acetate[17] in 65 mL of dry benzene was added 20.0 g (40.6 mmol) of technical (90%) $Pb(OAc)_4$, which had been dried in vacuo over KOH. The reaction mixture was heated at reflux for 2.5 h, cooled, filtered, and washed with saturated aqueous $NaHCO_3$. After drying ($MgSO_4$) the solvent was evaporated to give a solution containing 55% of 2, 7% of nopinone, and 37% of the 2,2-diacetate (GC/MS). This mixture was stirred with 185 mL of 10% aqueous acetic acid at 25 °C for 15 h. The mixture was diluted with 150 mL of water and extracted with hexanes, and the hexane solution was washed thoroughly with saturated aqueous $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed and the product distilled to give 2.30 g (59%) of 2, bp 63-64 °C (1.9 mmHg), contaminated with less than 5% of nopinone (analysis by GC/MS). The IR, ^1H NMR, MS, and specific rotation were identical with those of material prepared by the published procedure.[4]

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Acknowledgment. We thank the National Institute on Drug Abuse for support of this work under Grant DA-03590. We also thank Dr. Robert A. Archer of Eli Lilly Research Laboratories for a generous gift of dimethylheptylresorcinol and Patricia G. Lee for technical assistance. The high resolution mass spectral determination was performed by the Midwest Center for Mass Spectrometry, a National Science Foundation Instrumentation Facility (Grant CHE 8620177).

Supplementary Material Available: Summary of structural details, tables of atomic coordinates, bond lengths, bond angles, and anisotropic thermal parameters for the X-ray crystallographic analysis of 12, and ^{13}C NMR spectra of 10, 15, 16, and 19 (10 pages). Ordering information is given on any current masthead page.

Synthesis of (*R*)-2,3-Dihydro-2,5-dimethyl-2-isopropylfuran

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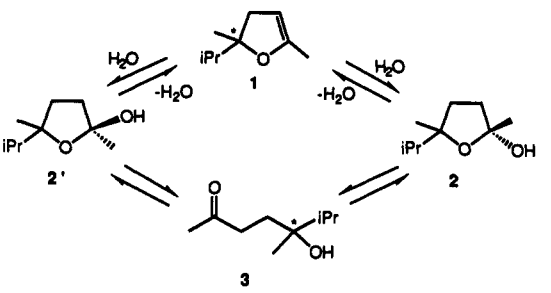
The synthesis of (*R*)-2,3-dihydro-2,5-dimethyl-2-isopropylfuran (1), an insect pheromone, via a 1,3-oxathiane is reported. Key steps are the preparation of (*S*)-2,3-dimethylbutane-1,2-diol (7) from isobutyryloxathiane 5 and reaction of lithiated acetone dimethylhydrazone with tosylated diol 8. NMR spectra of the key tautomeric precursors, 2/2′/3, to 1 have been analyzed in detail, and the enantiomeric excess of these precursors was determined by a chiral shift ^{13}C NMR experiment.

Introduction

The cyclic enol ether 2,3-dihydro-2,5-dimethyl-2-isopropylfuran (1) has been identified[1] as a sex-specific attractant from females of the beetle *Hylecoetus dermestoides* L. The structure of this pheromone was determined by comparison of its mass spectrum with that of its hydrogenation product and confirmed by a synthesis of its racemate.[1,2] Cyclic enol ether 1 is known to be very volatile and was originally observed only by GC in its pentane extract. As outlined in Scheme I, it can be obtained by dehydration of hemiketals 2 or 2′; however, in the presence of moisture the reverse process is rapid at room temperature.[3,4] Moreover, compounds 3, 2, and 2′ are in equilibrium. A preliminary bioassay showed that the racemic material obtained by reaction of isopropylmagnesium bromide with 1,5-hexanedione may act as a sex pheromone.[1]

A synthesis of the *S* enantiomer of this pheromone from a D-glucose derivative has been reported[3] but included no detailed structural analysis, such as NMR data, of 1 nor of its precursors. The overall yield in the ten-step synthesis was less than 2%. The low specific rotation ($[\alpha]_D$ −1.1, *c* = 0.83, pentane) of either the precursors 2/2′/3, or the mixture of these precursors with 1, was later found[4] to have been incorrectly assigned to compound 1. Both enantiomers of 1 were subsequently synthesized by Mori in 7-12% overall chemical yield in six steps from an allylic alcohol by a sequence that included Sharpless asymmetric epoxidation and involved a precursor of 86% ee (enantiomer excess).[4] The absolute configuration of 1, opposite to that reported previously, was confirmed by an independent synthesis of the *R* enantiomer from naturally occurring (*R*)-linalool.[4]

Scheme I



Two fundamental questions concerning this insect pheromone remain to be answered: (1) Which compound is the actual pheromone? Although previous workers have assumed cyclic enol ether 1 to be the sex-specific attractant, the rapid and spontaneous conversion of 1 to 2/2′/3 in the presence of adventitious moisture raises doubt on this point. (2) Which enantiomer is responsible for the biological activity? This question can only be answered, eventually, through bioassay of optically active material.

