Mini-Reviews in Organic Chemistry, **2008**, *5*, 345-354

Transformations of Terpenoids on Acidic Clays

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Abstract: The review considers the intra- and intermolecular transformations of terpenes and their oxygen-containing derivatives in the presence of acidic clays. Using clays as catalysts of terpenoid transformations leads to improved characteristics of known processes and often to reaction routes other than those that occur in the presence of the traditional acid catalysts. This opens up new prospects for the application of renewable plant raw materials in fine organic chemistry.

Keywords: Clay, montmorillonite, terpenes, transformations, rearrangements, selectivity.

1. INTRODUCTION

Terpenes and their derivatives are valuable renewable raw materials in organic chemistry. Their unique structure is often combined with high chemical lability and optical activity. Many terpenoids have used in the pharmaceutical and cosmetic industries, production of flavor additives and pesticides [1,2], and fine organic synthesis, including asymmetric synthesis of complex optically active compounds [3]. In acid media, terpenoids generally undergo various transformations. The complex mixtures of products obtained in these transformations are the major factors that hinder the wide use of these compounds in fine organic chemistry. However, due to the significant dependence of the product ratio on the type and characteristics of the acid catalyst used, one can occasionally select favorable conditions for the synthesis of the desired product, which stimulates the search for new catalytic systems and reaction conditions [4-6]. The acid catalysts of terpenoid transformations include various liquid Brönsted and Lewis acids, ion-exchange resins, zeolites, etc. Clays play an especially important role. These are inexpensive and accessible catalysts that often lead to new routes of terpenoid transformations or give other product ratios than other acid catalysts. The use of clays as catalysts of terpenoid transformations has not received due attention, although a number of publications reviewed their use for catalyzing various organic reactions [5,7-10]. At the same time, the reactions of labile and polyfunctional compounds such as terpenes are the best examples to show the unique catalytic properties of clays [11]. This review deals with acid-catalyzed transformations of terpenoids in the presence of acidic clays.

2. THE STRUCTURE OF CLAY MINERALS

The majority of important clay minerals are combinations of two basic types of layers. The first layer consists of sheets of $Si(O,OH)_4$ tetrahedra arranged in hexagonal ring subunits. Each silica ring is combined with two adjacent rings to form another 12-membered ring [12]. The second type of layer is usually composed of $A1_2(O,OH)_6$ or $Mg_3(O,OH)_6$ units that form octahedrally coordinated sheets. The octahedra are arranged in such a way that each oxygen atom is shared by two neighboring metal atoms. The identical symmetry and dimensions of these tetrahedral and octahedral sheets allow them to be combined by sharing the apical oxygens of the silica layers with the successive octahedral layers. The most widespread combinations of the tetrahedral (T) and octahedral (O) layers are 1:1 (TO; chrysolite, kaolinite) and 2:1 (TOT; montmorillonite, vermiculite, saponite, etc.), the latter being most important from the viewpoint of chemical applications [13].

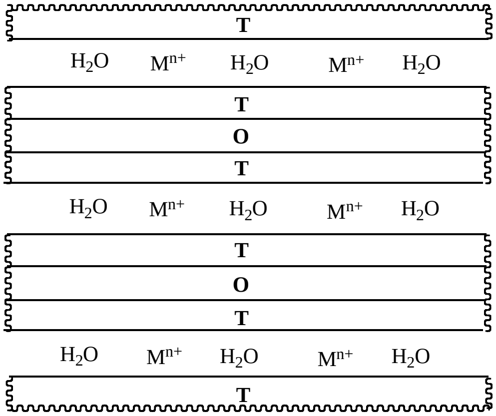

Fig. (1). Montmorillonite structure.

Some of the Si^{4+} cations in the T-net are isomorphically substituted by the Al^{3+}, Fe^{3+}, and other ions, while the $A1^{3+}$ cations in the O-net are replaced by the Mg^{2+}, Fe^{2+}, Li^+ and other ions. Substitution of cations by ions with lower valency gives rise to a negative charge in the layer, creating conditions for the formation of the acid properties of clays. In layered silicates with a TOT structure, the interlayer space is formed by the identical surfaces of the T-nets, and held by the dispersion forces of the silicon-oxygen tetrahedra and the electrostatic forces between the negatively charged opposite layers and the intermediate cations (mostly Na^+ and Ca^{2+} in natural clays) (Fig. **1**). In many layered minerals with a TOT structure such as montmorillonites, vermiculites, etc., the interlayer space contains water molecules, which hinder the complete coalescence of layers. Swelling in water and polar solvents is an important ability of clays (mainly, montmorillonites), in which case the interlayer distance directly depends on the nature of the solvent [12].

At high temperatures (above 200 °C) clay dehydration and the ensuing collapse of layers hinder the organic reactions in the interlayer space of montmorillonites (most often used as catalysts). The temperature limitations imposed by the collapse can be overcome by incorporating the thermally stable bulky oligomer hydroxyl cations (for example, the Keggin ion $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}$ [13]) in the interlayer space. These cations act as "pillars" that fix the layers at certain distances apart, hindering their coalescence after the removal of water. This method of layer fixation led to the creation of a new type of aluminosilicate catalysts, namely, pillared layered silicates (pillared clays) [10,14,15]. Layer fixation in clay minerals increased the upper boundary of thermal stability to 550-800 °C and yielded aluminosilicates with a regular structure and with voids significantly larger than those in large-pore zeolites.

A number of procedures are used to increase the catalytic activity of clays. These include treatment with mineral acids, thermal treatment and substitution of exchange cations by other cations. Acid treatment increases the active surface of layered aluminosili-

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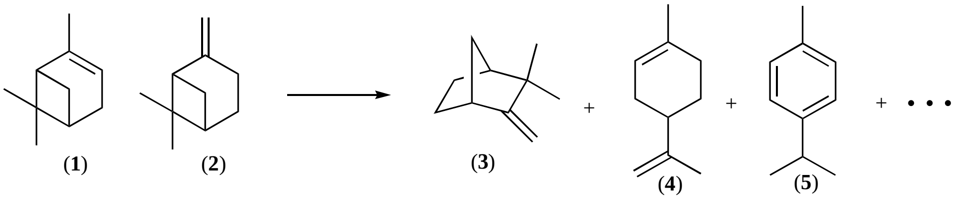


Scheme 1. Isomerization of pinenes.

cates, as well as the number of Lewis and Brönsted acid centers [14,16].

Clays (especially montmorillonites) can act as universal catalysts containing both Lewis and Brönsted acid centers with various power [17]. By varying the method for clay treatment and/or modification, one can change the power of these active centers, the ratio between them, and the interlayer distance. Clay pillaring affords thermally stable catalysts with a large interlayer distance.

3. ISOMERIZATION OF TERPENES IN THE PRESENCE OF CLAYS

Isomerization of α- (**1**) and β-pinenes (**2**) is the best studied reaction of terpenes in the presence of clays (Scheme **1**) because of the practical importance of camphene (**3**) and *dl*-limonene (dipentene) (**4**) obtained as the reaction products. The reaction also gives other mono- and bicyclic monoterpenes, dimers, and polymers.

The first works on the use of activated clay for isomerization of pinenes, dating back to the first half of the 20th century [18], revealed that this reaction formed camphene (**3**) with a yield of up to 50-55%. More recently, it was shown [19] that the primary products of isomerization of α-pinene (**1**) in the presence of Attapulgus clay were camphene (**3**) and limonene (**4**), which formed directly from α-pinene by relatively fast reactions. Other monocyclic terpenes and polymers formed by relatively slow secondary reactions, primarily, from limonene (**4**). It was first assumed [19] that the stereochemistry of terpene adsorption on clay affected the route of isomerization.

