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Double Heterocyclization in the Reaction of Unconjugated Dienes and Hydroxyolefins with Salicylaldehyde on the Askanite-Bentonite Clay

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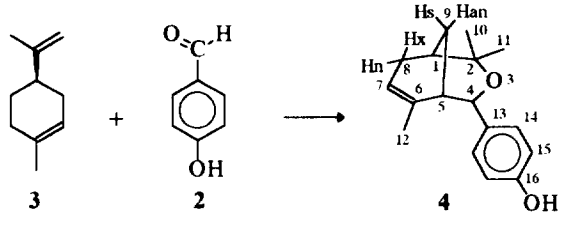
Abstract: The reaction of salicylaldehyde with some dienes and hydroxyolefins of natural origin on the askanite-bentonite clay under mild conditions was shown to lead to a double heterocyclization forming compounds with the xanthene framework, condensed with tetrahydropyran or tetrahydrofuran rings. Copyright © 1996 Elsevier Science Ltd

The reaction of dipentene and 1,2,4-trimethyl-4-isopropenylcyclohex-1-ene **1** with aliphatic and aromatic aldehydes on the askanite-bentonite clay was found by us earlier to lead to an unusual heterocyclization to give bicyclic ethers.[1] Now we have found that p-hydroxybenzaldehyde **2** also reacts with R-(+)-limonene **3** (askanite-bentonite clay, 20 °C, CH_2Cl_2, 2 hr.) with formation of 2,2,6-trimethyl-4-(4-hydroxyphenyl)-3-oxabicyclo[3.3.1]non-6-ene **4** in 39% yield (Scheme 1).

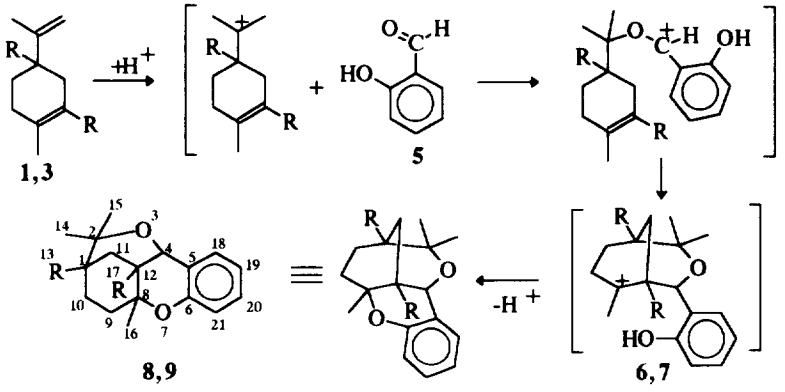


3 **2** **4**

Scheme 1

In the case of the interaction of dienes **1** or **3** with the ortho-isomer of aldehyde **2** - the salicylaldehyde **5** (askanite-bentonite clay, 20 °C, CH_2Cl_2, 6-9 hr.) the process does not stop, as in the previous cases, at the stage of the formation of bicyclic ethers. The cationic center in the presumed intermediates **6** and **7** could be trapped by the phenolic hydroxy group to yield 1,2,2,8,12-pentamethyl-3,7-dioxa-5,6-benzotricyclo-[6.2.2.$0^{4,12}$]dodecane **8** and 2,2,8-trimethyl-3,7-dioxa-5,6-benzotricyclo[6.2.2.$0^{4,12}$]dodecane **9**, respec-

tively (Scheme 2).



