Base-catalysed isomerisations of terpenes

By James Verghese, Synthite Industrial Chemicals Private Ltd. Cochin, India

The panorama of base-catalysed isomerisations of terpenes is an important part of aroma chemistry. Major contributions in this area are presented here under sections on hydrocarbons, alcohols, aldehydes, ketones, acids, esters, and epoxides.

Hydrocarbons

p-Menthenes. Pines and Eschinazi introduced sodium-organosodium catalysts, for example sodium-'benzylsodium' catalyst (prepared by treating an excess of sodium in toluene with o-chlorotoluene) for isomerising the title compounds.[1] One of their main findings is that when (+)-p-menth-1-ene (1), trans-p-menth-2-ene (2) or p-menth-3-ene (3) is refluxed at 168-175° for 20-22 hrs with the catalyst, the isomerisate is an equilibrium mixture of (3) (63%), (1) (32%), and p-menth-8(9)-ene (4) (5%). The rate of racemisation of (+)-(1) is relatively faster than that of its rate of isomerisation and (+)-trans-(2) reorganised to (+)-(1). There is no formation of p-cymene (5). The mechanism proposed involves intermediate carbanions.

More recently, Ferro and Naves studied the isomerisation of (1), (3), (4) (cis and trans) and p-menth-4(8)-ene (6) with sodium-organosodium catalyst (catalyst S, prepared according to Pines and Eschinazi,[1] xylene replacing toluene) and analysed (by GC) the products formed at reflux temperatures.[2] Under these experimental conditions, there is no equilibrium of the p-menthenes. Thus, (3) is obtained from (+)-(1) and cis-(4) in 52.1 and 78.6% in 48 and 6 hrs respectively; trans-(4), however, is less reactive than its stereoisomer.

Further, the behaviour of the p-menthenes toward n-lithioethylenediamine (catalyst L) at 50° and potassium tert-butoxide (t-BuOK) in dimethylsulfoxide (DMSO) (catalyst B) at 100° was evaluated. By a 4 hr treatment with catalyst L, (+)-(1) only a small amount of the racemate resulted and with catalyst B, the racemisation rate increases to 16% in 2 hrs without isomerisation. Reaction of cis-(4) and trans-(4) with catalyst L furnishes (6) in 76.9 and 48.6% (in 4 hrs) and with catalyst B, 77.0% (in 8 hrs) and 64.3% (beyond 12 hrs) respectively. Use of catalyst S is recommended for the preparation of (3) from (1) and of catalysts L and S to obtain (6) from (4) (cis and trans).[2]

Kinetically controlled regrouping of p-menthenes with calcium amide catalyst in the liquid phase gives equivalent mixtures of isomers with exo and endocyclic double bonds.[3]

o-Menthenes. Rearrangements similar to p-menthenes are observed in the interaction of the sister o-isomers with calcium amide catalyst.[3]

p-Menthadienes. Investigations on base-catalysed rearrangements of this family of hydrocarbons were reported by Pines and Eschinazi.[4] On refluxing (+)-limonene (7) with sodium-'benzylsodium' or sodium hydride catalyst, rapid racemisation occurs with evolution of hydrogen, providing p-cymene (5). Interruption of the reaction when the optical rotation drops to ~20% gives a catalysate that includes 20% of (+)-(7), 50% of (±)-(7) and 20% of a mixture consisting of p-mentha-2,4(8)- and p-mentha-3,8(9)-diene (8) and (9) in the approximate ratio 4:1 and 1% of (5). Without a promoter but in the presence of sodium at reflux temperature, (+)-(7) only undergoes racemisation without aromatisation. With the catalyst, the intermediates (8) and (9) are reversibly isomerised; on the other hand, (−)-α-phellandrene (10) loses optical activity and gets dehydrogenated to (5) with no signs of conjugation to (8) and (9). Invoking carbanions these changes have been explained.

Swiss investigators have also tracked—in the same way as p-menthenes—the transformations of p-menthadienes.[2] When reacted for 1 hr with catalyst L at 50°, (+)-(7) gives an equilibrium mixture of (8), (9), γ-terpinene (13) and α-terpinene (14) in the proportion 14:50:30:3 with increasing conversion to (5), depending on the reaction time. On processing with catalyst B, the substrate is practically effaced in 5 hrs at 100° and the equilibrium is realised. Under refluxing conditions, catalyst S generates (8) and (9) in the proportion 11:1.

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Terpinolene (11), isolimonene (p-mentha-2,8(9)-diene) (12) and γ-terpinene (13), with the exception made for the latter in the case of catalyst S, respond in a similar manner. With catalyst L, the equilibrium of (11), (12) and (13) is attained in 30 min and with catalyst B, in 15 min. Complete isomerisation is achieved in 6 hrs with catalyst S, leading to (8) and (9) in the approximate proportion 11:1. As against these, with catalyst S, (13) changes completely to p-cymene (5) in 15 hrs.

