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# INTERACTION OF (13S)-6-OXOLABD-7,14-DIEN-13-OL WITH PHENOLS ON THE CLAY ASKANITE-BENTONITE

**E. V. Kuzakov and É. N. Shmidt**

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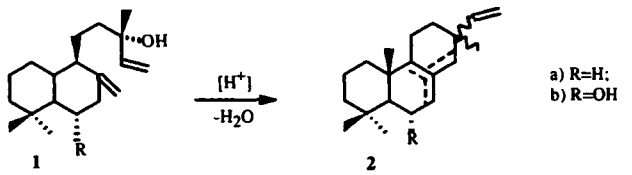
*The alkylation of some phenols with an allyl 6-oxolabdane alcohol in the presence of the clay askanite-bentonite has been investigated. It has been shown that during the reaction intermediate* ortho- *adducts of substitution in the aromatic nucleus are cyclized into chroman derivatives containing a bicyclic terpene residue — 2-methyl-2-(6′-oxo-$\Delta^{7}$-tetranorlabd-12′-yl)chromans. Performing the reaction in the presence of heterogeneous catalysts imposes limitations on the yields of certain products.*

Phenolic compounds containing an isoprenoid residue in their molecule are of interest in connection with the study of their biological activity, as is shown by the broad spectrum of such activity for natural terpenophenols [1—3]. The vitamin E activity of the tocopherols is widely known [4]; information on the synthesis of representatives of this class is also fairly voluminous [5]. However, reports of the activity of cyclic analogs of the tocopherols, which, in nature, are metabolites of some marine organisms [6], are still sparse, which is apparently explained by the small number of studies dealing with the synthesis of such compounds.

Thus, in the literature we have found only a paper by Gonzalez et al. [7] on the partial synthesis of a methyl ether of 3-deoxytaondiol from the tertiary labdane alcohol manool under acid-catalyzed conditions. As in the majority of methods for synthesizing tocopherols, here a two-stage scheme of obtaining the final product was used: initial alkylation of the phenol with the allyl alcohol followed by cyclization of the intermediate adduct into a chroman derivative.

In the present work we have shown the possibility of alkylating phenols with certain allyl alcohols of the labdane series under the conditions of catalysis by alumosilicates. The use of the latter presupposed the following changes in comparison with performing the reaction in a homogeneous medium. In the first place, it had been found previously that alumosilicates catalyze both the alkylation of phenols [8] and cyclization processes involving the hydroxy group of a phenol [9], in view of which we proposed a one-stage — i.e., without the isolation of intermediate products — preparation of the desired chroman derivatives. Then, in a possible scaling up of the process, its ecologically pure performance, with no waste waters, would be ensured. And, finally, the possibility of a nonstandard course of the process, as compared with a homogeneous medium, was not excluded.

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Initially, as potential alkylating agents it was proposed to use readily available labdane alcohols — 13-epimanool (**1a**) and larixol (**1b**) — which are easy to isolate from the oleoresin of conifers of the *Larix* genus. It had been found earlier [10] that the exocyclic position of the double bond in the molecules of these alcohols favored their rapid intramolecular cyclization in the presence of acid catalysts. In analogy with this, in our case, in the presence both of zeolites and of the clay askanite-bentonite, the alcohols (**1a**) and (**1b**), containing a $\Delta^{8(17)}$-bond predominantly underwent cyclization into the corresponding

Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, Novosibirsk, fax 8(3832) 3 54 752; e-mail: shreerd@nioch.nsc.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 653—662, September-October, 1998. Original article submitted January 12, 1998.