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In this context we report here a convenient, short, enantioselective synthesis of 1, which includes full characterization of the precursor mixture 2/2′/3 and measurement of its enantiomer excess (ee).

Results and Discussion

The enantioselective synthesis of (R)-1 from 1,3-oxathiane 4[5] (chiral auxiliary) involves two distinct stages (Scheme II): the preparation of optically active (S)-2,3-dimethylbutanediol (7)[6] and reaction of the tosylated butanediol 8 with lithiated acetone dimethylhydrazone (9) followed by hydrazone cleavage.[7]

Isobutyryloxathiane 5 obtained from 1,3-oxathiane 4[5] by an improved procedure[8] underwent Grignard addition to give the desired oxathianyl alcohol α-(S)-6 in 80% de (diastereomer excess) and 90% yield. The de of α-(S)-6 was increased to 96% with 77% yield by flash chromatography on silica gel. Cleavage of the oxathiane ring of α-(S)-6 as previously described[6] gave diol (S)-7, which was tosylated to (S)-8 exclusively at the primary hydroxy group. Reaction of (S)-8 with lithiated 9 in tetrahydrofuran (THF) for 20 h at 0–10 °C, presumably via an epoxide intermediate, yielded (R)-10, which, without purification, was subjected to removal of the dimethylhydrazone group by Corey's procedure[7] to give, in good yield, product (R)-3, shown (below) to be a tautomer mixture with 2 and 2′. The material solidified upon standing at low temperature (−22 °C). Its wide melting range (35–39.5 °C) suggested the existence of a tautomer mixture in the solid state. The solution NMR spectra of this mixture were analyzed in detail. A total of six doublets and six singlets representing 12 methyl groups (two singlets and two doublets for each of the above structures) were observed in the proton NMR spectrum (benzene-d_6). The two singlets at 0.84 and 1.68 ppm (CH_3CO)[9] and two doublets at 0.76 and 0.85 ppm are assigned to 3 on the basis of their similar relative intensities and the presence of a low-field (CH_3CO) signal in the set. These signals are about half as intense as the remaining methyl signals, which, in turn, were about equal in intensity. This indicated the ratio of 3 to 2 to 2′ to be about 1:2:2 in benzene (Mori et al.[4] obtained the tautomers in a ca. 1:1:1 ratio in $CDCl_3$). Altogether, 27 peaks (12 CH_3, 6 CH_2, 3 CH, and 6 C according to DEPT[10]) are observed in the ^{13}C NMR spectrum, which further demonstrates the presence of the three tautomers. Although the ^{13}C NMR spectrum of the separately synthesized racemate mixture (2/2′/3) in the presence of the chiral shift reagent Pr(hfc)$_3$ (hfc = (3-heptafluorobutyryl)camphor) is very complicated, at least one pair of characteristic, well-resolved signals provided the opportunity to determine the ee. This excess, determined by integration of the pair of ^{13}C NMR signals at 82.9 (major) and 82.7 ppm (minor) in the presence of Pr(hfc)$_3$, was 96 ± 4%, equal to the de of the oxathiane alcohol precursor α-(S)-6, implying that no racemization had occurred during the synthetic transformations. In GC-MS analysis the material displayed two GC peaks, the second of which was assigned to the product 2/2′/3. Its chemical (isobutane) ionization mass spectrum showed the protonated molecular peak (m/e 159, MH^+), and the electron impact MS demonstrated a base fragment at 115 (M − 43), indicating the loss of the isopropyl group. (The first GC peak was analyzed by MS to be compound 1, MH^+ 141). The dextrorotation of (R)-2/2′/3 agrees with the configurational assignment of the (+) isomer prepared by Mori.[4]

Thermal dehydration of tautomer mixture (R)-2/2′/3 gave cyclic enol ether (R)-1, a very moisture-sensitive compound, as the final product. In the presence of adventitious moisture, (R)-1 reverts to its precursors. Pure (R)-1 was obtained by preparative GC at elevated temperatures. Its proton and ^{13}C NMR spectra agree with those reported in literature.[4] The electron-impact GC-MS (97, M − 43) shows that the loss of the isopropyl group is again predominant.