The study with the conjugated dienes (8), (9), (14), and p-mentha-2,4-diene (15) has led to interesting results. Equilibrium between (8), (9), and (14) is attained by the action of catalysts L and B. Divergent behaviour is displayed with catalyst S; the cyclic dienes (14) and (15) only give (5) (100 and 90% in 24 hrs); (8) equilibrates with (9) in the approximate ratio 11:1. A modified carbanion mechanism has been advanced to explain this reaction.

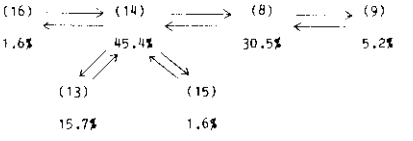
Using Pines and Eschinazi catalyst, isoterpinolene (8) has been synthesised from (+)-limonene (7).[5]

A kinetic study of the action of t-BuOK-DMSO system on (±)-limonene indicates that the initial products of isomerisation is a 5:3:1 mixture of (8), (13), and (14) and that the pseudo-first-order rate constant at 55° is 4.5×10^{-6} sec^{-1}. Under the experimental conditions, (8) and (14) afford the same products in 30 min. Hence the slow step in the isomerisation is the migration of the double bond to the exo position.

From the above synthetic mixture derived from (±)-limonene, by precise fractionation, (8) is recoverable in 11% yield. Since the sister isomers can also be reverted to this mixture and recycled, this is an elegant method for the large-scale preparation of this unusual hydrocarbon.

Whereas (±)-p-mentha-2,4(8)diene (8) is convertible to (±)-menthol isomers, it is the (+)-(8) that is higher priced, being a possible precursor in the synthesis of (−)-menthol.[7,8] Technically, a facile route to this hydrocarbon is from (+)-isolimonene (12) by contact with t-BuOk-DMSO combination at room temperature.[7]

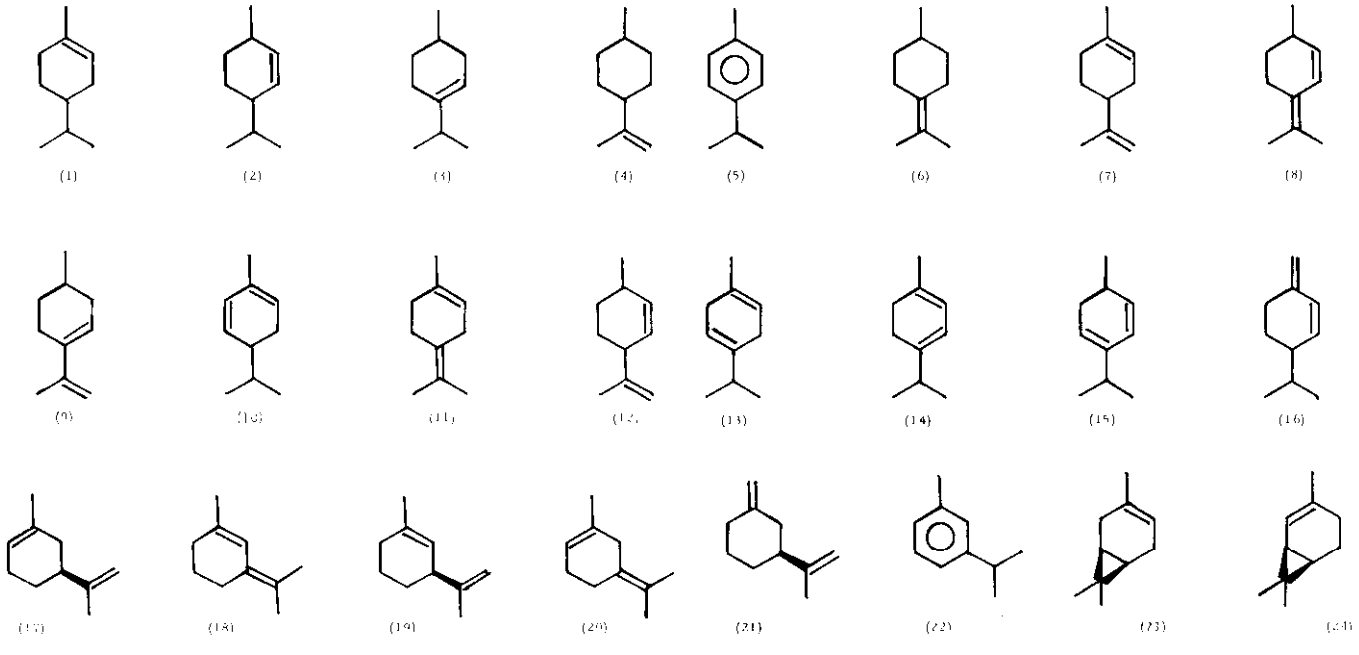
In the rearrangement of p-menthadienes catalysed by t-BuOK-DMSO at 55°, only three constituents of the isomerisate have been identified. A fuller picture of the equilibrium composition, conditions for achieving it with < 10% of side reactions, and rate constants for many of the possible interconversions of the isomers have emerged from the work of Bates and coworkers.[9] Starting from (9), (10), (13), and (14) and a 3:1 mixture of (10) and (16), the samples equilibrated with potassium-tert-butoxide in butanol exhibited identical PMR and GLC patterns. The percentages of the six isomers with an absolute value of rate constant $4.5 \pm 0.5 \times 10^{-2}$ sec^{-1} are listed in the following scheme. It is assumed that all interconversions proceed via pentadienyl carbanion intermediates.