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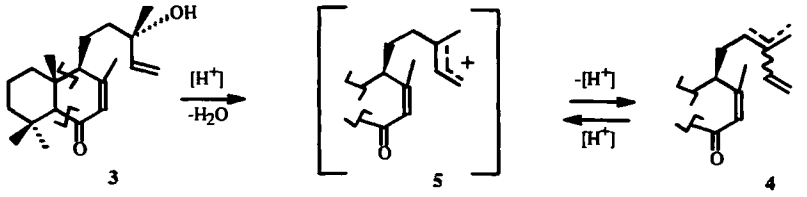
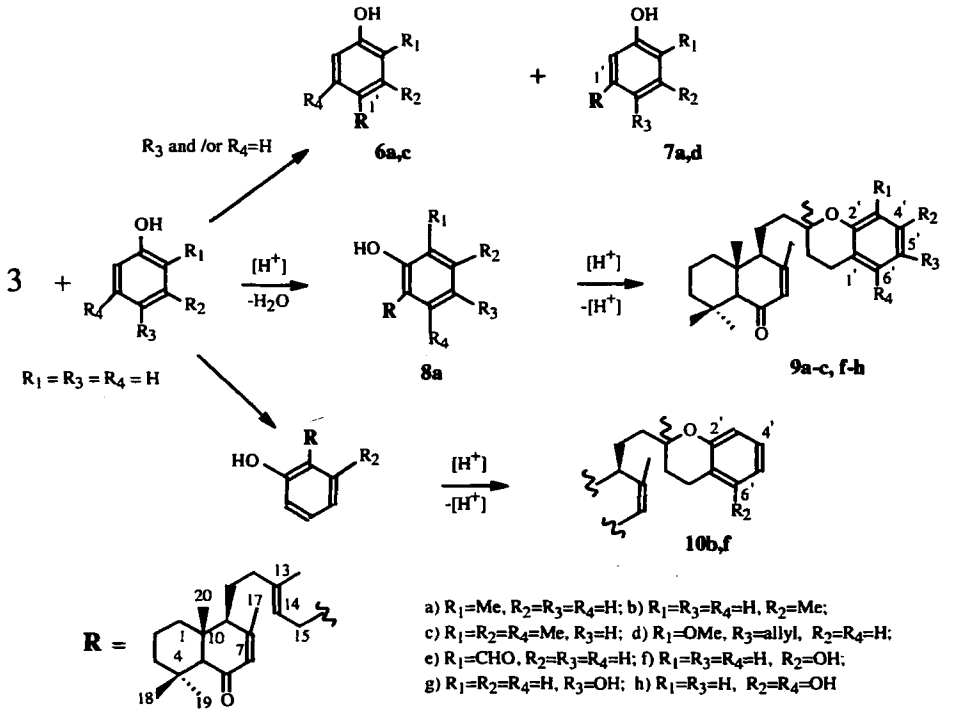
pimaradiene derivative (**2a**) or, partially, (**2b**).

A change in the order of addition of the reactants, the use of the less active zeolites NaY and NaX, and also the addition of alkylation promotors tested previously on zeolites [11], had practically no influence on the ratio of the rates of alkylation processes — intramolecular cyclization in the case of the alcohols (**1a, b**). Later, therefore, as the initial compound we chose an alcohol with an endocyclic double bond obtained in quantitative yield from larixol (**1b**) — (13S)-6-oxolabd-7,14-dien-13-ol (**3**). According to Gonzalez et al. [10], in the presence of zeolite HY the ketoalcohol (**3**) is converted only into a mixture of the unsaturated ketones (**4**) by dehydration, presumably via the ion (**5**).




The use of feebly active zeolites as alkylation catalysts sharply lowers the conversion of the substrate, while the use of the active β-zeolites leads to the formation of an appreciable amount of polymers. The best yields of the desired products of the chroman type, starting from the ketoalcohol (**3**), were obtained in the presence of the clay askanite-bentonite, and this was used subsequently as the catalyst.




a) $R_1$=Me, $R_2$=$R_3$=$R_4$=H; b) $R_1$=$R_3$=$R_4$=H, $R_2$=Me;
c) $R_1$=$R_2$=$R_4$=Me, $R_3$=H; d) $R_1$=OMe, $R_3$=allyl, $R_2$=$R_4$=H;
e) $R_1$=CHO, $R_2$=$R_3$=$R_4$=H; f) $R_1$=$R_3$=$R_4$=H, $R_2$=OH;
g) $R_1$=$R_2$=$R_4$=H, $R_3$=OH; h) $R_1$=$R_3$=H, $R_2$=$R_4$=OH

From the mixture of products obtained by keeping equimolar amounts of the ketoalcohol (**3**) and *ortho*-cresol on the clay askanite-bentonite ($CH_2Cl_2$, 25°C) [12], four condensation products were obtained: compounds (**6a—8a**), and also trace amounts of the desired product of further cyclization (**9a**), formed, as we have shown, from the *ortho*- isomer (**8a**). More severe temperature conditions are required for the more complete cyclization of the *ortho*- product (**8a**) into the chroman compound (**9a**): on the addition of benzene to the reaction mixture described above, followed by further boiling, the *ortho*- isomer was completely converted into the cyclized product (**9a**). However, the performance of the same sequence of reactions in dichloroethane led to the formation of compounds (**6a**, **7a**, and **9a**) in the ratio shown in Table 1. In the case of the reaction in boiling dichloroethane, the *ortho*- isomer (**8a**) was absent from the mixture, and we therefore used just this variant of the method subsequently for the most complete possible conversion of the intermediate products into cyclized chroman derivatives.