In conclusion, we have achieved a facile synthesis of (R)-1 in seven steps from readily accessible starting material. The absolute configuration of the product may be inferred from that of its precursors α-(S)-6[11] and (R)-(+)-2/2′/3.[4,13] Enantiomer (S)-1 could be synthesized, in principle, by using oxathiane 11[6,14] as a chiral template.[15] Intermediate 2/2′/3 has been fully characterized by both ^1H and ^{13}C NMR and its enantiomer excess determined by an NMR chiral shift experiment. The ready reversion of 1 to 2/2′/3 in the presence of moisture has been confirmed.

11

Experimental Section

General Procedure. Proton and carbon-13 NMR spectra were recorded in $CDCl_3$ (except where indicated) at 200.1 and 50.3 MHz, respectively. The ^1H NMR spectra of the target compound (R)-1 and new compounds α-(R)-6, α-(S)-6, and (S)-8 indicate purity of 95% or greater.

(1′S)-2-[1′,2′-Dimethyl-1′-hydroxypropyl]hexahydro-4,4,7-trimethyl-4H-1,3-benzoxathiin (α-(S)-6). A solution of 2.02 g (7.47 mmol) of ketone 5[8] in 10 mL of THF was added to a solution of 15 mL (22.5 mmol) of 1.5 M CH_3MgBr (THF/toluene (75/25)) in 50 mL of THF, and the solution was stirred for 3 h at −78 °C. The reaction mixture was quenched by addition of 25 mL of saturated NH_4Cl. The aqueous layer was extracted twice with diethyl ether (20 mL each). The combined organic layers were dried ($MgSO_4$) and concentrated to yield 2.78 g of crude product α-(S)-6 in 80% de determined on the basis of the integrated proton signals H(2). Purification by chromatography on silica gel with 5% ethyl acetate in hexanes gave two fractions of chemically pure carbinol α-(S)-6: 1.64 g (77% yield, 96% de) and 0.30 g (13% yield, 1% de). A diastereomerically pure sample of α-(R)-6 was obtained by preparative TLC purification on silica gel. α-(S)-6: ^1H NMR δ 0.85 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.4 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 1.14 (s, 3 H), 1.25 (s, 3 H), 1.38 (s, 3 H), 2.24 (s, 1 H), 3.40 (dt, J = 4.3, 10.4 Hz, 1 H), 4.83 (s, 1 H), and others; ^{13}C NMR δ 16.6 (CH_3), 17.5 (CH_3), 18.9 (CH_3), 22.0 (CH_3), 22.6 (CH_3), 24.3 (CH_2), 29.7 (CH_3), 31.3 (CH),

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(9) The relatively high field position of this methyl proton is undoubtly due to an ASIS shift caused by the solvent, benzene-d_6. In $CDCl_3$, in which the spectrum is less well ressolved, the CH_3CO signal is seen at 2.16 ppm.
(10) Doddrell, D. M.; Pegg, D. T.; Bendall, M. R. *J. Magn. Reson.* **1982**, *48*, 323.
(11) In all cases we have studied—cf. Eliel, E. L. *Phosphorus Sulfur* **1985**, *24*, 73 and especially Eliel, E. L.; Lynch, J. E. *Tetrahedron Lett.* **1987**, *28*, 4813—the addition of Grignard reagents to acyloxathianes analogous to 5 proceeds according to Cram's chelate rule, i.e., the addition is lk^{12} with respect to C(2) of the oxathiane.
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(13) The reason that the specific rotation of (R)-(+)-2/2′/3 prepared here is lower than that reported by Mori[4] may be due to its lesser content in tautomer 3.
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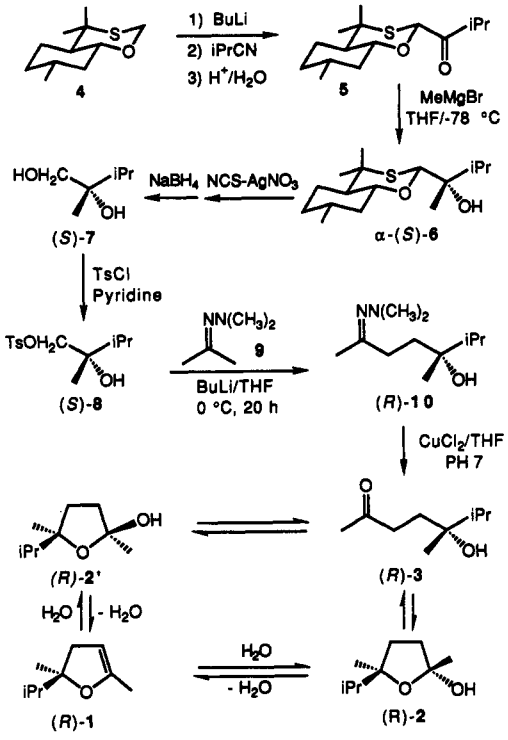
(15) Attempts to obtain the diastereomer of 6 by adding isopropylmagnesium chloride to the methyl ketone analogue of 5 produced a mixture of diastereomers and reduction products.