Equilibrium percentages of p-menthadienes

Terpinolene (11) rearranges in the presence of N-lithioethylene-diamine at 100° mainly to isoterpinolene (8) accompanied by (5), (13), and (14); on the other hand, dipentene (7) gives (5), (8), and (14).[10]

Finally, an interesting study has been reported on the transformations of terpinolene (11), (−)-limonene (7) and α-terpinene (14) on a weakly basic catalyst, CaO, by a pulse method.[11] Here the main trend is the rearrangement to (8), (9), (13), and (14) with concomitant aromatisation to p-cymene (5). Thermodynamic equilibrium is approached with respect to the propor-



tions of the terpinenes generated. It is assumed that the reaction intermediates are adsorbed ionic species that can be taken to behave like carbanions, and on this basis a mechanism has been advanced.

m-Menthadienes. Base-catalysed reactions of this series of hydrocarbons were relatively recently reported.

On treatment with N-lithioethylenediamine at 50-80°, m-mentha-6,8-diene (17) gives mainly m-mentha-1,3(8)- diene (18) (≥76.2%) with lesser amounts of m-mentha-1-8-diene (19), m-mentha-6, 3(8)-diene (20) m-mentha-1(7),8-diene (21), and m-cymene (22); at 100° aromatisation is complete.[12] By reaction with t-BuOK-DMSO system at 82±2° for 3 hrs, sylvestrene (17) affords (18) (45.0%), (19) (3.0%), (20) (5.5%), and (21) (0.9%)13. With the same catalyst, the hydrocarbon (18) largely resists rearrangement *but the sister isomer (20) smoothly conjugates* to (18).[13]

(+)-Car-3-ene. Ohloff and coworkers accomplished the base-catalysed conversion of (+)-car-3-ene (23) to (+)-car-2-ene (24).[14] The reaction of (23) with N-lithioethylenediamine for 1 hr at 100° results in an equilibrium mixture of the 3- and 2-isomers in the ratio 3:2, accompanied by cymenes equivalent to 2%. From the catalysate, enriched (+)-car-2-ene (80%) is obtained by fractionation. Others have followed this trail.[7,15-18] Theoretical reasons have been advanced to account for the greater stability of the 3- over the 2-isomer.[16] From the equilibrium constant 1.50, the free energy difference is extracted as 240 cal/mol at 25°.[17]

A disadvantage of the above technique is the concurrent release of the cymenes.[16] However, under regulated conditions, use of t-BuOK-DMSO catalyst eliminates this defect and the reaction generates a clean equilibrium mixture consisting of 40% (+)-car-2-ene and 60% (+)-car-3-ene.[16]

While today more advanced and different syntheses for (−) menthol are used, patents granted to Booth[7] combined with that to Webb[8] are classics of the technical exploitation of (+)-car-3-ene for a (−)-menthol synthesis. The outstanding step in the chain of reactions is the rearrangement of the terpene to the 2-isomer. In general, basic catalysts recommended consist of strong bases, applied under conditions when carbanions of a hydrocarbon can be formed and these include simple or complex alkali metal alkyls, also strong bases such as alkali metal alkoxides, and alkali metal amides which are advantageously used in media that encourage the maturing of their basicity. Examples of the catalysts are activated sodium of the Pines type, sodium and/or potassium derivative of γ-picoline, t-BuOK in DMSO, N-lithioethylenediamine, and Na or K metal on Al_2O_3.

Here we may digress a little. Above 180°, in the presence of the basic catalyst, (+)-car-2-ene (24) decyclises to (+)-isolimonene (12) and the latter conjugates to (+)-p-mentha-2, 4(8)-diene (8), the pivotal hydrocarbon in a (−)-menthol synthesis. The next stage is the migration of the exo double bond of (8) to give an equilibrium mixture of α-terpinene (14)

(50%), γ-terpinene (13) (20%), isoterpinolene (8) (25%) and p-mentha-3, 8-diene (9) (5%). Finally the p-menthadienes get dehydrogenated to p-cymene (5).[7] For these reasons, the correct temperature and time must be chosen to terminate the reaction at the isoterpinolene stage. Catalysts which rearrange (+)-car-3-ene to (+)-car-2-ene will also perform this function.