TABLE 1. Results of the Interaction of the Ketoalcohol (3) with Certain Phenols on the Clay Askanite -Bentonite (boiling in dichloroethane, equimolar ratio of reactants)

| Name of the phenol | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Amounts of products in the mixture (%, GLC) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 6 | 7 | 9 | 10 |
| *ortho*-Cresol (a) | Me | H | H | H | 30*'*** | 20*' *** | 25 | |
| *meta*-Cresol (b) | H | Me | H | H | - | - | 50 | 10 |
| 2,3,5-Trimethylphenol (c) | Me | Me | H | Me | 3* | - | 10 | |
| Eugenol (d) | OMe | H | Allyl | H | - | 7* | Tr. | |
| Salicylaldehyde (e) | CHO | H | H | H | - | - | - | |
| Resorcinol (f) | H | OH | H | H | - | - | 78* | 8 |
| Hydroquinone (g) | H | H | OH | H | - | - | ~20*'** | |
| Phloroglucinol (h) | H | OH | H | OH | - | - | <5*'** | |

* In the form of methyl ethers of phenols.

**Partially oxidized during chromatography.

***Ratio of the isomers determined from the PMR spectrum of their mixture.

As was found, a variation in the structure of the phenol did not entail appreciable changes in the direction of the process but affected only the yield of alkylation products. Below we give the results of the interaction of the ketoalcohol (**3**) with various phenols in the presence of askanite-bentonite (see Table 1). The structures of adducts (**8a**) and (**9a** and **f**) were established on the basis of their $^{1}H$ and $^{13}C$ NMR spectra, while the structures of (**6a** and **c**, **7a** and **d**, **9b**, **c**, **g**, and **h**, and **10b** and **f**) are proposed on the basis of an analysis of the chemical shifts and multiplicities of the signals of the protons in the PMR spectra (Tables 2—4).

TABLE 2. Chemical Shifts* ($\delta_H$, ppm), Multiplicities, and SSCCs (Hz) of the Signals of the Protons of the Terpenoid Fragment of the Molecules of Compounds (**6a** and **c**, **7a** and **d**, **9b**, **c**, **g**, and **h**, and **10b** and **f**) in the PMR Spectra, $CDCl_3$

| | 6a | 6c | 7a | 7d | 9b | 9c | 9g | 9h | 10b | 10f |
|---|---|---|---|---|---|---|---|---|---|---|
| H-7 | 5.75 br.s | 5.73 br.s | 5.75 br.s | 5.72 br.s | 5.70 br.s | 5.74 br.s | 5.72 br.s | 5.71 br.s | 5.70 br.s | 5.72 br.s |
| H-14 | 5.27 t, J=7.0 | 5.27 t, J=7.0 | 5.30 t, J=7.0 | 5.24 br.t., J=7.0 | | | | | | |
| 2H-15 | 3.22 dm, J=7.0 | 3.27 m | 3.22 dm, J=7.0 | 3.20 dm, J=7.0 | 2.60 m | 2.59 dm, J=8.0 | 2.71 m | 2.85 m | 2.71 m | 2.68 m |
| 3H-16 | 1.72 s | 1.80 s | 1.72 s | 1.70 s | 1.23 s | 1.25 s | 1.25 s | 1.23 s | 1.16 s | 1.28 s |
| 3H-17 | 1.86 s | 1.82 s | 1.92 s | 1.89 s | 1.81 s | 1.79 s | 1.77 s | 1.90 s | 1.83 s | 1.80 s |
| 3H-18 | 1.11 s | 1.10 s | 1.13 s | 1.10 s | 1.12 s | 1.11 s | 1.10 s | 1.11 s | 1.13 s | 1.12 s |
| 3H-19 | 1.14 s | 1.13 s | 1.16 s | 1.12 s | 1.14 s | 1.14 s | 1.13 s | 1.12 s | 1.15 s | 1.13 s |
| 3H-20 | 0.82 s | 0.84 s | 0.87 s | 0.80 s | 0.85 s | 0.85 s | 0.83 s | 0.85 s | 0.84 s | 0.83 s |

*For each compound taken individually, the signals of the 3H-18 and 3H—19 methyl proton may be interchanged. The spectrum of the isomers (**6a**) and (**7a**) was recorded for an equimolar mixture of them; the signals for corresponding protons of these compounds may be interchanged.

