oxidation product to saturated K_2CO_3 at room temperature led to a 70:30 mixture of the expected sulfoxide and the title compound. The latter was isolated in 23% yield by flash chromatography (silica gel 60, 80:20 hexane–ether): ^1H NMR ($CDCl_3$, Me_4Si) δ 1.61 (s, 3 H), 1.72 (s, 3 H), 2.97 (t, J = 7 Hz, 2 H), 5.16 (tt, J = 7, 1.5 Hz, 1 H), 6.06 (ddt, J = 16, 8, 1.5 Hz, 1 H), 6.82 (dt, J = 16, 7 Hz, 1 H), 9.53 (d, J = 8 Hz, 1 H).

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Registry No. 1, 79499-64-2; 7, 79499-65-3; 8, 79499-66-4; 9, 22842-10-0; 10, 22850-55-1; 11, 79499-67-5; 12, 79499-68-6; isoprenyl bromide, 870-63-3; geranyl bromide, 6138-90-5; 2-methyl-5-(phenylsulfinyl)-2-hepten-6-yne, 79499-69-7; 6-methyl-2,5-heptadienal, 79499-70-0.

Polymer-Catalyzed Protection of Alcohols

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Alcohols can be protected by reaction with dihydropyran to form tetrahydropyranyl ethers under acid catalysis (hydrochloric acid,[1,2] phosphorus oxychloride,[3] boron trifluoride etherate,[4] or *p*-toluenesulfonic acid[5,6,7]). These THP ethers have found wide use in organic synthesis because they are stable to alkali, Grignards, lithium aluminum hydride, chromium trioxide, and many other common reagents. THP ethers are easily converted back into the alcohols by dilute acid. In general, THP ether formation works better for primary and secondary alcohols than for tertiary alcohols. For example, Auterhoff and Egle[8] prepared the THP ether of cholesterol in 89% yield (*p*-toluenesulfonic acid catalyst) compared to only 32% for 2-methyl-2-pentanol. Perhaps steric hindrance and dehydration side reactions adversely affect the yields with tertiary alcohols.

Miyashita, Yoshikoshi, and Grieco[9] recently reported a new and efficient catalyst for tetrahydropyranylation: pyridinium *p*-toluenesulfonate. This work prompted us to test a variety of related polymeric salts for catalytic activity in alcohol protection. Easy reaction workup, in which a recyclable catalyst can be separated by filtration, was one desired goal. The other goal was to secure reasonable isolated yields (>80%) with tertiary alcohols under conditions where conventional catalysts are unsatisfactory.[10,11]

Table I. Tetrahydropyranylation of Alcohols in Benzene with Poly(4-vinylpyridinium *p*-toluenesulfonate) and Poly(2-vinylpyridinium *p*-toluenesulfonate) at 24 °C

	P-4VPTS		P-2VPTS	
alcohol	rctn time, h	isolated yield,[a] %	rctn time, h	isolated yield,[a] %
1-dodecanol	4	95	6	93
cyclohexanol	4.5	87	6	97
nopol[b]	5	90	7	90
geraniol	6	86	8	87
3-acetyl-1-propanol	6	75	4	72
cholesterol	7	95	8	90
benzhydrol	5	92	7	91
2-phenyl-2-propanol	4	81[c]	4	76[c]
1-methylcyclohexanol	3	85[c]	3	84[c]

[a] All products showed satisfactory spectral data and chromatographic purity. [b] 6,6-Dimethylbicyclo[3.1.1]-hept-2-ene-2-ethanol. [c] The molar ratio of dihydropyran to alcohol was 1.5 except with the two tertiary alcohols for which the ratio was 3. The tertiary alcohols gave over twice the yields achieved with pyridinium *p*-toluenesulfonate[9] under comparable conditions.

Three types of polymeric analogues to pyridinium *p*-toluenesulfonate proved useless in the tetrahydropyranylation of alcohols at 25 °C and 3–6 h reaction time: (1) the pyridinium salt of a sulfonated cation exchange resin, Dowex 50X8-50, (2) the *p*-toluenesulfonate salt of an anion-exchange resin, Amberlite IRA-400, and (3) the trifluoromethanesulfonate salt of poly(4-vinylpyridine). On the other hand, synthetically exploitable catalytic activity was observed for the *p*-toluenesulfonate salts of commercially-available poly(4-vinylpyridine) and poly(2-vinylpyridine). Isolated yields at the 0.5–2.0-g scale (room temperature, 3–8 h) exceeded 80% for most alcohols (Table I). As seen from the Experimental Section, reaction workup was simple. Two of the nine alcohols examined were tertiary but, nonetheless, gave good yields of tetrahydropyranyl ethers. Thus, both major objectives of the project were achieved.

Heterogeneous polymer-catalyzed protection of alcohols in roughly 3 times faster with a benzene solvent than with ether. Benzene swells the polymer and increases the rate. Catalysis apparently takes place on the polymer surface since stirring the polymer for several hours with benzene gave no detectable acid in the solvent phase. Polymer recovered after a reaction can be washed with solvent and used again with no impaired yield.

Experimental Section

Preparation of Catalyst. Poly(2-vinylpyridine) (Aldrich) or poly(4-vinylpyridine) (Polysciences) was added to methanol (1.05 g/25 mL) and the mixture was stirred at room temperature until dissolution. *p*-Toluenesulfonic acid monohydrate (1.90 g) was then added to the methanol followed, after a few minutes of stirring, by 9.00 g of Celite. The mixture was stirred well until the polymer derivative uniformly coated the inert support. Solvent removal with the aid of a rotary evaporator produced the catalysts, which was ground to a fine powder and dried under reduced pressure (25 °C, 3 mm) overnight. The product (11.1 g) was stored in a desiccator. The poly(4-vinylpyridinium *p*-toluenesulfonate) seemed to give the faster tetrahydropyranylation reactions es-

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pecially with nonaromatic solvents.