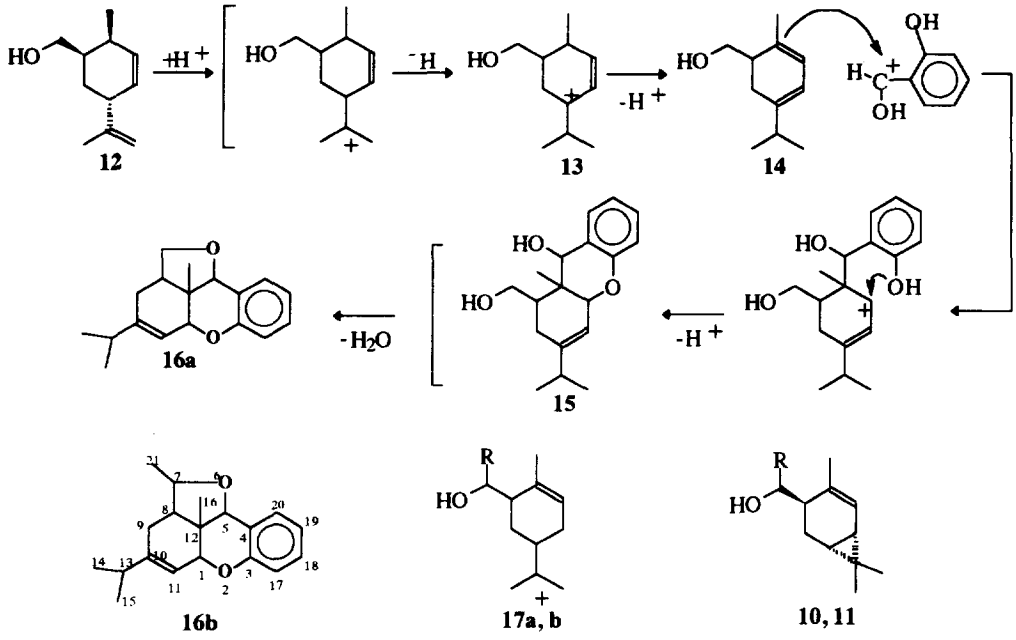
1, 6, 8 - R=CH_3; **3, 7, 9** - R=H

Scheme 2

Compound **8** (yield 75%) and **9** (yield 28%), containing the xanthene framework, condensed with a tetrahydropyran ring, were isolated from the reaction mixtures by consecutive chromatography on SiO_2 (40-100 μ) and Al_2O_3 (neutral).

The reaction of aldehyde **5** with the hydroxyolefins of the carane and menthane series, - trans-4-hydroxymethyl-2-carene **10**, trans-4-(1-hydroxyethyl)-2-carene **11** and (1S,4R,6R)-6-hydroxymethyl-p-mentha-2,8(9)-diene **12** (askanite-bentonite clay, 20-40 ^{0}C, CH_2Cl_2, 0.5-4 hr.) also gave products containing the xanthene framework. However, in these examples, a tetrahydrofuran ring is appended. This, together with the different location of the alkyl substituents, indicates transformation via another route is occurring.

The tentative mechanism of the reaction is presented in Scheme 3 for the case of the interaction between the hydroxyolefin **12** and the aldehyde **5**. In the first step, protonation of the exocyclic double bond occurs, followed by a [1,2] hydrogen shift to give the ion **13**. After loss of a proton the intermediate **14** reacts with the protonated aldehyde **5**. A further possibility consists of two intramolecular heterocyclizations to form the intermediate **15** which dehydrates to give the end product **16a** - 12-methyl-10-isopropyl-2,6-dioxa-3,4-benzotricyclo[6.3.1.$0^{5,12}$]dodec-10-ene in 18% yield. The reaction of hydroxyolefins **10** and **11** with aldehyde **5** under similar conditions occurs presumably by a similar route to give ions **17a** and **17b** (after the protonation, followed by the opening of the cyclopropane ring) and, finally, the compounds **16a** (yield 62%) and 7,12-dimethyl-10-isopropyl-2,6-dioxa-3,4-benzotricyclo[6.3.1.$0^{5,12}$]dodec-10-ene **16b** (yield 20%) respectively.