TABLE 3. Chemical Shifts* ($\delta_H$, ppm), Multiplicities, and SSCCs (Hz) of the Signals of the Protons of the Phenol** Fragment of the Molecules of Compounds (**6a** and **c**, **7a** and **d**, **9b**, **c**, **g**, and **h**, and **10b** and **f**) in the PMR Spectra, $CDCl_3$

| | **6a** | **6c** | **7a** | **7d** | **9b** | **9c** | **9g** | **9h** | **10b** | **10f** |
|---|---|---|---|---|---|---|---|---|---|---|
| H-2' | 6.83 d, J=2.5 | - | 6.85 d, J=2.5 | 6.62[a]s | - | - | - | - | - | - |
| H-3' | - | - | - | - | 6.60 d, J=2.5 | - | 6.72 d, J=8.5 | 8.11[a]d, J=2.5 | 6.63[a]dd, J=8.5; 2.5 | 6.75[a]dd, J=8.5; 2.5 |
| H-4' | - | - | - | - | - | - | 6.60 dd, J=8.5; 2.5 | - | 7.05 t, J=8.5 | 6.33 d, J=8.5 |
| H-5' | 6.63 d, J=8.5 | 6.41 s | 6.64 d, J=8.5 | 6.73[a]s | 6.57 dd, J=8.5; 2.5 | 6.49 s | - | 8.14[a]d, J=2.5 | 6.95[a]dd, J=8.5; 2.5 | 6.77[a]dd, J=8.5; 2.5 |
| H-6' | 6.78 dd, J=8.5; 2.5 | - | 6.79 dd, J=8.5; 2.5 | - | 6.87 d, J=8.5 | - | 6.49 d, J=2.5 | - | - | - |

*The proton signals marked with the same letter within a single column may be interchanged. The signals of corresponding protons in compounds (**6a**) and (**7a**) may be interchanged.

**The chemical shifts of the methyl groups attached to the aromatic ring in adducts (**6a** and **c**, **9b** and **c**, and **10b**) and those of the allyl and methoxy groups in compound (**7d**) correspond to those for the initial phenols.

The following conclusions can be drawn from the results obtained. In the first place, some characteristic features observed previously in the alkylation of phenols in a homogeneous medium have been confirmed. In particular, phenols containing acceptor groups (salicylaldehyde) do not take part in the reaction to an appreciable extent. When there is no difference in steric hindrance the rate of the reaction in the case of a nonconcerted electronic influence of substituents in the phenol is far lower (hydroquinone in comparison with resorcinol). When there is an alternative possibility of alkylation in the *ortho-* or *para-* position to the phenolic hydroxyl there is a tendency, observed earlier [13] in the presence of Lewis acids and aluminum alcoholates, to the formation of the *ortho-* isomers (**8**), leading subsequently to cyclization products of type (**9**) (*meta*-cresol, 2,3,5-trimethylphenol).

Further, the presence of a heterogenous catalyst introduces a substantial limitation to the steric control of the reaction. In particular, attack of the hypothetical ion (**4**) at an unsubstituted aromatic carbon atom having two substituents different from hydrogen in the *ortho-* positions is strongly hindered even when the substituents exert a favorable orienting influence. Thus, in the cases of phloroglucinol and 2,3,5-trimethylphenol alkylation is possible only at such aromatic carbon atoms, which leads to low over-all yields of products. However, in the cases of resorcinol and *meta*-cresol the influence of the same factor leads to the selective formation of products of type (**9**).

According to $^{13}C$ NMR spectra, in the cases of resorcinol and *ortho*-cresol the corresponding products with the (**9**) structure each consists of a mixture of isomers — apparently the 13R- and 13S- epimers — in a ratio of 1:1, since the maximum difference $\Delta\delta_C$ for each of the two pairs of epimers (**9a**) and (**9f**) was observed for the signal of the C-13 atom and its environment. According to calculations performed for the geometrically optimized molecules of the 13R- an 13S- epimers of product (**9c**), the latter possess practically identical standard heats of formation $\Delta H^0_f$: -184.9 and -185.2 (MM+) and -192.7 and -193.2 (AM1) kcal/mole, respectively; in the case of their precursor — compound (**8f**) — the barrier ($\Delta G^{\#}$) to free rotation around the C14—C15 bond averages 1.75 kcal/mole (MM+) and, therefore, the two isomers have identical thermodynamic and kinetic stabilities, which agrees with the given ratio of the epimers of product (**9a**).