Ferro and Naves[18] found that Ohloff's reaction[14] when conducted at 110° for 5 hrs gives an equilibrium mixture of (+)-car-3-ene (23) and (+)-car-2-ene (24) (55:45) with cymenes (12%); an 18 hr run augments aromatisation (20.4%). Also, the findings of Acharya and Brown[40] using t-BuOK-DMSO have been fully substantiated.

There are valuable data on the isomerisation of (+)-car-3-ene (23) over basic catalysts such as MgO, CaO, SrO_2, Y_2O_3, La_2O_3 and ZrO_2 by the pulse method.[19,20] The reaction has been tracked in detail over MgO (I) and MgO (II) and CaO (II) catalysts.[20] Rearrangement of (23) to (24) is the dominant change, but synchronised two-way decyclisation leads to α-terpinene (14) and m-mentha-1,5-diene 25) and further dehydrogenation to p-cymene (5) and m-cymene (22). From a tracer study with deuterium it is inferred that the double bond shift is most likely to proceed via II-allylic anion (26).

(+)-Car-2-ene. A study has established that the equilibration of (+)-car-2-ene (24) with t-BuOK-DMSO system gives as in the case of (+)-car-3-ene (23), a distribution of (+)-(23) (60%) and (+)-(24) (40%).[16]

α-Pinene. Economic conversion of α-pinene (27) to the less available β-pinene (28) has occupied several chemists since the β-isomer is an excellent substrate for the manufacture of resins and aroma chemicals.

α-Pinene is more stable than the β-variety.[21] This is contrary to the recent assertion,[22] as is shown by the heats of combustion[23]; thermodynamically, the transition from the α- to the β-isomer is also pronounced as unfavourable.[24]

H^+catalysed isomerisation of α-pinene gives the β-isomer.[25,26] Unfortunately, the poor yield of the desired hydrocarbon coupled with dissipating conversions to other hydrocarbons render this route uneconomical.

Webb has developed a simple process for converting α-pinene to β-pinene by agitating with a solution of KOH in DMSO (NaOH and LiOH are also active) at a temperature of 110-225°.[27] A suitable weight ratio of KOH to DMSO is *ca* 1 to 4, but ratios of 4 to 1 and 1 to 25 have provided good conversions. The equilibrium between α- and β-pinenes is a mixture of *ca* 95% α- and 5% β-pinene, the exact equilibrium depending on temperature. At the end of the reaction, it suffices to separate the lower DMSO-KOH phase and fractionate the pinenes.

Another route comprises contacting α-pinene with high surface elemental sodium.[28-30,33] Thus, operating the reaction at 200° for 4 hrs, pure α-pinene modifies to 4.5% β-pinene, 3% limonene and the rest α-pinene.[28,33] In the case of "sour" α-pinene, sodium performs the twin function of "sweetener" and isomerising catalyst.[29,33]

Following is a discussion of the rearrangement of α-pinene to β-pinene with t-BuOK.

Defer has patented the isomerisation of α- to β-pinene by homogenous catalysis with t-BuOK-DMSO system.[28,30] On maintaining equimolecular quantities of α-pinene with t-BuOK in DMSO for 5 hrs at 65-70°, the reaction mixture analysed for 3.5% β-pinene; the balance α-pinene is free of other isomerisation and disproportionation products. Utilisation of this system in establishing the equilibrium between the pair of pinenes has been further confirmed.[18,31]

Mere refluxing of α-pinene with t-BuOK (in the ratio 3:1) at 165-175° for 2-40 hrs apparently gives β-pinene but the reaction is vitiated by extensive resinification.[32]

L. Givaudan & Cie, S. A. has patented the isomerisation of α- to β-pinene with an organo-alkali metal catalyst, viz. amylsodium, activated by 1-chloropentane[34]; the rearrangement has also been effected with Pines-type catalyst.[18]

Soviet chemists introduced calcium amide to isomerise (27) to (28) with negligible formation of by-products.[32,35] Only 2% of the b-isomer is present in the equilibrium concentration.[32] Thus, in the vapour phase, (27) is rearranged to (28) over the catalyst at 170-220°. In a different technique, the b-isomer is prepared from (27) in high yield (over 30% in 120 hrs) by conducting the isomerisation in a flask fitted with a continuous rectifying column to tap off (28) and to return (27) for reprocessing.

In contrast to the findings of Joshi et al,[36] reaction of α-pinene and N-lithioethylenediamine for 5 hrs at 110° has afforded 3-4% of β-pinene. The strongly basic character and high catalytic activity of evacuated MgO, CaO, SrO and BaO induces the rearrangement of α-pinene to β-pinene.[37] Thus, stirring of (27) for 1 hr with CaO prepared by calcining the guaranteed reagent in *vacua* at various temperatures showed that the catalytic activity of CaO begins to appear when the catalyst is evacuated at 500° and attains the optimum efficiency at *ca* 600° and thereafter decreases on evacuation at higher temperatures. The equilibrium constant of (27) to (28) is *ca* 0.03. Compared to CaO, the activity of MgO or BaO is very or slightly low respectively. BaO evacuated at 1100-1300° displays the maximum activity. The selectiveness of MgO and BaO are almost on a par with that of CaO and SrO.