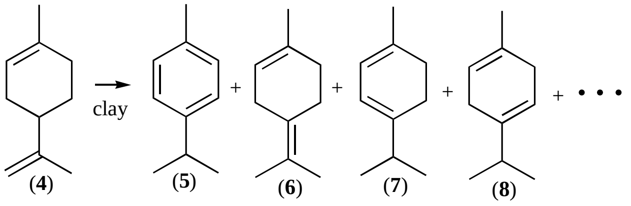
Montmorillonite clays were generally the most popular catalysts of pinenes isomerization, although kaolinitic clay was also successfully used for this purpose [20]. Preliminary acid treatment of clays had a considerable effect on the conversion of pinenes and the product ratio [21]; the amount of the acid used [22,23], its concentration [24,25], and the temperature of acid treatment [22,26] were reported to be important factors in this case. The data about the dependence of the catalytic activity of acidic clays and isomerization selectivity on the nature of acid centers, obtained in these works, indicated that the transformations of pinenes (1,2) into camphene (3) occurred predominantly on the Brönsted acid centers [24,27,28].

Studies of the effects of the exchange cation on the isomerization of α-pinene (**1**) showed [27,28] that montmorillonite clays containing the Fe^{3+} cation exhibited the highest activity. Isomerization of α-pinene (**1**) in the presence of acid-treated polycation-exchanged montmorillonite clay led to a considerably increased yield of camphene (**3**) compared with the yield obtained in the presence of the non-polycation-exchanged equivalents [29]. Investigation of the applicability of montmorillonite clays containing organic cations (tetramethylammonium, dodecyltrimethylammonium and octadecyltrimethylammonium) as exchange cations to isomerization of α-pinene (**1**) revealed that only organoclays pretreated with an acid possessed high catalytic activity [30,31]. The Al^{3+} exchange cations used in combination with tetramethylammonium proved less effective in isomerization of α-pinene (**1**) than Al^{3+}-exchange clays because conversion decreased substantially when the tetramethylammonium content increased [32]. Alumina pillared clays demonstrated [33] good activity and high selectivity with respect to camphene (**3**).

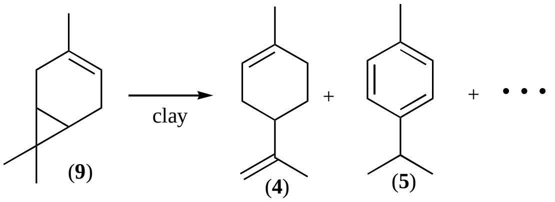
The selectivity of the best catalysts based on clays in isomerization of compound (**1**) generally was 40-65% with respect to camphene (**3**) and 15-40% with respect to limonene (**4**), while conversion of α-pinene (**1**) was 70-90%.

The major goal of acid-catalyzed isomerization of limonene (**4**) is the synthesis of *p*-cymene (**5**), but the reaction also forms large amounts of isomeric *p*-menthane terpenes (terpinolene (**6**), α-(**7**) and γ-(**8**) terpinenes, etc.) (Scheme **2**). The use of acid-activated bentonite (montmorillonite type clay) as a catalyst in this reaction led to high conversion (95%), but the selectivity with respect to *p*-cymene (**5**) was up to 15% [34]. A comparison of Al^{3+}-bentonite (with maximum Brönsted acidity) and Ni^{2+}-bentonite (basically a Lewis acid) did not support the enhanced production of *p*-cymene (**5**) over the Lewis acid sites [35]. *p*-Cymene (**5**) was obtained as the major product (with a selectivity of over 22%) during isomerization of limonene (**4**) in the presence of pillared alumina clays [33].

Heating of 3-carene (**9**) to 170 °C in the presence of activated clay gave limonene (**4**) as the primary product of isomerization (Scheme **3**) [36]. Further transformations of limonene (**4**) under the reaction conditions involved the displacements of the double bonds, formation of *p*-cymene (**5**), and polymerization.

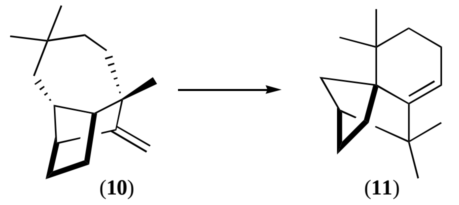


Scheme 2. Isomerization of limonene.

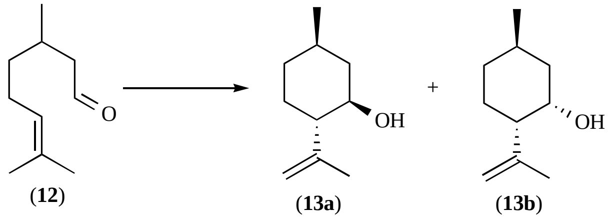


Scheme 3. Isomerization of 3-carene.

Isolongifolene (**11**) and various other isolongifolene-based products are commercially important chemicals that find applications in perfumery and fragrance industries. Isomerization of longifolene (**10**) to isolongifolene (**11**) (Scheme **4**) in the presence of clays (montmorillonite, pillared clay and modified pillared clay) was studied in [37]. An analysis of the results confirmed that the total acid strength along with the acid site distribution played a vital role in selective isomerization of longifolene (**10**) to isolongifolene (**11**). Catalysts with a very low and very high total acidity with large numbers of weak acid sites were not suitable for this isomerization because side reactions dominated the reaction pathway. The use of Al- and Zr-pillared clays at 180 °C yielded reaction mixtures with more than 70% isolongifolene (**11**).



Scheme 4. Isomerization of longifolene.



Scheme 5. Isomerization of citronellal, products are racemic.

Thus, clays proved quite effective catalysts of terpene isomerizations, while the conversion of the starting compounds and the process selectivity could be changed by varying the activation parameters and/or modifying clays. These reactions generally formed the same major products as reactions in the presence of other acid catalysts.

4. ISOMERIZATION OF OXYGEN-CONTAINING TERPENOIDS IN THE PRESENCE OF CLAYS

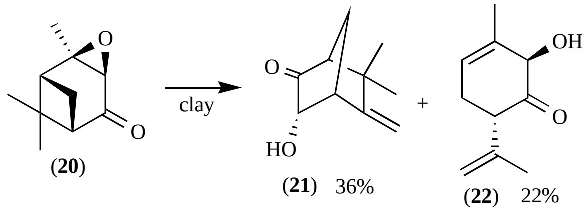
For terpenes isomerized on clays, the major effect on the product ratio is exerted by the nature and strength of acid sites, while for oxygen-containing terpenes, other characteristics of clays as catalysts are also very important, namely, the three-dimensional crystal structure, the mutual arrangement of active centers, etc. As a result, unlike the case with the traditional acid catalysts, the presence of clays favors activation of particular functional groups and particular terpenoid conformations can be fixed in the course of adsorption, and these factors can determine the direction and stereoselectivity of transformations.

Montmorillonite containing Zr^{4+} as an exchange cation proved to be a highly selective catalyst of isomerization of citronellal (**12**) to racemic isopulegol (**13**) [38] (Scheme **5**). The product yield reached 98% at an isomer ratio of (**13a**):(**13b**) 9:1. The use of the H^+ form of K-10 montmorillonite clay instead of Zr^{4+}-montmorillonite led to a lower product yield, but did not substantially affect the isomer ratio.

Verbenol epoxide (**14**) in the presence of K-10 clay transformed into a mixture of three compounds, namely, diol (**15**), ketoalcohol (**16**), and α-hydroxyaldehyde (**17**) (Scheme **6**) [39]. It should be noted that the expected product of this reaction was only ketoalcohol (**16**), obtained previously by isomerization of verbenol epoxide (**14**) in the presence of $ZnBr_2$. In the presence of clay, compound (**16**) formed only as a minor product, while *trans*-diol (**15**) was the major product.