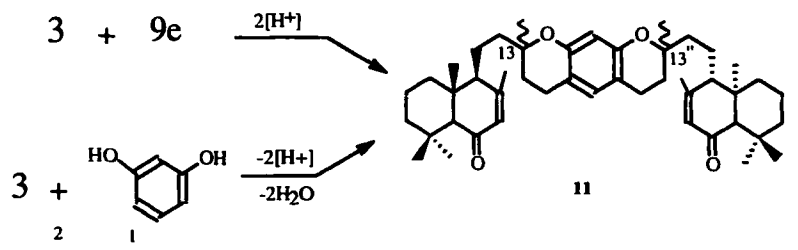
We have also shown that the reaction of ketoalcohol (**3**) with resorcinol, while giving the highest yield of chroman products (**9f**), can be used as a selective method of obtaining double-substitution products. Thus, in the case of a twofold excess of compound (**3**) in the reaction, just as in the interaction of adduct (**9f**) with the ketoalcohol under its conditions, the dimeric alkylation—cyclization product (**11**) was formed almost quantitatively.

TABLE 4. Chemical Shifts* and Multiplicities of the Signals in the $^{13}C$ NMR Spectra of Compound (**8a**), Mixtures of the 13R- and 13S-Epimers of Compounds (**9a** and **f**), and (**11**) in $CDCl_3$, $\delta_C$, ppm

| C atom | 8a | 9a | 9f | 11 |
|---|---|---|---|---|
| 1 | 38.49 t | 38.76 t | 38.56 t | 38.66 t |
| 2 | 18.06 t | 18.19 t | 18.01 t | 18.11 t |
| 3 | 43.03 [a] t | 43.26 [a] t | 43.03 a t | 43.27 [a] t |
| 4 | 32.14 s | 32.31 s | 32.12 s | 32.17 s |
| 5 | 55.52 d | 56.68 d | 56.71 d | 56.70 d |
| 6 | 200.16 s | 199.12 s | 200.91 s | 199.92 s |
| 7 | 128.44 d | 128.70 d | 128.12 d | 128.48 d |
| 8 | 158.69 s | 157.78 s | 159.58 s | 158.44 s |
| 9 | 63.48 d | 63.71 d | 63.57 d | 63.59 d |
| 10 | 41.78 s | 42.67 s | 42.00 s | 38.62 s |
| 11 | 25.28 t | 21.64 t | 20.63 t | 20.74 t |
| 12 | 29.57 t | 22.19 t | 21.21 t, 22.39 t | 21.72 t, 21.91 t |
| 13 | 137.12 s | 75.46 s ,75.48 s | 75.48 s, 75.80 s | 75.95 s, 75.68 s |
| 14 | 120.11 d | 31.28 t, 31.40 t | 30.49 t, 31.09 t | 31.16 t, 31.17 t |
| 15 | 43.03 [a] t | 43.15 [a] t | 43.39 [a] | 43.10 [a] t |
| 16 | 21.38 [b] q | 21.53 [b] q | 23.62 q, 23.90 q | 23.65 q, 23.82 q |
| 17 | 21.93 [b] q | 21.91 [b] q | 21.68 [b] q | 21.27 [b] q |
| 18 | 33.31 q | 33.53 q | 32.16 q | 33.35 q |
| 19 | 15.73 q | 16.06 [a] q | 21.03 [b] q | 20.68 [b] q |
| 20 | 14.58 q | 14.78 q | 14.56 q | 14.59 q |
| 1' | 123.95 s | 119.84 s | 112.55 s | 112.69 s |
| 2' | 151.82 s | 151.67 s | 154.57 [c] s | 152.97 s |
| 3' | 127.29 s | 125.85 s | 129.77 d | 129.28 d |
| 4' | 123.07 [c] d | 119.21 [d] d | 155.48 [c] s | - |
| 5' | 127.29 [c] d | 126.90 [d] d | 108.50 d | - |
| 6' | 128.85 [c] d | 128.46 [d] d | 103.74 d | 104.64 d |
| 7' | 16.17 q | 16.08 [c] q | - | - |

*Within any one column, the values of the chemical shifts marked with the same letters should possibly be interchanged.

