27, 2005 (1971).

74. G.W. Dauben, J.P. Hubbel and N.D. Vietmeger, J. Org. Chem. 40, 479 (1975).

75. Y. Naha and Y. Hirose, Chem. Lett. 133, 727 (1973).

76. D. Baines, J. Forvester and W. Parker, J.C.S. Perkin I., 1598 (1974).

77. A. Nickon, T. Iwadere, F.J. McGuire, J.R. Mahajan, S.A. Narang and B. Umezawa, J. Am. Chem. Soc. 92, 1688 (1970).

78. cf. G. Mehta and B.P. Singh, Tetrahed. Lett., 3961 (1975).

79. Y. Ashima, and T. Tsukamoto, J. Pharm. Soc. Japan 484, 463 (1922); 491, 1202 (1929).

80. Sukh Dev, Curr. Science (India) 20, 296 (1951).

81. J.B. Stother, C.T. Tan. A. Nickon, F. Huang, R. Sridhar, and R. Weglein, J. Am. Chem. Soc. 94, 8581 (1972).

82. A. Aebi, D.H.R. Barton, A.W. Burgstahler and A.S. Landrey, J. Chem. Soc., 4629 (1954).

83. W. Parker, R.A. Raphael and J.R. Robert, J. Chem. Soc.'C', 2634 (1969).

84. A. Nickon, F.Y. Edamma, T. Ewadare, K. Matsuo, F.J. McGuire and J.S. Roberts, J. American Chem. Soc. 90, 4196 (1968).

85. F.Y. Edamura and A. Nickon, J. Org. Chem. 35, 1509 (1970).

86. C. Enzell, Acta, Chem. Scand. 16, 1553 (1962).

87. W.G. Dauben, and E.I. Aoyagi, Tetrahed. Lett. 2675 (1964).

88. W.G. Dauben, L.E. Friedrich, P. Oberhausli and E.I. Aoyagi, J. Org. Chem. 37, 9 (1972).

89. H.U. Daeniker, A.R. Hochstetler, K. Kaiser and G.C. Kitchens, J. Org. Chem. 37, 1 (1972).

90. K.B. Wiberg and G. Szeimies, J. Am. Chem. Soc. 90, 4195 (1968); 92, 571 (1970).

91. W.G. Dauben and E.I. Aoyagi, Tetrahed. Lett., 1735 (1967).

92. W.G. Dauben and E.I. Aoyagi, Tetrahedron 26, 1249 (1972).

93. Z. Majerski and P. von. R. Schleyer, J. Am. Chem. Soc. 93, 665 (1971).

94. Y. Hikino and P.de Mayo, Chem. Comm., 550 (1965).

95. J. Tadanier, J. Org. Chem. 31, 2124 (1966).

96. S.W. Palletier, S. Nakamura and Y. Simizy, Chem. Comm., 727 (1966).

97. W.G. Dauben and P. Oberhanski, J. Org. Chem. 31, 315 (1966).

98. B. Nann, O. Gravel, R. Schorta, H. Wehrli, K. Schaffner and Jeger, Helv. Chim. Acta. 46, 2473 (1963).

99. B. Nann, H. Wehrli, K. Schaffner and O. Jeger, Helv. Chim. Acta. 48, 1680 (1965).

100. S. Domb and K. Schaffner, Helv. Chim. Acta 53, 1765 (1970).

101. K. Ishikawa and T.B.H. McMurry, J.C.S. Perkin I. 914 (1973).

102. D.S.R. East, K. Ishikawa and T.B.H. McMurry, J.C.S. Perkin I., 2563 (1973).

103. D.S.R. East, T.B.H. McMurry and R.R. Talekar, J.C.S.Perkin I., 433 (1976).

104. T.B.H. McMurry and R.R. Talekar, J.C.S. Perkin I, 442 (1976).

105. R.D.H. Murray, R.W. Mills and J.M. Young, Tetrahed. Lett., 2393 (1971); and also see: A. Martin and R.D.H. Murray, J. Chem. Soc.'C', 2023 (1970); 2529 (1968).

106. A.H. Kapadi and Sukh Dev, Tetrahed. Lett., 1255 (1965).

107. A. Yoshikoshi, M. Mitandani and Y. Kitahara, Tetrahedron 23, 1175 (1967).

108. R.D.H. Murray, R.W. Mills, A.J. McAlees and R. McCrindle, Tetrahedron 30, 3399 (1974).

109. E. Wenkert and Z. Kumazawa, Chem. Comm., 140 (1968).

110. O.E. Edward and R.S. Rosich, Can. J. Chem. 46, 1113 (1968).

111. J. Fourrey, J. Polonsky and E. Wenkert, Chem. Comm., 714 (1969).

112. S. Borry and C. Asselinew, Bull. Soc. Chim. Fr., 341 (1959).

113. L. Ruzicka, Experentia 9, 357 (1953).

114. J.D. Conolly, R. McCrindle, R.D.H. Murray and K.H. Overton, J. Chem. Soc.'C', 273 (1966).

115. T. McCreadie and K.H. Overton, Chem. Comm., 288 (1968).

116. O.E. Edward and B.S. Mootoo, Can. J. Chem., 47, 1189 (1969).

117. R. Stevenson, T. Tsuyuki, R. Aoyagi and T. Takahashi, Bull. Chem. Soc. Japan, 44, 2567 (1971).

118. R. Aoyagi, T. Tsuryuki, T. Takahashi and R. Stevenson, Tetrahed. Lett.,3397 (1972).

119. R.M. Coates, Tetrahed. Lett., 4143 (1967).

120. E.J. Corey and J.J. Ursprung, J. Am. Chem. Soc. 78, 5041 (1956).

121. L. Ruzicka, Proc. Chem. Soc., 341 (1959).