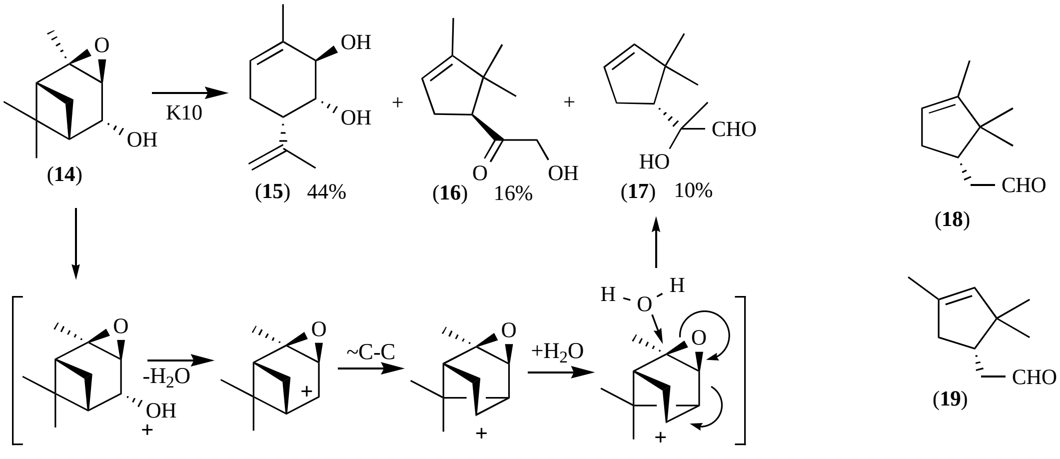
The structure of compound (**17**) was extremely unusual. Its formation could not be explained by the usual rearrangements into substances with a cyclopentane framework (analogs of campholene (**18**) and isocampholene (**19**) aldehydes), which are traditional for α-pinene epoxides. It was assumed [39] that the mechanism of the formation of α-hydroxyaldehyde (**17**) from compound (**14**) included the skeletal rearrangements in the intermediate carbocation before cleavage of the epoxy group. It is important that isomerization of verbenol epoxide (**14**) to compound (**17**) is stereoselective without any decrease in the optical purity of the compound.

The use of the natural acidic montmorillonite clay askanite-bentonite for isomerization of verbenone epoxide (**20**) led to α-keto alcohols (**21**) and (**22**) [40] (Scheme **7**), while compounds with a cyclopentane framework did not form at all. Again the terpenoids showed a radical difference in reactivity on clay and in the presence of $ZnBr_2$, when the only product was the analog of campholene aldehyde [41]. The formation of compound (**21**) with a camphane framework as the major product proved unexpected because rearrangements of this kind are characteristic for α- and β-pinenes (**1**,**2**) themselves, but not for their derivatives.

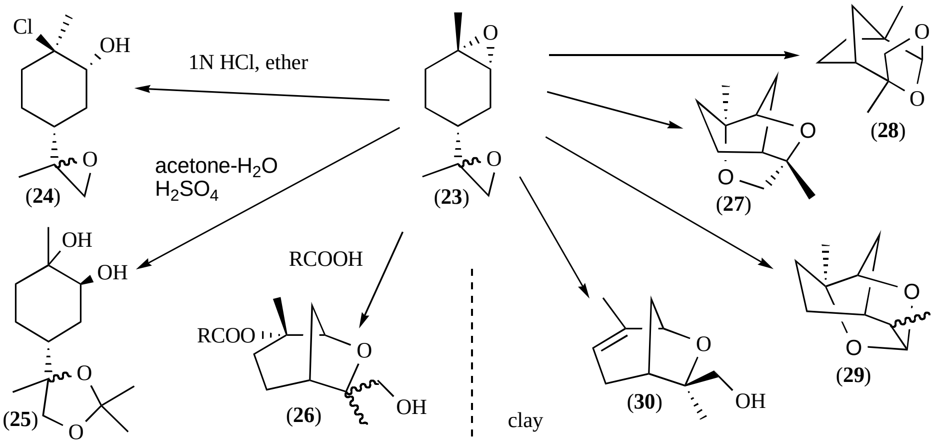


Scheme 7. Isomerization of verbenone epoxide on clay.

When limononene diepoxide (**23**) was stored in homogeneous acid media, the reactions always involved an external nucleophile. The carbocation formed by cleavage of the protonated epoxide ring either reacted immediately with the external nucleophile, giving the products of the independent cleavage of the epoxide rings, (**24**) and (**25**) [42,43], or experienced intramolecular cyclization into a cation



Scheme 6. Isomerization of verbenol epoxide on clay.



Scheme 8. Isomerization of limonene diepoxide.

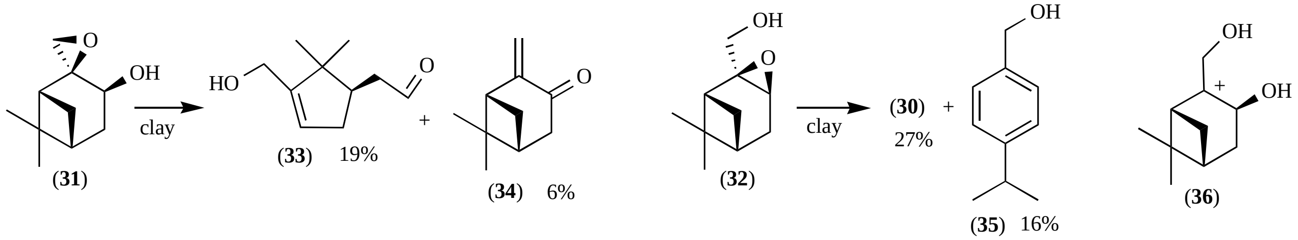
with an 6-oxabicyclo[3.2.1]octane framework, trapped by the external nucleophile to give compound (**26**) [43] (Scheme **8**).

Isomerization of compound (**23**) in the presence of clays (askanite-bentonite, K-10) did not involve the external nucleophile and led to a set of optically active bi- and tricyclic oxygen-containing compounds, among which compound (**27**) was the major product, and compounds (**28**)-(**30**) were minor products [44]. The use of sulfated Zr pillared clay as a catalyst of this reaction led to a more complex reaction mixture [45].

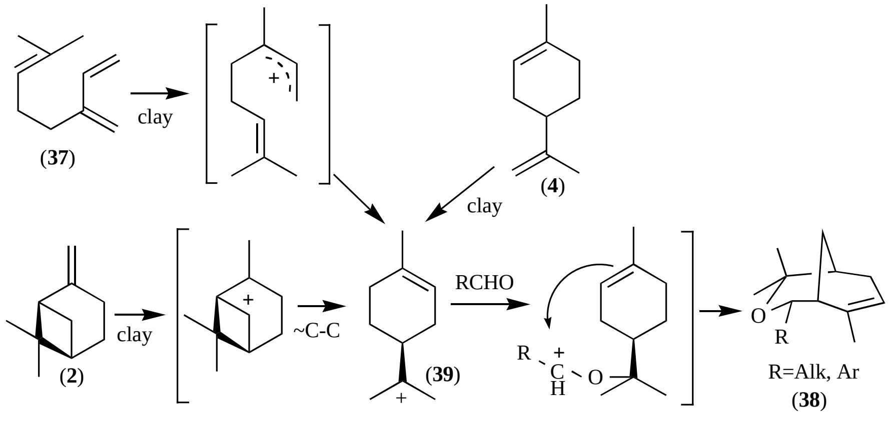
In the presence of askanite-bentonite clay, pinocarveol (**31**) transformed into compound (**33**), an analog of campholene aldehyde, and pinocarvone (**34**) (Scheme **9**). The transformations of myrtenol epoxide (**32**) on clay gave aldehyde (**33**) and an aromatic alcohol with a *p*-menthane framework (**35**) [46]. Synthesis of compound (**33**) was quite expected in these reactions, while the formation of "nonoverlapping" products (**34**) and (**35**) was not. Indeed, after protonation in acid media, compounds (**31**) and (**32**) gave the same intermediate carbocation, (**36**), and hence one could expect the formation of the same products in both cases. This discrepancy between the expected and real results might be the consequence of the peculiarities of the adsorption of epoxy alcohols (**31**) and (**32**) on clay.

5. INTERMOLECULAR REACTIONS OF TERPENES IN THE PRESENCE OF CLAYS

Investigation of the reactions of β-pinene (**2**), limonene (**4**), and myrcene (**37**) with aliphatic and aromatic aldehydes in the presence of askanite-bentonite clay led to the development of a simple and effective procedure for the preparation of bicyclic ethers with an 3-oxabicyclo[3.3.1]nonane framework (**38**) (Scheme **10**) [47,48]. The highest yield of the target product (up to 56%) was observed when β-pinene (**2**) was used as a substrate [48]. Interest in these bicyclic



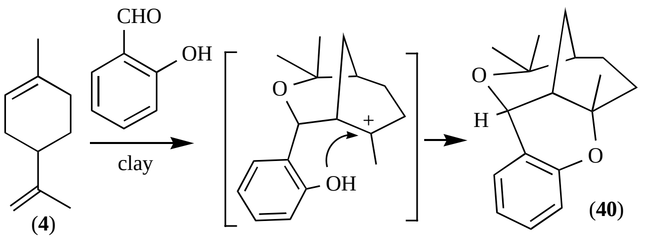
Scheme 9. Isomerization of pinocarveol and myrtenol on clay.