β-Pinene. The alkaline earth metal oxides which we considered just now can also rearrange β-pinene to α-pinene. Of singular interest is the fact that β-pinene is converted almost completely to the equilibrium value of α-pinene over SrO evacuated at 900-1100° at room temperature in 15 min. Such distinguished activity and selectivity are apparently unheard of with any heterogeneous catalyst.[37] In fact, in

homogenous catalysis, using t-BuOK-DMSO combination at 65°, the half-period of the reaction protracted to several hours.[31]

Quantitative rearrangement of β-pinene to α-pinene has been accomplished with N-lithioethylendiamine.[36]

Recently, potassium-3-aminopropylamine, KNH $(CH_2)_3NH_2H_2N(CH_2)_3NH_2$, has been introduced for the isomerisation of (−)-β-pinene to give 95% (−)-α-pinene of optical purity 98.7%.[38]

Kirkpatrick has achieved the isomerisation of α- and β-pinenes to dipentene (7) without formation of p-menthadienes, notably α-terpinene (14), utilising a dissolved water-soluble inorganic base catalyst or a dissolved organic base catalyst.[39] Catalysts that are especially desirable in carrying out the process are sodium hydroxide, potassium hydroxide, potassium carbonate, sodium carbonate, potassium silicate, trisodium-phosphate, sodium sulphate, sodium silicate, potassium sulphate, cesium hydroxide, rubidium hydroxide, and so forth. Organic bases such as a tetramethyl ammonium hydroxide, guanidinium hydroxide, piperidinium hydroxide, ammonium hydroxide, triethanol amine, diamyl amine, triamyl amine, aniline, and so forth are also recommended.

Thus, α-pinene (100 parts) and 1% aq. sodium hydroxide (100 parts) are agitated in silver-lined auto clave for a period of 2 hrs at a temperature of 250° to give a steam volatile material which on fractionation afforded 28.15 parts of pure dipentene and the intermediate cut (29.7 parts), boiling below dipentene and above α-pinene, on further fractionation yielded 55% dipentene.

In another example, a mixture of β-pinene (660 parts), distilled water (750 parts) and diamyl amine (15 parts) is agitated in a silver-lined autoclave for 16 min at 280°. Usual workup afforded a steam distillate which included 23% dipentene (b.p. 176-177°). Similar runs on the lines indicated above for α- and β-pinenes are listed in Table I.

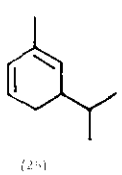
Table I. Rearrangement of α- and β-pinenes to dipentene

Terpene*	Catalyst*	Temperature °C	Time min	% Dipentene recovered
α-Pinene	1% aq. Na_3PO_4	250	120	40
α-Pinene	1% aq. diamylamine	260	30	30
β-Pinene	1.66% aq. triethanol amine	280	15	35

* 100 parts

(+)-Sabinene. Reagents that induce rearrangements in the carane and pinane systems (see above) serve (+)-sabinene (29) also.

Overnight stirring of (+)-(29) with N-lithioethylenediamine at room temperature gives a mix-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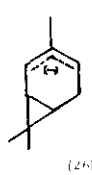
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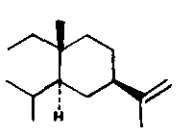
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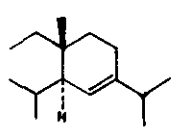
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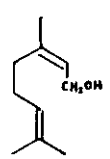
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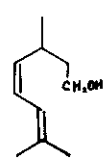
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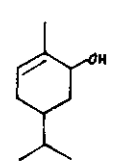
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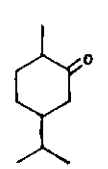
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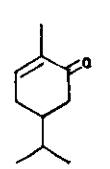
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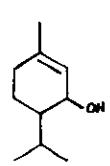
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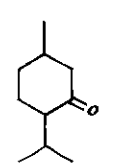
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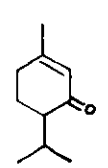
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ture of (−)-α-thujene (30) (68%), (+)-sabinene (7%) admixed with p-cymene (5) (25%).[40] On the other hand, operating at 50°, a 5 hr processing furnishes a catalysate consisting of (30), (29) and (5) in 89.0, 5.3 and 2.5% respectively.[18]

A Pines-type catalyst is less active, requiring 50 hrs refluxing to deliver a mixture of (30) (60.7%) and (29) (42.7%).