In the PMR spectrum of compound (**11**), the signals of the protons corresponding to the terpene fragments have a doubled intensity in comparison with the signals of the aromatic protons. In the $^{13}C$ NMR spectrum, paired signals were observed for some carbon atoms, obviously, as in the case of the product of monoalkylation (**9f**), corresponding to the R- and S- configurations of the asymmetric centers at the C-13 atoms. Judging from everything, compound (**11**) was a mixture of three diastereomers: (13R,13"R), (13R,13"S), and (13S,13"S).




In all cases, we also isolated from the reaction mixture the unsaturated ketones (**4**) — products of the dehydration of the

initial ketoalcohol — the amount of which was a maximum at the start and gradually decreased as the reaction proceeded. The employment of these compounds in the reaction with phenols led to the same set of products as in the case of the alcohol (**3**), but at the same time it became necessary to lengthen the reaction time and to increase the amount of catalyst. The acidity of the clay is apparently sufficient for the protonation of the side-chains of these compounds, which expands the list of potential substrates for this reaction. In particular, the same system of conjugated double bonds in the side chain is present in widespread components of conifer oleoresins — *cis*- and *trans*-abienols, neoabienol, and communic acids.

We have not found in the literature any of the products of initial alkylation, (**6a** and **c**, **7a** and **d**, and **8a**) or those of subsequent cyclization (**9a**—**c** and **f**—**h**, and **10b** and **f**) or, again, of compound (**11**).

Thus, we have shown the possibility of alkylating phenols with tertiary allyl 6-oxolabdane alcohols and also with the conjugated dienes (**4**) in the presence of a clay. The intermediate *ortho*-alkylation products (**8**) may undergo cyclization to form chroman derivatives of type (**9**) or (**10**), depending on the structure of the phenol. It has been found that the presence of the catalyst imposes restrictions on the yields of certain reaction products. A series of cyclic analogs of tocopherols has been obtained and it has been shown that where there is a favorable conjunction of factors the selective formation of products of double alkylation—cyclization is possible.

## EXPERIMENTAL

Melting points were measured on a Kofler stage. Specific rotations were determined on a Polamat A polarimeter at 578 nm for solutions in $CHCl_3$. The recording of the mass spectrum of compound (**11**) was made on a Finnigan MAT 8200 spectrometer.

$^1H$ and $^{13}C$ NMR spectra* were recorded on Varian-WP 200SY (200 MHz for $^1H$) and Bruker AC-200 (200.13 MHz for $^1H$ and 50.21 MHz for $^{13}C$) spectrometers for 2—18% solutions in $CDCl_3$. Chloroform was used as an internal standard: $\delta_H$ 7.24 ppm; $\delta_C$ 79.60 ppm.

Details of the $^{13}C$ NMR spectra are given in Table 4.

GLC was conducted on a Chrom-5 instrument with a 0.3 × 125 cm column; liquid phase, 5% of SE-30 on Chromaton; carrier gas, nitrogen, at a rate of feed of 0.8—1.0 ml/min; detector, flame-ionization; evaporator temperature 180—270°C.

Mixture of compounds were separated by CC on KSK silica gel with grain sizes of 63—71, 71—90, and 90—125 μm, the eluent being mixtures of pentane or hexane with increasing proportions of diethyl ether (DE).

Monitoring was carried out on Silufol-254 (UV) or Merck Kieselgel-60 (F 254) plates. To detect the spots we used a UV lamp, iodine vapor, and/or treatment of the chromatograms with concentrated $H_2SO_4$.

The askanite-bentonite was obtained by acid activation of bentonitic clays of the Askan group of deposits (Makharadze, Georgia; it corresponded to GOST [State Standard] 113—12—86—82) and was passed through a sieve with cell dimensions of 760 μm. The clay was additionally activated by heating at 120—130°C for 3—3.5 h immediately before the reactions.

Zeolites of types NaY and NaX were industrial products; the β-zeolites were synthesized in Institute of Catalysis, Siberian Division of the Russian Academy of Sciences. Before use in a reaction, the freshly calcined catalysts were cooled in a desiccator with $P_2O_5$ for 5 min.

For the performance of the reactions in the presence of the alumosilicates we used anhydrous solvents.