Scheme 10. Reactions of β-pinene, limonene and myrcene with aldehydes on clay.

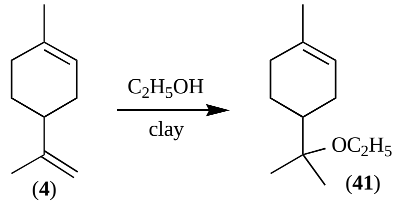
ethers arises, above all, from their recently detected selectivity of binding with estrogen α- and β-receptors [49]. The mechanism of the transformations of the three monoterpenes to compound (**38**) suggested in references [47,48] includes the formation of the same intermediate carbocation (**39**) with a *p*-menthane framework, which further interacts with the aldehyde molecule. It is interesting that α-pinene (**1**), whose protonation should form the same tertiary carbocation as in the case of β-pinene (**2**), did not react with aldehydes in the presence of clay.

When limonene (**4**) reacts with salicylic aldehyde on askanite-bentonite clay in methylene chloride, the reaction does not stop at the stage of the bicyclic ether formation (Scheme **11**). The sterically favorable arrangement of the hydroxyl group in the intermediate carbocation facilitates double heterocyclization, which leads to the synthesis of tricyclic compound (**40**) with a 28% yield [50].



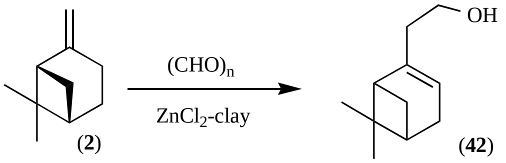
Scheme 11. Reaction of limonene with salicylic aldehyde on clay.

Later, it was found that stepwise application of substrates on clay in a solvent, further evaporation of the latter by distillation, and storage of the reaction mixture without a solvent increased the yield of product (**40**) to 73% [51]. The order of reagent application was important; thus, if limonene (**4**) was applied first or both substrates were applied at once, the reaction rate decreased considerably relative to the rate in the case with salicylic aldehyde applied first. This method also proved effective for the reaction of limonene (**4**) with ethanol (Scheme **12**) in the presence of askanite-bentonite clay [51]; the reaction gave a 95% yield of (**41**) (conversion of limonene (**4**) was 60%), which exceeded by far the yield (31%) obtained with sulfuric acid used as a catalyst [52].



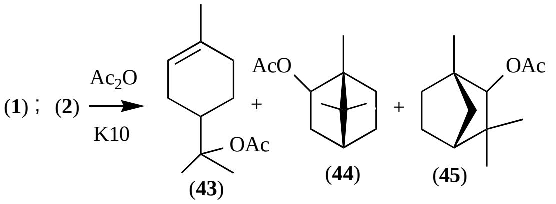
Scheme 12. Reaction of limonene with ethanol on clay.

The reaction of β-pinene (**2**) with formaldehyde in the presence of the $ZnCl_2$ impregnated montmorillonite catalyst formed nopol (**42**) with 97% selectivity and 75% conversion of β-pinene (**2**) (Scheme **13**) [53]. In this case, the conversion and yield exceeded those observed previously in the same reaction in the presence of unsupported $ZnCl_2$. This was attributed to the adsorption of β-pinene (**2**) and carbocation formed in the reaction of formaldehyde with $ZnCl_2$ on the clay surface [53].



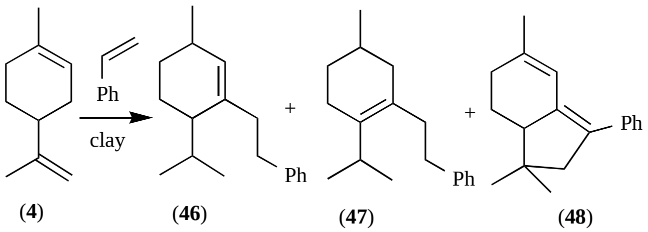
Scheme 13. Reaction of β-pinene with formaldehyde on clay.

The reactions of pinenes (**1**) and (**2**) with acetic anhydride on clay K-10 gave not only products (**43**) and (**44**) (Scheme **14**) formed as a result of the isomerization of the pinane framework to the *p*-menthane and bornane frameworks, respectively, but also compound (**45**), which resulted from a more profound rearrangement of the pinane framework [54]. Although both pinenes were expected to give the same cation after protonation, the composition of the reaction mixture depended on the structure of the starting pinene; the ratio of products (**43**), (**44**), and (**45**) in the reaction mixture was 2.5:3:1 in the case of α-pinene (**1**) and 4:2:1 in the case of β-pinene (**2**).



Scheme 14. Reactions of pinenes with acetic anhydride on clay.

The reaction of limonene (**4**) with styrene in the presence of askanite-bentonite clay occurred with unusual transformations to compounds (**46**), (**47**), and (**48**) in a ratio of 3:1:1.5 (GLC), respectively (Scheme **15**) [55, 56]. Compounds (**46**) and (**47**) might be regarded as the products of formal alkylation at a saturated carbon atom and hydrogenation, while compound (**48**) might be the result of the [3C + 2C]-cycloaddition and dehydrogenation. In the presence of clay, limonene (**4**) did not react with styrenes having donor or acceptor substituents. It seems that the electronic effects of substituents introduced in the benzene ring are less significant than steric hindrances created by them during the adsorption of the substrate on the catalyst. These transformations did not occur when β-zeolite was used as a catalyst. Investigation of the effects of various cation-exchange modifications of askanite-bentonite clay on the total yield of products in this reaction showed that the best results were achieved on Cr^{3+}- and Zn^{2+}-modified clays and on acidic clay, while the use of Co^{2+}-, Fe^{3+}-, and especially Al^{3+}-modified clays decreased the product yield considerably [56].

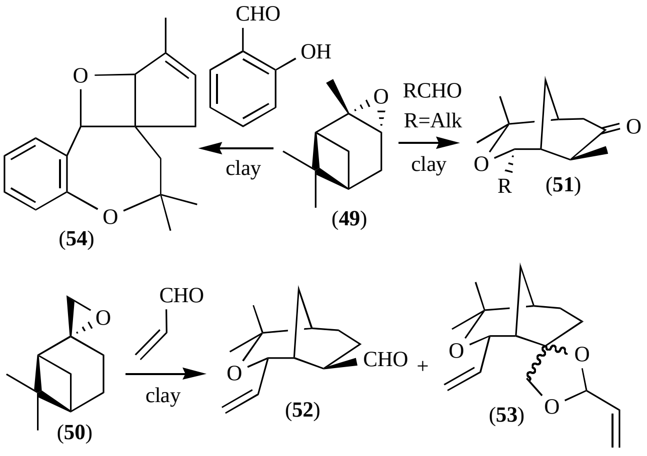


Scheme 15. Reaction of limonene with styrene on clay.

6. INTERMOLECULAR REACTIONS OF OXYGEN-CONTAINING TERPENOIDS IN THE PRESENCE OF CLAYS

In the presence of montmorillonite clays, α-(**49**) and β-(**50**)-pinene epoxides enter the intermolecular reactions with aldehydes (Scheme **16**). Compounds (**51**)-(**53**) formed in the reactions of these terpenoids with aliphatic aldehydes [57] have the same 3-oxabicyclo-[3.3.1]nonane framework but different sets of functional groups compared with bicyclic ethers obtained in reactions of β-pinene (**2**) with aldehydes (Scheme **10**).