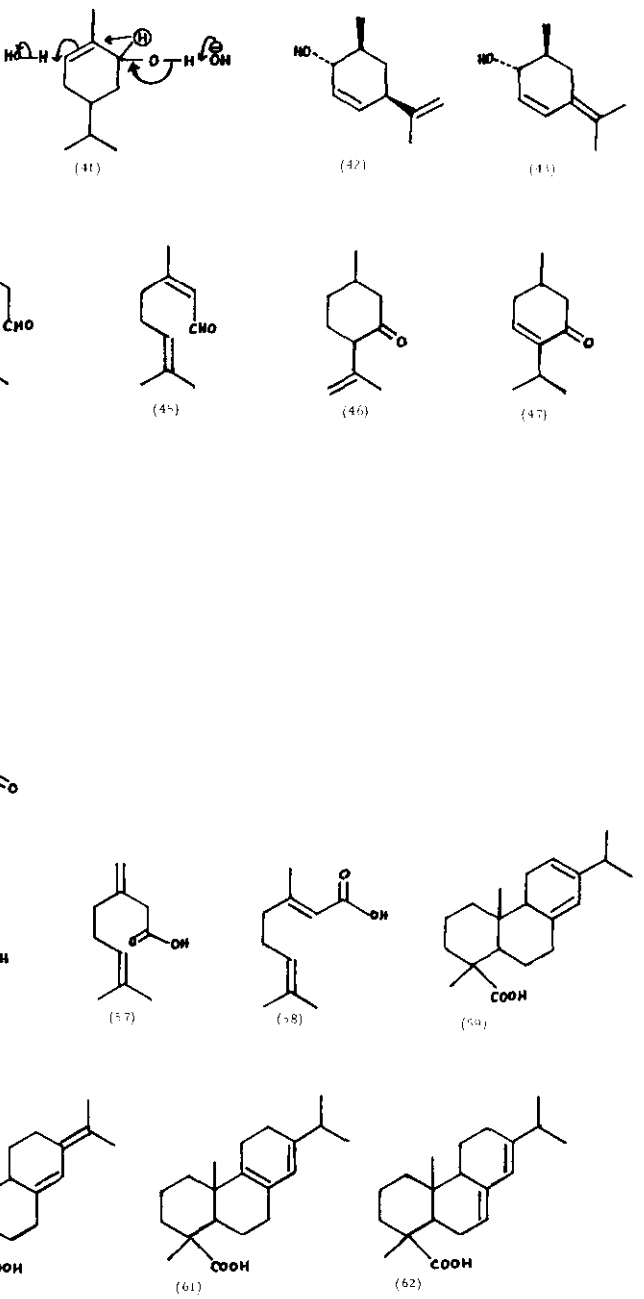
t-BuOK-DMSO system is the most outstanding, isomerising (+)-(29) by a 1 hr processing at 90° to give an equilibrium mixture of 91% (−)-(30) and 9% (+)-(29)[40]; the same result is achieved in 1 hr at 100°.[18] This rearrangement provides a viable synthetic route to (−)-α-thujene from readily available (+)-sabinene.[40]

Tetrahydroelemene. On exposure to N-lithioethylenediamine, the double bond in tetrahydroelemene (31) migrates to give the endocyclic olefine (32).[36]

Alcohols

Not many cases are known of the base-catalysed isomerisation of terpene alcohols. An interesting approach is that of geraniol (33) to the conjugated diene alcohol (34) on refluxing with N-lithioethylenediamine.[41]

Isomerisation of α, β-unsaturated alcohols of the p-series to ketones on distillation with powdered KOH is a more recent contribution.[42] Thus, carvotanacetol (35) rearranges to carvomenthones (36);



carvotanacetone (37) is also formed. Likewise, piperitol (38) yields menthone (39) and piperitone (40). It is believed that (36) arises directly by the concerted mechanism depicted in (41); the unsaturated ketone (37) is ejected by premature termination of the concerted process. A similar mechanism accommodates the changes observed in the alcohol (38).

In the m-series, (−)-cis-m-mentha-4, 8(9)-dien-trans-6-ol (42) gives (−)-m-mentha-4, 3(8)-dien-trans-6-ol (43) by gentle contact with ethylenediaminelithium.[43]

Aldehydes

An elegant isomerisation in this family is in the stereospecific synthesis of geranyl skeleton in which the final step is the conversion of the aldehyde (44) into geranial (45) with a catalytic amount of t-BuOK.[44]

Ketones

Partial isomerisation of isopulegone (46) to p-menth-3-en-5-one (47) occurs in the reaction with N-lithioethylene-diamine.[41]

Perfumery technology has provided delicate rearrangements of ketones having a carane ring. Thus, 4-acetyl-car-3-ene (49) and 2-acetyl-car-2-ene (51) are derived from 4-acetyl-car-2-ene (48) and 2-acetyl-car-3-ene (50) respectively using sodium methoxide-methanol catalyst.[45-48] For converting (48) to (49), sodium hydride-benzene is preferred.[48]