10, 17a - R=H **11, 17b** - R=CH_3

Scheme 3

The discovered reactions do not proceed in the absence of clay or in acetic acid medium. Compounds **16a** and **16b** appear to be unknown in literature and the compounds **8** and **9** have a novel ring skeleton. The structure of all new compounds was determined with the aid of ^1H and ^{13}C NMR.[2]

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REFERENCES AND NOTES

1. a) Volcho, K. P.; Tatarova, L. E.; Korchagina, D. V.; Salakhutdinov, N. F.; Aulchenko, I.S.; Ione, K. G.; Barkhash, V. A. *Zh. Org. Khim.* **1994**, 30, 641-653.
2. Analytical data for **4**: HRMS m/e for $C_{17}H_{22}O_2$: calcd. 258.1617, obsd. 258.1619. $[\alpha]^{20}_{580}$ +171.4^0 (c. 5.5, $CHCl_3$); mp: 141-142 ^{0}C, IR (ν_{max} cm^{-1}, $CHCl_3$): 3625, 3390. ^1H NMR (400.13 MHz, $CDCl_3$) δ: 0.90 (ddd, J 2.5, 2.5, 2, CH_3-12), 1.31 and 1.37 (s, CH_3-10 and CH_3-11), 1.53 (dddd, J 6.5, 3, 3, 1, H-1), 1.69 (ddd, J 12.5, 3, 3, H-9s), 2.06 (dddq, J 18.5, 6.5, 3, 2.5, H-8x), 2.11 (ddd, J 3, 3, 2.5, H-5), 2.31 (dddd, J 12.5, 3, 3, 1.5, H-9an), 2.38 (dm, J 18.5, H-8n), 4.81 (d, J 2.5, H-4), 5.43 (m, H-7), 6.69 (d, J 8, 2H-15), 7.14 (d, J 8, 2H-14). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 33.9 (d, C-1), 75.3 (s, C-2), 73.9 (d, C-4), 41.5 (d, C-5), 133.1 (s, C-6), 123.1 (d, C-7), 27.6 (t, C-8), 28.1 (t, C-9), 28.5 (q,

C-10), 23.8 (q, C-11), 24.0 (q, C-12), 134.9 (s, C-13), 126.8 (d, C-14), 114.7 (d, C-15), 154,2 (s, C-16).

Analytical data for **8**: oil, HRMS m/e for $C_{19}H_{26}O_2$: calcd. 286.1932, obsd. 286.1939. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 0.76 and 0.80 (s, CH_3-13 and CH_3-17), 1.15 and 1.34 (s, CH_3-14 and CH_3-15), 1.25 (ddd, J 14, 14, 5, H-10a), 1.40 (d, J 14, H-11), 1.42 (d, J 1, CH_3-16),1.48 (ddd, J 12.5, 5, 2, H-9e), 1.80 (dd, J 14, 3.5, H-11), 1.98 (dddd, J 14, 5, 3.5, 2, H-10e), 2.77 (dddd, J 14, 12.5, 5, 1, H-9a), 4.15 (s, H-4), 6.78 (d, J 8, H-21), 6.85(td, J 8, 1.5, H-19), 7.16 (d, J 8, H-18), 7.17 (td, J 8, 1.5, H-20). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 35.0 (s, C-1), 77.7 (s, C-2), 73.1 (d, C-4), 121.2 (s, C-5), 152.7 (s, C-6), 79.5 (s, C-8), 34.2 (t, C-9), 34.6 (t, C-10), 41.1 (t, C-11), 34.4 (s, C-12), 21.0 and 21.3 (q, C-13 and C-17), 24.2 and 25.4 (q, C-14 and C-15), 22.4 (q, C-16), 131.1 (d, C-18), 119.7 (d, C-19), 129.2 (d, C-20),116.5 (d, C-21).