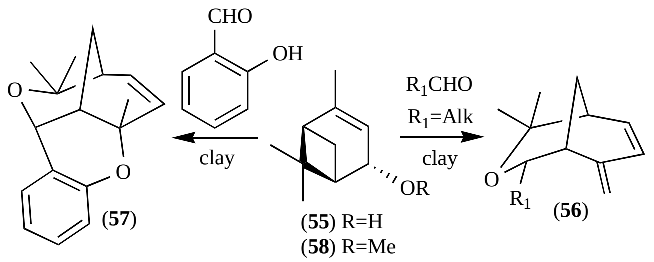
The reaction of α-pinene epoxide (**49**) with salicylic aldehyde on askanite-bentonite clay (Scheme **16**) occurred in a different way [57]. It led to a profound rearrangement of the pinane framework. An unusual tetracyclic ether, (**54**), was isolated in a 17% yield as the sole product of intermolecular reaction. To explain the formation of this product, the authors suggested [57] a reaction scheme that included more than 10 stages.



Scheme 16. Reactions of pinene epoxides with aldehydes on clay.

The reactions of *trans*-verbenol (**55**) with aliphatic aldehydes and salicylic aldehyde in the presence of askanite-bentonite clay afforded products (**56**) and (**57**) (Scheme **17**), which were similar in structure to the compounds synthesized in reactions of limonene (**4**) with these aldehydes on clay (Schemes **10**,**11**) [46]. Investigation of the behavior of the steric isomer of compound (**55**), *cis*-verbenol, in the presence of clay showed that the reaction formed the optical antipodes of heterocyclic compounds (**56**) obtained from (+)-*trans*-verbenol (**55**) [46]. Thus, it appeared that the relative position of the hydroxyl group in the starting verbenol did not affect the occurrence and direction of the intermolecular reactions. Moreover, substitution of the hydroxyl group by the methoxy group in *trans*-verbenol to obtain its methyl ether (**58**) did not change the reaction route either.

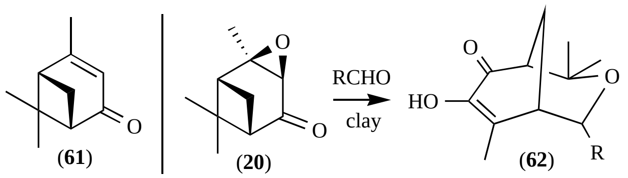
Other reactions were observed when verbenol epoxide (**14**) reacted with aldehydes on clay [46]. The reactions of (**14**) with aromatic aldehydes in the presence of askanite-bentonite clay gave the products of intermolecular reactions compounds (**59**) with a tetrahydrobenzodioxine framework; the reaction with crotonic aldehyde yielded not only compound (**59**), but also product (**60**) with a hexahydrochromene framework (Scheme **18**). The possibility for diol (**15**) to be involved in the formation of (**60**) was confirmed by the reaction of (**15**) with crotonic aldehyde on clay, which indeed gave compound (**60**).



Scheme 17. Reactions of verbenol with aldehydes on clay.

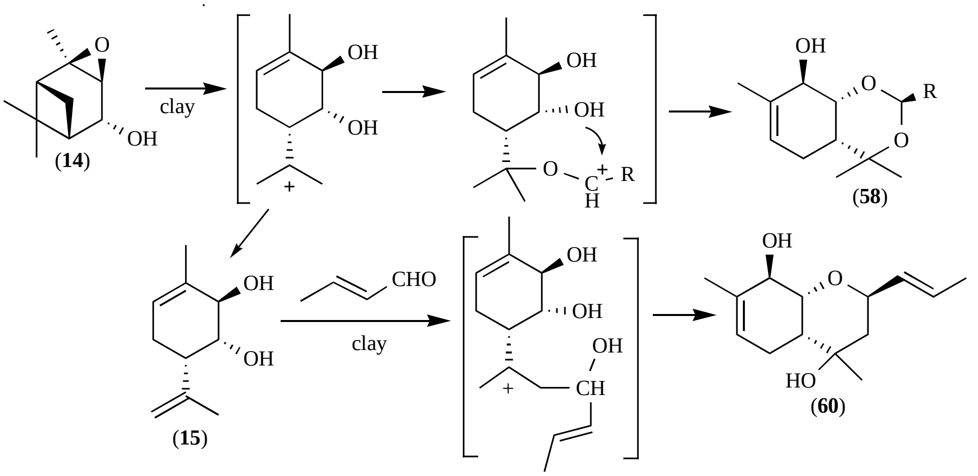
It can be seen that the reactivity of verbenol epoxide (**14**) in intermolecular reactions with aldehydes in the presence of clay differs radically from the reactivity of β-pinene (**2**), verbenol (**55**), and α-pinene epoxide (**49**) in these transformations. This was attributed [46] to the differences in the reaction mechanisms; the hypothetical mechanism that forms compounds (**58**) and (**60**) involves heterocyclization at the last stage (Scheme **18**), but not carbocyclization suggested for compounds (**38**), (**51**), and (**56**) (Scheme **10**).

In contrast to verbenol (**55**), verbenone (**61**) did not react with aldehydes in the presence of clays [40]. At the same time, the reactions of verbenone epoxide (**20**) with aldehydes on askanite-bentonite clay formed ketoenols (**62**) with an oxabicyclo[3.3.1]nonene framework (Scheme **19**) [40].

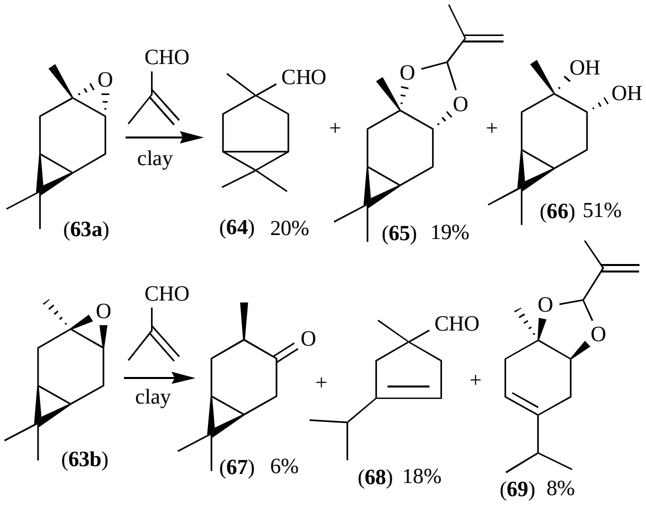


Scheme 19. Reactions of verbenone epoxide with aldehydes on clay.

The structure of the products of the intermolecular reaction differed radically from the structure of the substances formed in reac-



Scheme 18. Reactions of verbenol epoxide with aldehydes on clay.



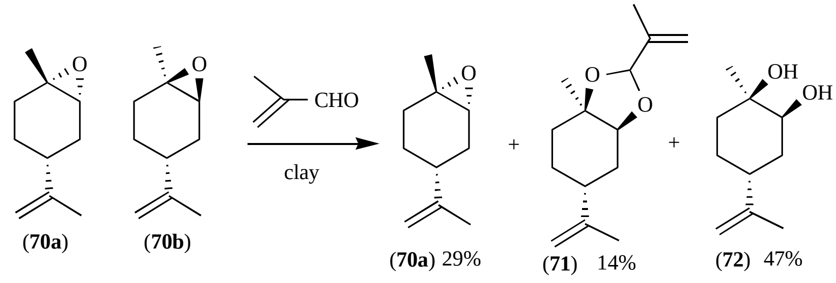
Scheme 20. Reactions of 3-carene epoxides with α-methylacrolein on clay.

tions of verbenol epoxide (**14**) on clay (Scheme **18**). It seems that compounds (**62**) formed by a mechanism similar to the one shown in Scheme **10** [40].