Deconjugation of (+)-verbenone and (−)-verbenone (52 and 53) with sodium hydride in THF to (+) and (−)-2(10)-pinen-4-ones (54 and 55) respectively giving access to optically active ipsdineol (56) is one of the base-catalysed processes recorded in terpene syntheses.[49]

Acids

Again, in the stereospecific synthesis of the geranyl structure, we come across an interesting example of a base-catalysed isomerisation of an acid, viz. that of (57) to geranic acid (58) with NaH/THF.[44]

Conjugated resin acids, namely levopimeric (59), neoabietic (60), and palustric acid (61) on treatment with excess of t-BuOK in DMSO at 189° for 2 min converge on abietic acid (62).[50] Most probably, the products are in equilibrium since abietic acid gives a spectrum of products as from the other three acids and approximately in the same proportions. Anion intermediates are postulated as precursors of the acids.

Esters

As an example, we may recall the rearrangements of car-2-ene-4α-carboxylic acid, methyl ester (63) to car-3-ene-4α-carboxylic acid, methyl ester (64) on exposure to methanolic sodium methoxide.[48]

Epoxides

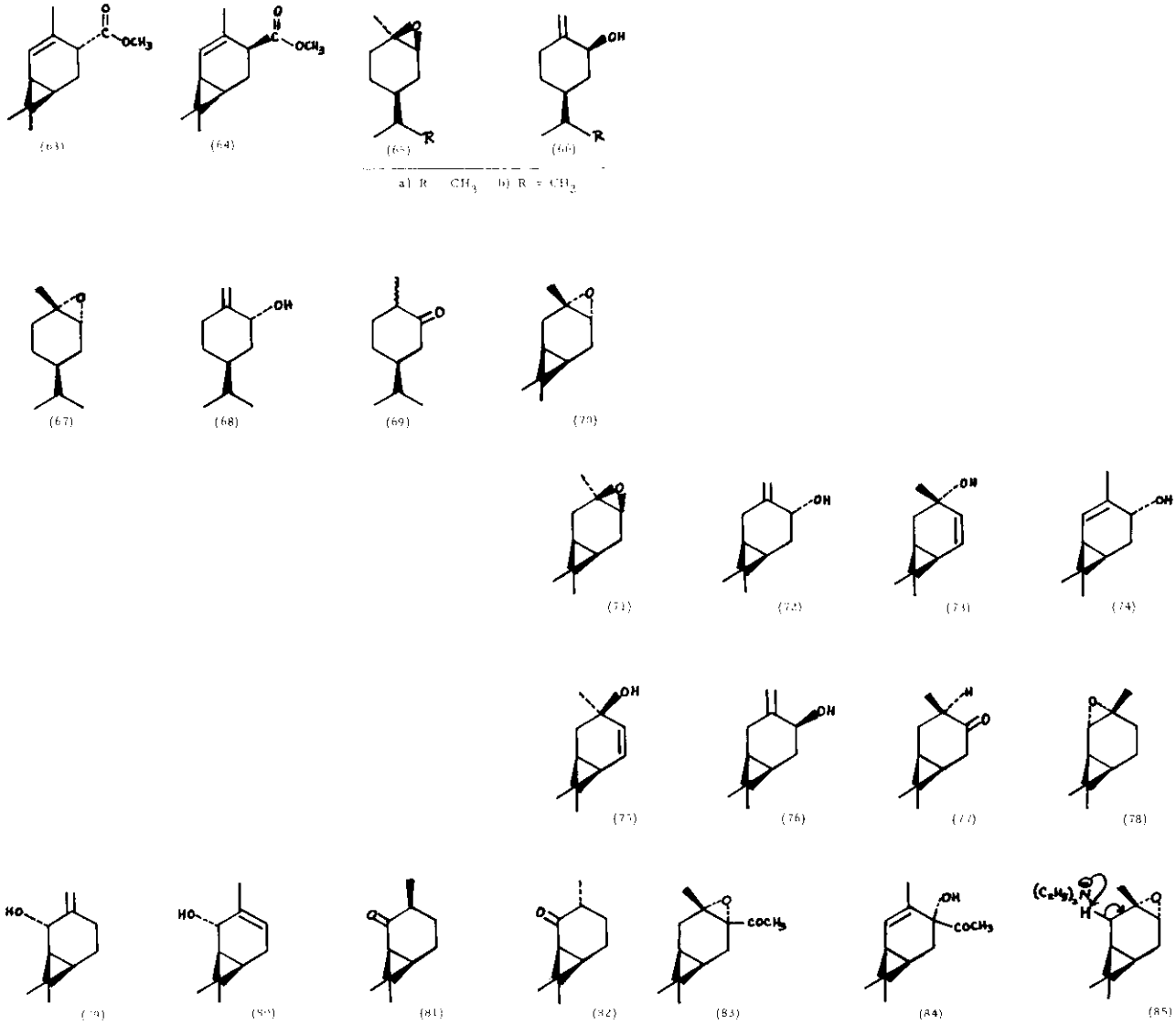
An extensive literature exists on base-catalysed regrouping of epoxides belonging to the p-menthane, carane and pinane systems. Cleavage of the oxirane ring of 1,2-epoxy-trans-p-menthane (65a) by powdered Na[51] and t-BuOK in aprotic solvents[52] results in cis-p-menth-1(7)-en-2-ol (66a).