**Interaction of the Ketoalcohol (3) with *ortho*-Cresol on the Clay Askanite-Bentonite.** A solution of 0.090 g of the ketoalcohol (**3**) and 0.050 g of *o*-cresol in 2.5 ml of $CH_2Cl_2$ was added to 0.5 g of a suspension of the clay in 2.0 ml of $CH_2Cl_2$. The mixture was stirred at room temperature for 3 h, after which the catalyst was removed, the products (0.150 g) were dissolved in DE, and the solution was treated with 5% NaOH, and washed with water. The alkaline solution was brought to a weakly acid reaction and was extracted with DE (3 × 10 ml). The ethereal extract was washed with water and dried with anhydrous $Na_2SO_4$. After elimination of the solvent, we obtained: 0.090 g of a neutral fraction (NF) with the composition (%; GLC of the mixture methylated with dimethyl sulfate): unsaturated ketones (**4**) — 20; the adduct (**8a**) — 25; a mixture of compounds (**6a** and **7a**) — 50. The acid fraction (AF), 0.010 g, consisted wholly of unchanged *o*-cresol. By chromatographing the NF on 3.0 g of $SiO_2$ (63—71 μm) with 5 to 15% of DE in hexane as eluent, we isolated: 0.018 g of a mixture of unsaturated ketones (**4**), the NMR spectra of which agreed with those given in the literature [10], 0.020 g of the alkylation product (**8a**), and 0.041 g of the sum of the isomers (**6a**) and (**7a**).

**2-(6′-Oxolabd-7′,13′-dien-15-yl)-6-methylphenol (8a).** Oily liquid, $[\alpha]_D^{21}$ +25.2° (*c* 1.748). PMR spectrum:0.83 (s, 3H-

*The numbering of the atoms in the $^1H$ and $^{13}C$ NMR spectra is given in accordance with the trivial numbering for terpene compounds.

20), 1.12 (s, 3H-18 or 3H-19), 1.15 (s, 3H-19 or 3H-18), 1.80 (s, 3H-16), 1.90 (br. s, 3H-17), 2.23 (s, Ar-Me), 3.39 (dm, $J_{15,14}$=7.0, 2H-15), 5.38 (t, $J_{14,15}$=7.0, H-14), 5.71 (qd, $J_{7,17}$ = 2.0 and $J_{7,9}$=1.5, H-7), 6.74 (d, $J_{ortho}$=8.5, H-5'), 6.97 (dd, $J_{ortho}$=8.5, and $J_{meta}$=2.5, H-4' or H-6'), 6.98 (dd, $J_{ortho}$=8.5, and $J_{meta}$=2.5, H-6' or H-4').

**Cyclization of the Adduct (8a).** A solution of 0.020 g of compound (**8a**) in 3.0 ml of benzene was treated with 0.05 g of askanite-bentonite. The mixture was boiled for 3 h, and then the catalyst and the solvent were eliminated, and the products were chromatographed on $SiO_2$ (71—90 μm). Elution with pentane—DE (93:7) led to the isolation of 0.015 g of compound (**9a**).

The alkylation of *ortho*-cresol with the ketoalcohol (**3**) (see above) was repeated, starting with 0.210 g of the ketoalcohol (**3**), 0.100 g of *ortho*-cresol, and 0.6 g of catalyst; after stirring in $CH_2Cl_2$ (5.0 ml) for 2 h the solvent was evaporated off, and then 5 ml of benzene was added and the mixture was boiled for 3 h and was worked up as described above. Part of the products was methylated with dimethyl sulfate and analyzed by GLC. Composition (%): unsaturated ketones (**4**) — 15; the chroman (**9a**) — 25; the adducts (**6a**) and (**7a**) — about 50. Boiling (5 h) the ketoalcohol (**3**) and *ortho*-cresol on clay in dichloroethane while observing the same ratio of the reactants yielded a mixture with the same composition.

**(2R, 2S)-2,8-Dimethyl-2-(13', 14',15',16'-tetranor-6'-oxo-Δ$^{7'}$-labd-12'-yl)-chroman (9a).** Oily liquid, $[\alpha]^{21}$+14.0° (*c* 3.566). PMR spectrum:0.84 (s, 3H-20), 1.08 (s, 3H-18 or 3H-19), 1.09 (s, 3H-19 or 3H-18), 1.13 (s, 3H-16), 1.74 (dd, $J_{17,7}$=2.0, $J_{17,9}$=1.5, 3H-17), 2.13 (s, Ar-Me), 2.76 (dm, J=12.0, 2H-15), 5.71 (dm, J=2.0,and 1.5, H-7), 6.69 (t, $J_{ortho}$=8.5, H-5'), 6.81 (dd, $J_{ortho}$=8.5, and $J_{meta}$=2.5, H-4' or H-6'), 6.86 (dd, $J_{ortho}$=8.5, and $J_{meta}$=2.5, H-6' or H-4').