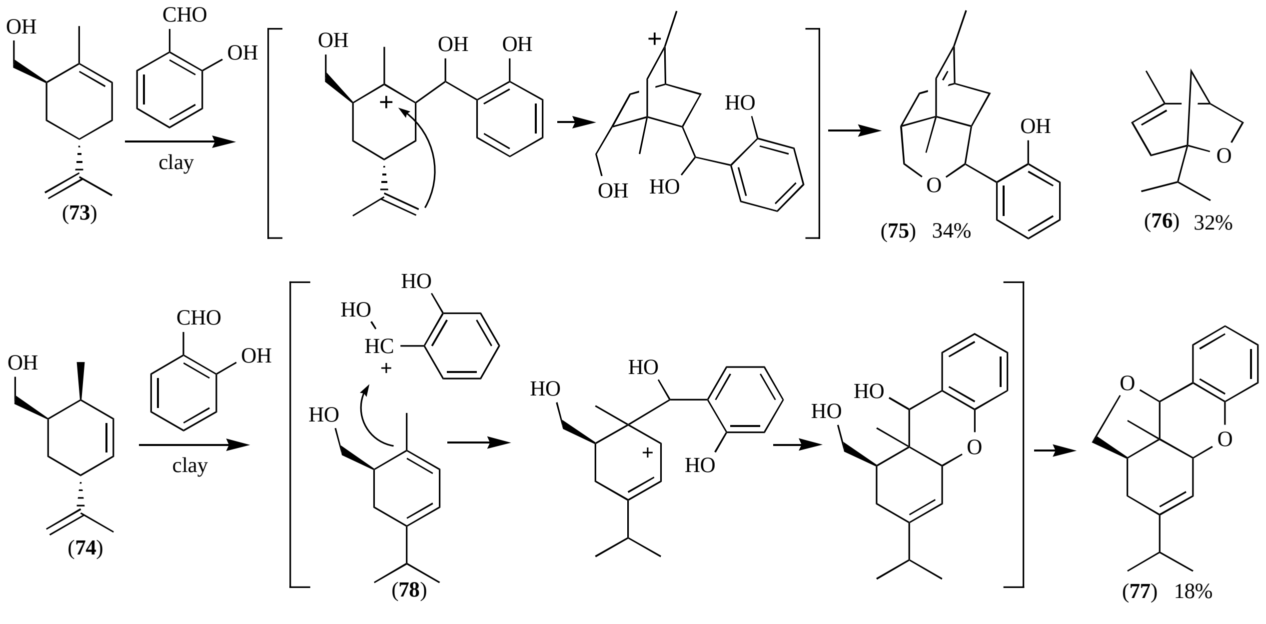
The reactions of 3-carene *trans*-(**63a**) and *cis*-(**63b**)-epoxides with α-methylacrolein on askanite-bentonite clay are described in [58] (Scheme **20**). Apart from the isomerization products, namely, compounds (**64**), (**67**), and (**68**), the products of intermolecular reactions, (**65**), (**66**), and (**69**), were isolated from the reaction mixtures. *cis*-Diol (**66**) was evidently formed by hydrolysis of cyclic acetal (**65**) because direct hydrolysis of the starting epoxide (**63a**) should lead to the appropriate *trans*-diol. The total yield and product ratio in the intra- and intermolecular processes largely depended on the structure of the starting epoxide. While 3-carene *trans*-epoxide (**63a**) mainly gave the products of intermolecular reactions (total yield 70%), 3-carene *cis*-epoxide (**63b**) led to only 8% yield of (**69**) (the total yield of isomerization products was 24%).

Interaction of the 1:1 mixture of limonene *cis*-(**70a**)- and *trans*-(**70b**) 1,2-epoxides with α-methylacrolein on askanite-bentonite clay (Scheme **21**) led to the formation of a reaction mixture containing unchanged limonene *cis*-epoxide (**70a**) and the products of the reaction of limonene *trans*-epoxide (**70b**) with α-methylacrolein, compounds (**71**) and (**72**) (the yield is given based on the changed limonene epoxide) [58]. Acetal (**71**) was readily hydrolyzed into *cis*-diol (**72**) in the course of the reaction on clay and in the course of separation on silica gel. Thus, due to the different reactivities of limonene *cis*- and *trans*-1,2-epoxides in the presence of clay, it was possible to selectively obtain one stereoisomer, *cis*-diol (**72**), without preliminary separation of the epoxide mixture. The compounds (**71**) and (**72**) was optically active, but *ee* of these compounds wasn't measured.

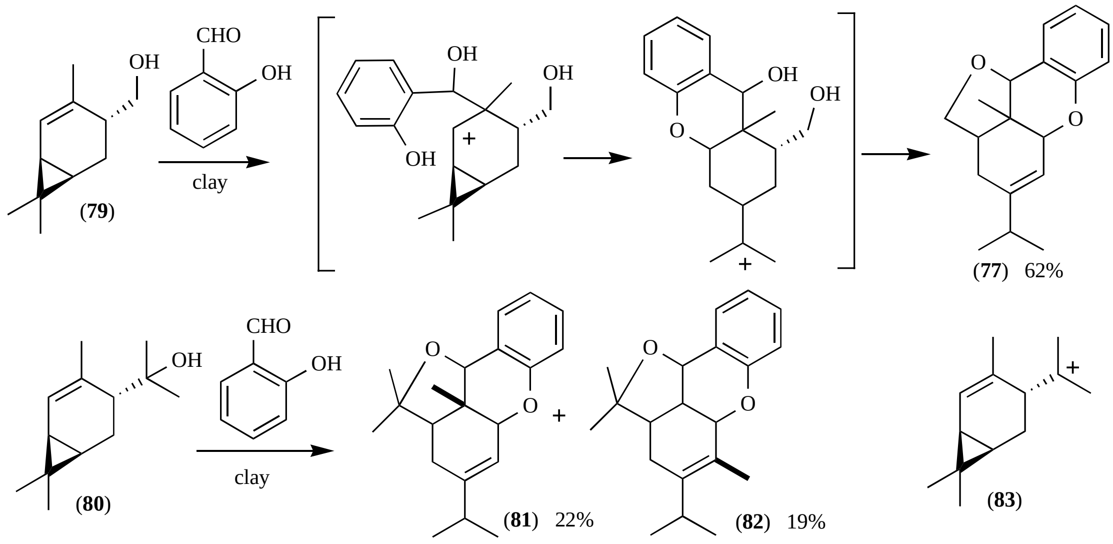
The reactions of isomers with different positions of the double bond, 6-hydroxymethyl-limonene (**73**) and 6-hydroxymethyl-*iso*-



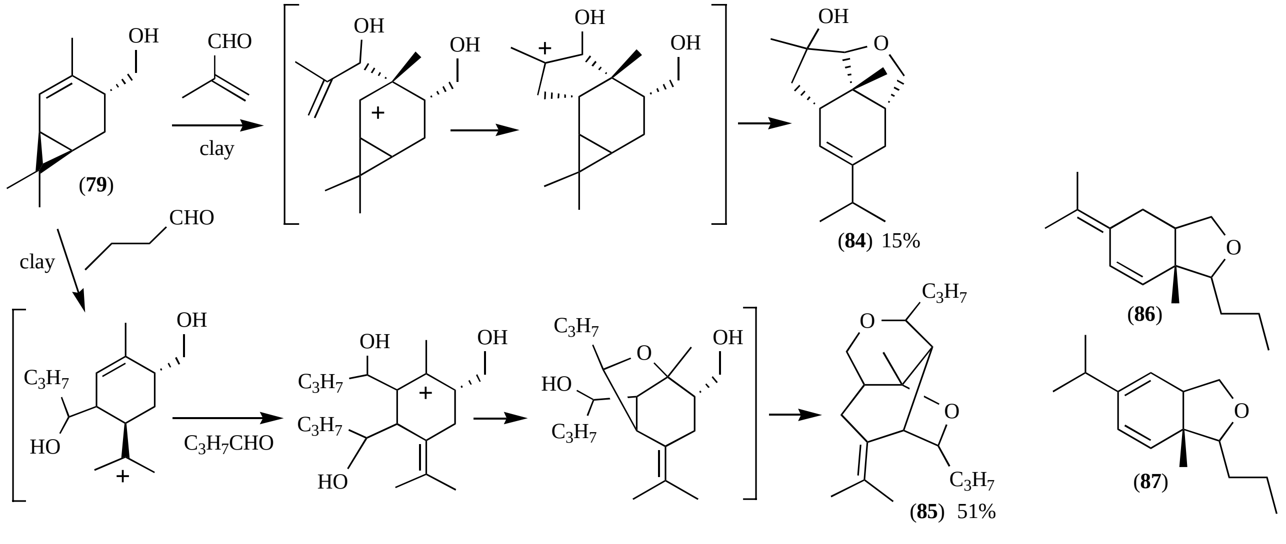
Scheme 21. Reaction of limonene epoxides with α-methylacrolein on clay.