Two Typical Runs. P-4VPTS (1.00 g) was added to a mixture of 1-dodecanol (932 mg, 5 mmol) and Aldrich 2,3-dihydropyran (631 mg, 7.5 mmol) in 25 mL of dry benzene (hood!). Magnetic stirring at room temperature was continued for 4 h after which the catalyst was removed by filtration and washed; the combined filtrate and washings were stripped to produce crude product. Thick-layer chromatography (Merck silica gel GF-254 type 60 with a 5:1 hexane/ether eluant) gave 2-(1-dodecyloxy)-tetrahydro-2*H*-pyran (1.28 g, 95%) as a clear liquid with satisfactory NMR, IR, and GLC data. The same procedure worked successfully on a somewhat larger scale (20 mmol of alcohol), using column chromatography.

Cholesterol (1.93 g, 5 mmol) was treated exactly as the 1-dodecanol except that the stirring lasted 6 h. Removal of the solvent gave a solid residue which was dried for 2 h under reduced pressure. Recrystallization from ethyl acetate yielded white needles (2.24 g, 95%) with a melting point of 151–152 °C (lit.[1] mp 154–155 °C).

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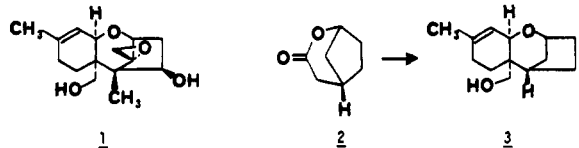
Registry No. 1-Dodecanol, 112-53-8; cyclohexanol, 108-93-0; nopol, 128-50-7; geraniol, 106-24-1; 3-acetyl-1-propanol, 1071-73-4; cholesterol, 57-88-5; benzhydrol, 91-01-0; 2-phenyl-2-propanol, 617-94-7; 1-methylcyclohexanol, 590-67-0; 1-dodecanol THP ether, 63588-79-4; cyclohexanol THP ether, 709-83-1; nopol THP ether, 79433-80-0; geraniol THP ether, 59632-99-4; 3-acetyl-1-propanol THP ether, 1012-10-8; cholesterol THP ether, 6252-45-5; benzhydrol THP ether, 79373-25-4; 2-phenyl-2-propanol THP ether, 79373-26-5; 1-methylcyclohexanol THP ether, 72347-38-7; P-4VPTS, 29323-86-2; P-2VPTS, 79373-27-6.

Communications

Synthesis of a Bicyclic Precursor to Verrucarol: Application of a Trimethylsilyl-Controlled Diels–Alder Reaction and Wagner–Meerwein Rearrangement Sequence†

Summary: A synthesis of lactone 4, which corresponds to the bicyclic nucleus of verrucarol (1), is described. The key steps of this synthesis are the $BF_3{\cdot}Et_2O$ catalyzed Diels–Alder reaction of 7 with methyl acrylate and the oxidative conversion of cycloadduct 8 into epoxy alcohols **10a** and **10b**. A trimethylsilyl group plays a crucial role in both of these transformations.

Sir: Verrucarol (1) possesses the 12,13-epoxytrichothecene skeleton common to the trichothecene family of terpene antibiotics.[1] The remarkable biological properties of many of these compounds, particularly some of the macrocyclic di and triester derivatives of verrucarol, have stimulated considerable interest in their synthesis.[2] We recently described a synthetic approach to the trichothecene ring system, exemplified by the stereospecific synthesis of 3

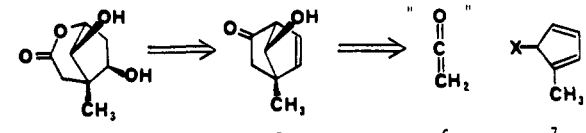


1 2 3

from lactone 2.[3] We describe herein a stereoselective synthesis of lactone 4, a bicyclic compound bearing all of the functionality necessary for elaboration to verrucarol.

Our solution to the synthetic problem posed by 4 has its genesis in the analysis summarized in Scheme I.

Scheme I



4 5 6 7

Certain structural features of 4, notably the lactone and the C-4 hydroxyl group, suggested that bicycloheptenone 5, or a suitable synthetic equivalent, might be an appropriate precursor. This, in turn, suggested a Diels–Alder construction involving a ketene equivalent, 6, and a disubstituted cyclopentadiene, 7. There are, of course, a number of obvious pitfalls to such a strategy. First, disubstituted cyclopentadienes such as 7 are not, in general, readily available. More important, the thermal stability of 7 (e.g., X = OR) relative to other tautomers would be a problem ([1,5] hydrogen shifts), except in cases where 7 could be synthesized and worked with at low temperature.[4] Finally, all known ketene equivalents[5] would be expected to add to 7, preferentially, in the undesired regiochemical sense, leading to the carbonyl-transposed isomer of 5. On the assumption that the first two problems could be solved, some means of inverting the orientational preference of 6 with an appropriate cyclopentadiene would be required, or, alternatively, some controlled means of reorganizing the functional group relationships in the initial bicycloheptene Diels–Alder adduct would need to be employed. Our synthesis of 4, which in fact follows the latter logic, involves use of 7 (X = $SiMe_3$; Scheme II). The choice of a trimethylsilyl group not only simplifies the synthesis of 7[6] but also serves to ensure a sufficient

† This communication is dedicated to Professor George H. Büchi on the occasion of his 60th birthday.

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