Upon reaction with lithium amides—notably lithium diisopropylamide—limonene epoxides (65b and 67) furnish the following mixture: trans-isocarveol (68), trans-carveol (69), cis-isocarveol (66b) and dihydrocarvone (69).[53] Formation of cis-isocarveol is also noted in reaction of (65b) with finely divided Na.[54] Contact of the trans-epoxide (65b) with t-BuOK in aprotic solvents, on the other hand, affords the cis-alcohol (66b).[52]

Arbuzov's group[55,56(a)] explored the reaction of (+)-3, 4-epoxycarane (70) with lithiumdiethylamine and found that it leads to unsaturated alcohols which include (−)-trans-car-3(10)-en-4-ol (72). A rather sketchy mechanism has been suggested. The derivative (72) also originates from (70) by reaction with CH_3ONa-CH_3OH.[56(b)]

Using n-propyllithium, Polish workers have probed deep into the isomerisation of (70) and of (−)-3,4-epoxycarane (71).[57] Rearrangement of (70) provides (−)-trans-car-3(10)-en-4-ol (72), (−)-cis-car-4-en-3-ol (73) and (+)-trans-car-2-en-4-ol (74) in the ratio 8:59:33. For (71), reshuffling gives (−)-trans-car-4-en-3-ol (75), (+)-cis-car-3(10)-en-4-ol (76), and (+)-cis-caran-4-one [(+)-4-isocaranone] (77) in the proportion 36:34:30. The generation and the isomerisation of (77) ranks as the best route to this ketone. Interpretation has illumined the stereochemistry of these transformations.

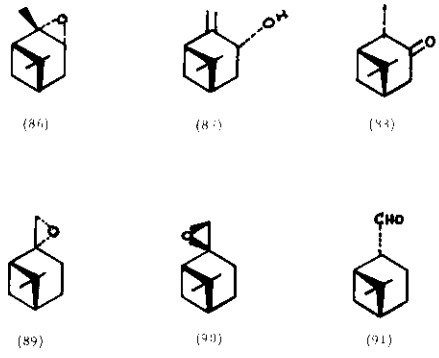
With t-BuOK in aprotic solvents, (70) gives (74) in 90% yield.[52] Joshi and Dev have demonstrated that Al_2O_3-NaOH matrix induces rearrangement of (70) to give essentially the alcohols (72) and (74).[58] Carenols (79) and (80) are the main products of isomerisation of 2α, 3α-epoxycarane (78) by lithiumdiethylamine; the



isomeric caranones (81) and (82) also formed, though to an insignificantly small extent.[59]

Another interesting study covers the isomerisation of 4β-acetyl-α-3,4-epoxycarane (83).[60] In the reaction with lithiumdiethylamine, it is easily regrouped into 4-acetyl-car-2-en-4-ol (84), according to the mechanism of β-elimination process followed by an E_2 reaction as depicted in (85).

Epoxides of the pinane series are also susceptible to base-catalysed modifications. On contact with CH_3ONa-CH_3OH, 2,3-epoxypinane (86) isomerises to trans-pinocarveol (87) and trans-pinocamphone (88). Substantial conversion to (87) is achieved with lithiumdiethylamine,[56(b),55,61,62] t-BuOK in DMF, DMSO or pyridine,[62,63] and Al_2O_3-NaOH.[58] This remarkably clean high yield reaction, particularly with lithiumdiethylamine, has some preparative value.[64] This rearrangement of 2,10-epoxypinanes (89 and 90) with Al_2O_3-NaOH furnishes trans-myrtanal (91).[58]



Conclusion

We have projected in the foregoing survey significant advances in the isomerisation of terpenes by base catalysis. Invoking this technique, it is seen how many of the delicate reactions are smoothly accomplished, adding new dimensions to terpene technology. To recall, modifications of (+)-sabinene to (−)-α-thujene, verbenones to optically active ipedienols, and the (−)3β,4β-epoxycarane to (+)-cis-caran-4-one are notable examples in synthesis. A remarkable achievement is the conversion of (+)-car-3-ene to (−)-menthol realised through base-induced isomerisation to (+)-car-2-ene. Again, the rearrangement of α- to β-pinene, which is a key substrate in perfumery material chemistry, and of acetyl-carenes, which enrich the perfumer's shelves, are landmarks in the aroma field. How terpenes, which are notoriously sensitive to thermal and proton impact, have been engineered in the desired direction through base catalysis is an important chapter in the history of terpene chemistry.

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