Scheme 22. Reactions of compounds (**73**) and (**74**) with salicylic aldehyde on clay.



Scheme 23. Reactions of compounds (**79**) and (**80**) with salicylic aldehyde on clay.



Scheme 24. Reactions of compound (**79**) with aldehydes on clay.

limonene (**74**), with salicylic aldehyde in the presence of askanite-bentonite clay occurred differently (Scheme **22**) [47,59].

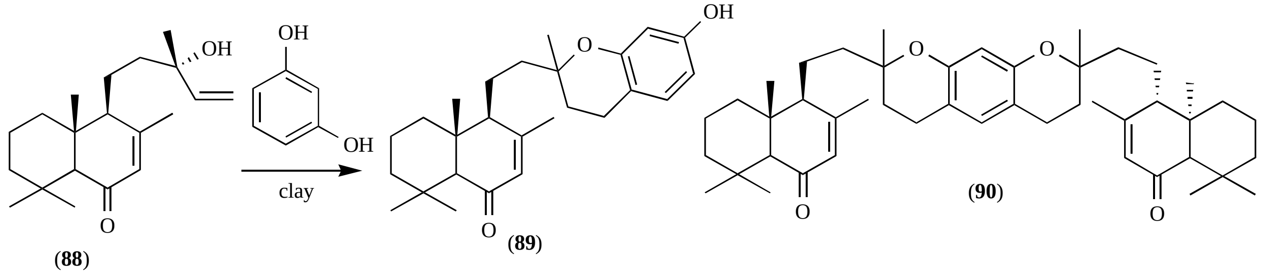
While the reaction of enol (**73**) with salicylic aldehyde afforded compound (**75**) with an oxatricyclo[5.3.1.0^{5,10}]un-decene framework (the reaction mixture also contained the product of cyclization of (**73**), the bicyclic ether (**76**)), the reaction of 6-hydroxymethyl-*iso*-limonene (**74**) with this aldehyde gave a compound with a dioxabenzotricyclo[6.3.1.0^{5,12}]dodecene framework, (**77**), as the sole product of intermolecular reaction. To explain the formation of this compound, the authors assumed [47] that the reaction formed compound (**78**) as an intermediate (Scheme **22**), which further reacted with protonated salicylic aldehyde. However, storage of compound (**74**) under the reaction conditions failed to give the expected intermediate (**78**) [59].

Note that, although it includes the framework of limonene (**4**), 6-hydroxymethyl-limonene (**73**) reacted with salicylic aldehyde in a quite different way than limonene (Schemes **11**, **22**).

The reaction of 4-hydroxymethyl-2-carene (**79**) with salicylic aldehyde on askanite-bentonite clay unexpectedly gave in a good yield compound (**77**) (Scheme **23**) [47] previously obtained from 6-hydroxymethyl-*iso*-limonene (**74**).

A transition from enol (**79**) to compound (**80**) containing two extra methyl groups afforded compounds (**81**) and (**82**) in equal proportion [47]. Compound (**81**) probably formed by the same mechanism as (**77**); however, the case was opposite for (**82**), whose structure was quite unexpected. The different positions of the methyl group (boldfaced on Scheme **23**) in compounds (**81**) and (**82**) suggest that the reaction followed different routes. It was assumed [47] that the multistep mechanism that formed (**82**) started with dehydration of (**80**) and gave tertiary carbocation (**83**), which further reacted with salicylic aldehyde. The authors did not indicate the stereochemistry of these compounds.

Compound (**79**) reacted with aliphatic aldehydes in the presence of askanite-bentonite clay; the structure of the products depended on the structure of the aldehydes used [47,60]. For example, the reaction of monoterpenoid (**79**) with α-methylacrolein gave compound (**84**) with an indeno[1,7-bc]furan framework as the major product of intermolecular reaction; however, in the reaction of hydroxyolefin (**79**) with butyric aldehyde, the major product was the



Scheme 25. Reactions of compound (**88**) with resorcinol on clay.

product of the addition of two aldehyde molecules to terpenoid, namely, compound (**85**) with a 6,10-dioxatri-cyclo[5.4.0.0^{4,8}]undecane framework (Scheme **24**). The reaction of enol (**79**) with butyric aldehyde on clay yielded not only compound (**85**), but also the products of the addition of one aldehyde molecule to the terpenoid, compounds (**86**) and (**87**) with an isobenzofuran framework (Scheme **24**) [47]. By varying the reaction conditions, one can radically change the reaction route to produce either (**85**) (preliminary deposition of butyric aldehyde on the catalyst) or (**86**) (simultaneous deposition of the reagents and lowering the reaction temperature to 0 ^{o}C).

The reactions of labdane alcohol (**88**) with phenols in the presence of askanite-bentonite clay led to terpenylchromanes (Scheme **25**), the products of alkylation and subsequent heterocyclization [61]. Attempts to use zeolites for these transformations failed because of considerable polymerization of the starting terpenoid. The product yield depended significantly on the structure of the starting phenol, which was explained by the effect of the heterogeneous catalyst. The highest yield was obtained when resorcinol was used as the phenol reagent; the yield of (**89**) was 63%. When resorcinol reacted with an excess of (**88**), the product was compound (**90**), obtained by the addition of two terpene residues to phenol (85% yield).

7. CONCLUSION

Using clays (primarily, montmorillonites) for acid-catalyzed intra- and intermolecular transformations of terpenoids proved a rather fruitful approach. Apart from the traditional advantages of heterogeneous acid catalysts such as no acid wastes, facile treatment of the reaction mixture, catalyst regeneration and recycling, etc., it has a number of other specific features. First, it provides the possibility of "fine" adjustment of a catalyst to a particular reaction by varying the method of acid and/or thermal activation of clay, introducing a suitable exchange cation in the interlayer space, impregnating clays with metal salts (for example, $ZnCl_2$), using pillared clay, etc. Second, for intermolecular transformations and reactions of polyfunctional compounds as substrates, of great importance are such factors as preferable fixation of definite conformations of substrates or intermediates on the surface of clay, definite mutual orientation of reactant molecules, etc. As a result, terpenoid transformations on clays often occur in other ways than transformations in the presence of traditional acid catalysts, giving new interesting products (often not available by other synthetic procedures) from renewable plant raw materials under the ecologically clean conditions. The transformations of terpenoids in the presence of clays are generally stereoselective processes. The information about these transformations obtained during the last decade allows us to pass from the reactivity studies of terpenoids on clays to practical application of the products, for example, in asymmetric synthesis.