Analytical data for **9**: oil, $[\alpha]^{20}_{580}$ +10.7^0 (c. 9.39, $CHCl_3$), HRMS m/e for $C_{17}H_{22}O_2$: calcd. 258.1619, obsd. 258.1622. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 1.23 and 1.43 (s, (s, CH_3-14 and CH_3-15), 1.40 (dddd, J 4, 3, 3 ,3, H-1), 1.53 (d, J 1, CH_3-16), 1.55 (m, H-10a, H-9e), 1.82 (br. ddd, J 3, 3, 3, H-12), 1.87 (ddd, J 13.5, 3, 3, H-11), 2.08 (ddddd, J 13.5, 5, 3, 3, 3, H-10e), 2.32 (dddd, J 13.5, 3, 3, 3, H-11), 2.64 (br. ddd, J 13.5, 13.5, 5, H-9a), 4.62 (d, J 3, H-4), 6.81 (d, J 8, H-21), 6.85 (td, J 8, 1.5, H-19), 7.17 (dd, J 8,1.5, H-18), 7.18 (td, J 8, 1.5, H-20). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 34.5 (d, C-1), 74.6 (s, C-2), 66.4 (d, C-4), 121.9 (s, C-5), 153.1 (s, C-6), 77.4 (s, C-8), 32.1 (t, C-9), 25.9 (t, C-10), 26.4 (t, C-11), 36.5 (d, C-12), 28.2 and 24.1 (q, C-14 and C-15), 26.6 (q, C-16), 130.3 (d, C-18), 119.6 (d, C-19), 129.4 (d, C-20), 116.7 (d, C-21).

Analytical data for **16a**: oil, $[\alpha]^{20}_{580}$ -25.2^0 (c. 8.7, $CHCl_3$); HRMS m/e for $C_{18}H_{22}O_2$: calcd. 270.1619, obsd. 270.1622. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 1.042 (d, J 7, CH_3-14), 1.044 (d, J 7, CH_3-15), 1.13 (s, CH_3-16), 2.14 (dd, J 17, 3, H-9), 2.23 (dddd, J 17, 6.5, 2, 1.5, H-9), 2.30 (br. qq, J 7, 7, H-13), 2.45 (dddd, J 9, 8, 6.5, 3, H-8), 3.66 (dd, J 9, 8, H-7), 3.97 (dd, J 8, 8, H-7), 3.98 (br. d, J 4.5, H-1), 4.50 (s, H-5), 5.64 (br. d, J 4.5, H-11) 6.95 (d, J 8, H-17), 6.97 (td, J 8, 1.5, H-19), 7.23 (td, J 8, 1.5, H-18), 7.27 (dd, J 8, 1.5, H-20). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 78.1 (d, C-1), 156.4 (s, C-3), 126.7 (s, C-4), 83.1 (d, C-5), 73.0 (t, C-7), 44.5 (d, C-8), 24.5 (t, C-9), 146.5 (s, C-10), 116.9 (d, C-11), 46.3 (s, C-12), 34.6 (d, C-13), 20.8 (q, C-14), 20.6 (q, C-15), 23.8 (q, C-16), 117.4 (d, C-17), 129.5 (d, C-18), 121.8 (d, C-19), 129.4 (d, C-20).

Analytical data for **16b**: oil, $[\alpha]^{20}_{580}$ -24.9^0 (c. 3.1, $CHCl_3$); HRMS m/e for $C_{19}H_{24}O_2$: calcd. 284.1776, obsd. 284.1772. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 1.02 (d, J 7, CH_3-14), 1.03 (d, J 7, CH_3-15), 1.18 (s, CH_3-16), 1.23 (d, J 6.5, CH_3-21), 1.98 (dd, J 15, 6, H-9), 2.11 (ddd, J 8, 6, 6, H-8), 2.29 (m, H-9), 2.30 (br. qq, J 7, 7, H-13), 4.13 (d, J 5, H-1), 4.25 (qd, J 6.5, 6, H-7), 4.36 (s, H-5), 5.64 (ddd, J 5, 1.5, 1 5, H-11), 6.94 (dd, J 8, 1.5, H-17), 6.96 (td, J 8, 1.5, H-19), 7.21 (td, J 8, 1.5, H-18), 7.31 (dd, J 8, 1.5, H-20). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 79.6 (d, C-1), 155.9 (s, C-3), 125.1 (s, C-4), 82.0 (d, C-5), 76.7 (d, C-7), 51.1 (d, C-8), 24.9 (t, C-9), 151.9 (s, C-10), 117.9 (d, C-11), 48.4 (s, C-12), 34.6 (d, C-13), 20.8 (q, C-14), 20.3 (q, C-15), 26.7 (q, C-16), 117.8 (d, C-17), 129.9 (d, C-18), 121.8 (d, C-19), 129.3 (d, C-20), 15.4 (q, C-21).

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