Subsequently, the reactions of the ketoalcohol with phenols were conducted under the conditions of boiling in dichloroethane in the presence of askanite-bentonite. The treatment with a solution of alkali described above was used only in the case of monobasic phenols; in other cases the excess of the phenol, as the most polar compound in the mixture was separated in the process of chromatography. Below there are given the amounts of reactants taken (in grams): the ketoalcohol (**3**), the appropriate phenol (**b—d, g, h**), the catalyst, and the main cyclocondensation product (**9b—d, g, h**) isolated after chromatography of the total products: b) 0.110, 0.050, 0.50, and 0.070; c) 0.450, 0.210, 1.00, and 0.030; d) 0.150, 0.070, 0.40, and 0.015; g) 0.110, 0.045, 0.45, and 0.020; h) 0.200, 0.160, 0.60, and 0.015.

**Cyclocondensation of the Ketoalcohol (3) and Resorcinol.** A solution of 0.150 g of resorcinol in 3.0 ml of dichloroethane was added to 1.2 g of askanite-bentonite, and then, over 20 min, a solution of 0.420 g of the ketoalcohol (**3**) in 3.0 ml of dichloroethane was introduced. The mixture was boiled for 7 h, the catalyst was filtered off, and the solvent was evaporated to give 0.560 g of reaction products. Chromatography on $SiO_2$ (71—90 μm) with the eluent pentane—DE (from 5 to 20% of the latter) resulted in the isolation of 0.020 g of unsaturated ketones (**4**), 0.015 g of the isomeric cyclocondensation product (**10f**), 0.026 g of the dimer (**11**), and 0.340 g of the adduct (**9f**).

**(2R,2S,8R,8S)-2,8-Dimethyl-2,8-di(13',14',15',16'-tetranor-6'-oxo-Δ$^{7'}$-labd-12'-yl)-3,4,7,8-tetrahydro-benzo[1,2-b; 5,4-b']dipyran (11).** Amorphous powder, mp 72—84°C (hexane—ethyl acetate (9:1)), $[\alpha]^{21}$+21.9° (*c* 3.829). Found: 682.4958. Calculated for $C_{46}H_{66}O_4$ 682.4961. Mass spectrum, *m/z* (%): 682 ($M^+$, 100 ).PMR spectrum: 0.83 (s, 2×3H-20), 1.10 (s, 2× 3H-18 or 2×3H-19), 1.13 (s, 2×3H-19 or 2×3H-18), 1.26 (s, 2×3H-16), 1.82 (br. s, H-17), 2.69 (m, 2×2H-15), 5.72 (2H, m, 2×1H-7), 6.19 (s, H-3'), 6.72 (s, H-6').

**(2R, 2S)-2-Methyl-2-(13',14',15',16'-tetranor-6'-oxo-Δ$^{7'}$-labd-12'-yl)-7-hydroxychroman (9f).** Mp 158—163°C (hexane—ethyl acetate, 9:1), $[\alpha]^{21}$+17.5° (*c* 3.321). PMR spectrum:0.84 (s, 3H-20), 1.11 (s, 3H-18 or 3H-19), 1.14 (s, 3H-19 or 3H-18), 1.26 (s, 3H-16), 1.82 (br. s, 3H-17), 2.69 (m, 2H-15), 5.72 (br. s, H-7), 6.27 (d, $J_{meta}$=2.5, H-3'), 6.33 (dd, $J_{ortho}$ = 8.5, $J_{meta}$ =2.5, H-5'), 6.88 (d, $J_{ortho}$ =8.5, H-5' or H-6').

**Reaction Forming the Dimer (11).** a) A solution of 0.50 g of the ketoalcohol (**3**) and 0.10 g of resorcinol in dichloroethane was boiled for 4 h in the presence of 0.15 g of clay. After working up, the mixture was chromatographed with elution by 7% DE in hexane, leading to the isolation of 0.045 g of the dimer (**11**). Yield 85% of theoretical. b) A dichloroethane solution of 0.040 g of the adduct (**9a**) was added to a solution of 0.010 g of resorcinol in dichloroethane in the presence of 0.1 g of clay. After being boiled for 4 h, the mixture was worked up and the product was subjected to chromatography with elution by pentane—DE (85:15). This gave 0.045 g of the dimer (**11**). Yield 90%.

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