REFERENCES

[1] Monteiro, J.L.F.; Veloso, C.O. *Top. Catal.*, **2004**, *27*, 169.
[2] Swift, K.A.D. *Top. Catal.*, **2004**, *27*, 143.
[3] Liu, W. In *Studies in Handbook of Chiral Chemistry, Second Edition*; D. Ager, Ed.; Taylor&Francis: Boca Raton, **2006**; pp. 59-74.
[4] Swift, K.A.D. In *Fine chemicals through heterogeneous catalysis*; Sheldon, R. A.; van Bekkum, H. Eds.; Wiley-VCH: Weinheim, **2001**, pp. 242-246.
[5] Maki-Arvela, P.; Holmbom, B.; Salmi, T.; Murzin D. Yu. *Catal. Rev.*, **2007**, *49*, 197.
[6] Salakhutdinov, N.F.; Barkhash, V.A. *Usp. Khim.*, **1997**, *66*, 376.
[7] Corma, A.; Garcfa, H. *Catal. Today*, **1997**, *38*, 257.
[8] Varma, R.S. *Green Chem.*, **1999**, 43.
[9] Centi, G.; Perathoner, S. *Microporous Mesoporous Mater.*, **2008**, *107*, 3.
[10] Gil, A.; Gandia, L.M. *Catal. Rev. Sci. Eng*., **2000**, *42*, 145.
[11] Shults, E.E.; Raldugin, V.A.; Volcho, K.P.; Salakhutdinov, N.F.; Tolstikov G.A. *Russ. Chem. Rev.*, **2007**, *76*, 655.
[12] McCabe, R.W. In *Inorganic Materials*; Bruce, D.W.; O'Hare, D. Eds.; Wiley & Sons Ltd: Weinheim, **1992**, pp. 295-351.
[13] Campanati, M.; Vaccari, A. In *Fine chemicals through heterogeneous catalysis*; Sheldon, R. A.; van Bekkum, H. Eds.; Wiley-VCH: Weinheim, **2001**, pp. 61-79.
[14] Busca, G. *Chem. Rev.*, **2007,** *107*, 5366.
[15] De Stefanis, A.; Tomlinson, A.A.G. *Catal. Today*, **2006**, *114*, 126.
[16] Ravichandran, J.; Sivasankar, B. *Catal. Present Future,* **1995**, 161.
[17] Fraile, J.M.; Garcia, J.I.; Gracia, D.; Mayoral, J.A.; Tarnai, T.; Figueras F. *J. Mol. Catal. A. Chem.*, **1997**, *121*, 97.
[18] Rudakov, G.A. *Zhur. Obsh. Khim.*, **1946**, *16*, 261.
[19] Wystrach, V.P.; Barnum, L.H.; Garber M. *J. Am. Chem. Soc.*, **1957**, *79*, 5786.
[20] Volzone, C.; Masini, O.; Comelli, N.A.; Grzona, L.M.; Ponzi, E.N.; Ponzi, M.I. *Mater. Chem. Phys*., **2005**, *93*, 296.
[21] Volzone, C.; Masini, O.; Comelli, N.A.; Grzona, L.M.; Ponzi, E.N.; Ponzi, M.I. *Appl. Catal. A. Gen*., **2001**, *214*, 213.
[22] Besun, N.; Ozkan, F.; Gunduz, G. *Appl. Catal. A. Gen*., **2002**, *224*, 285.
[23] Gündüz, G.; Murzin, D.Yu. *React. Kinet. Catal. Lett*., **2002**, *75*, 231.
[24] Yadav, M.Kr.; Chudasama, C.D.; Jasra, R.V. *J. Mol. Catal. A. Chem.*, **2004**, *216*, 51.
[25] Batalova, S.B.; Mukitanova, T.R.; Dzhakisheva, R.D. *Izv. Akad. Nauk. Kaz. SSR Ser. Khim.*, **1977**, *2*, 71.
[26] Ovcharenko, F.D.; Dimov, I.Ya.; Tarasevich, Yu.I. *Ukr. Khim. Zh.*, **1983**, *49*, 24.
[27] Brown, D.R.; Rhodes, C.N. *Catal. Lett*., **1997**, *45*, 35.
[28] Hart, M.P.; Brown, D.R. *J. Mol. Catal. A. Chem*., **2004**, *212*, 315.
[29] Breen, C.; Watson, R. *Appl. Clay Sci.*, **1998**, *12*, 479.
[30] Breen, C.; Watson, R.; Madejova, J.; Komadel, P.; Klapyta, Z. *Langmuir*, **1997**, *13*, 6473.
[31] Breen, C.; Moronta, A. *J. Phys. Chem. B*, **1999**, *103*, 5675.
[32] Breen, C.; Moronta, A. *J. Phys. Chem. B*, **2000**, *104*, 2702.
[33] De Stefanis, A.; Perez, G.; Ursini, O.; Tomlinson, A.A.G. *Appl. Catal. A. Gen.*, **1995**, *132*, 353.
[34] Fernandes, C.; Catrinescu, C.; Castilho, P.; Russo, P.A.; Carrott, M.R.; Breen, C. *Appl. Catal. A. Gen.*, **2007**, *318*, 108.
[35] Catrinescu, C.; Fernandes, C.; Castilho, P.; Breen, C. *Appl. Catal. A. Gen.*, **2006**, *311*, 172.
[36] Rudakov, G.A.; Artamonov, G.A. *J. Gen. Chem.*, **1945**, *15*, 75.
[37] Singh, B.; Patial, J.; Sharma, P.; Agarwal, S.G.; Qazi, G.N.; Maity, S. *J. Mol. Catal. A. Chem.*, **2007**, *266*, 215.
[38] Tateiwa, J.; Kimura, A.; Takasuka, M.; Uemura, S. *J. Chem. Soc. Perkin Trans. 1*, **1997**, 2169.
[39] Ardashov, O.V.; Il'ina, I.V.; Korchagina, D.V.; Volcho, K.P.; Salakhutdinov, N.F. *Mendeleev Commun*., **2007**, *17*, 303.
[40] Il'ina, I.V.; Volcho, K.P.; Korchagina, D.V.; Barkhash, V.A.; Salakhutdinov, N.F. *Helv. Chim. Acta*, **2006**, *89*, 507.
[41] Bessiere-Chretien, Y.; Montheard, J.P.; El Gaied, M.M.; Bras, J.P. *C. R. Acad. Sci. Ser C.*, **1971**, *273*, 272.
[42] Mukhamedova, L.A.; Nasybullina, F.G.; Kudryavtseva, M.I. *Izv. Akad. Nauk. SSSR Ser. Khim*., **1979**, *28*, 847.
[43] Salomatina, O.V.; Yarovaya, O.I.; Korchagina, D.V.; Gatilov, Yu.V.; Polovinka, M.P.; Barkhash, V.A. *Russ. J. Org. Chem*., **2006**, *42*, 1313.

[44] Salomatina, O.V.; Yarovaya, O.I.; Korchagina, D.V.; Polovinka, M.P.; Barkhash, V.A. *Mendeleev Commun*., **2005**, 59.

[45] Salomatina, O.V.; Kuznetsova, T.G.; Korchagina, D.V.; Paukshtis, E.A.; Moroz, E.M.; Volcho, K.P.; Barkhash, V.A.; Salakhutdinov, N.F. *J. Mol. Catal. A. Chem*., **2007**, *269*, 72.

[46] Il'ina, I.V.; Volcho, K.P.; Korchagina, D.V.; Barkhash, V.A.; Salakhutdinov, N.F. *Helv. Chim. Acta*, **2007**, *90*, 353.

[47] Salakhutdinov, N.F.; Volcho, K.P.; Il'ina, I.V.; Korchagina, D.V.; Tatarova, L.E.; Barkhash, V.A. *Tetrahedron*, **1998**, *54*, 15619.

[48] Il'ina, I.V.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Zh. Org. Khim*., **1999**, *35*, 491.

[49] Hamman, L.G.; Meyer, J.H.; Ruppar, D.A.; Marschke, K.B.; Lopez, F.G.; Allegretto, E.A.; Karanewsky, D.S. *Bioorg. Med. Chem. Lett*., **2005**, *15*, 1463.

[50] Volcho, K.P.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Tetrahedron Lett*., **1996**, *37*, 6181.

[51] Volcho, K.P.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **1999**, *35*, 1554.

[52] Royals, E.E. *J. Am. Chem. Soc*., **1949**, *71*, 2568.

[53] Yadav, M.K.; Jasra, R.V. *Catal. Commun*., **2006**, *7*, 889.

[54] Volcho, K.P.; Tatarova, L.E.; Suslov, E.V.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **2001**, *37*, 1418.

[55] Volcho, K.P.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Zh. Org. Khim*., **1994**, *30*, 941.

[56] Tatarova, L.E.; Yarovaya, O.I.; Volcho, K.P.; Korchagina, D.V.; Salakhutdinov, N.F.; Ione, K.G.; Barkhash, V.A. *Zh. Org. Khim*., **1995**, *31*, 982.

[57] Il'ina, I.V.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **2000**, *36*, 1446.

[58] Volcho, K.P.; Tatarova, L.E.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **2000**, *36*, 32.

[59] Volcho, K.P.; Korchagina, D.V.; Gatilov, Yu.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **1997**, *33*, 607.

[60] Il'ina, I.V.; Volcho, K.P.; Korchagina, D.V.; Salakhutdinov, N.F.; Barkhash, V.A. *Russ. J. Org. Chem*., **1999**, *35*, 673.

[61] Kuzakov, E.V.; Shmidt, E.N. *Chem. Nat. Comp*., **1998**, *34*, 594.

Received: April 01, 2008 **Revised: April 29, 2008** **Accepted: May 04, 2008**