Scheme II



33.7 (CH), 34.6 (CH_2), 41.6 (CH_2), 42.5 (C), 50.7 (CH), 75.8 (C), 77.6 (CH), 85.3 (CH); CI MS for (MH^+) $C_{16}H_{31}O_2S$ found m/e 287.2040, calcd m/e 287.2046. (*R*)-**6** (minor): ^1H NMR δ 0.90 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.93 (d, J = 6.9 Hz, 3 H), 1.12 (s, 3 H), 1.25 (s, 3 H), 1.39 (s, 3 H), 2.32 (bs, 1 H), 3.39 (dt, J = 4.2, 10.5 Hz, 1 H), 4.89 (s, 1 H), and others; ^{13}C NMR δ 16.5, 17.3, 19.6, 22.1, 22.7, 24.4, 29.7, 31.5, 33.8, 34.7, 41.7, 42.9, 50.9, 75.9, 77.6, 84.0.

(*S*)-2,3-Dimethyl-1,2-butanediol (7). A solution of 1.64 g (5.72 mmol) of α-(*S*)-**6** (96% de) in 7 mL of diethyl ether and 13 mL of acetonitrile was added to 1.53 g (11.4 mmol) of *N*-chlorosuccinimide and 1.94 g (11.4 mmol) of $AgNO_3$ in 70 mL of acetonitrile–water (80/20), and the solution was stirred for 15 min. Then saturated aqueous Na_2SO_3, Na_2CO_3, and NaCl (7 mL each) were successively added at intervals of 2 min. The mixture was filtered and the filter cake was washed with 40 mL of acetonitrile. $NaBH_4$ (1.35 g) was added to the combined filtrates with stirring for 1 h. Acetone (13 mL) was added with brief stirring. The mixture was filtered and the filter cake was washed with 25 mL of diethyl ether. The organic layer was separated, dried ($MgSO_4$), and concentrated to give 1.83 g of crude product, which was subjected to flash chromatography on silica gel to yield 404 mg (60%) of (*S*)-**7** and 923 mg of cyclic sultine.[6] (*S*)-**7**: ^1H NMR δ 0.86 (d, J = 6.9 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 1.05 (s, 3 H), 1.80 (septet, J = 6.9 Hz, 1 H), 1.86 (bs, 2 H), 3.41 and 3.53 (AB, J = 10.9 Hz, 2 H); ^{13}C NMR δ 16.6 (CH_3), 17.6 (CH_3), 18.7 (CH_3), 34.1 (CH), 68.3 (CH_2), 75.2 (C).

Racemic **7** was prepared according to a literature procedure[16] and its NMR spectra were identical with those above.

(*S*)-2,3-Dimethyl-1-(tosyloxy)-2-butanol (8). A solution of 827 mg (4.34 mmol) of *p*-toluenesulfonyl chloride in 1 mL of pyridine was added to 410 mg (3.39 mmol) of (*S*)-**7** in 1.5 mL of pyridine, stirred for 0.5 h at 0 °C, and then placed in a refrigerator overnight. Water (1 mL) was added with brief stirring. The mixture was extracted with 20 mL of diethyl ether and the organic solution was washed 3 times with 2 N aqueous HCl (3 mL each), dried ($MgSO_4$), and concentrated to yield 808 mg of crude product, which was purified by flash chromatography on silica gel with ethyl acetate/hexanes (20/80) to give 696 mg (75%) of product (*S*)-**8**: ^1H NMR δ 0.83 (d, J = 6.9 Hz, 3 H), 0.91 (d, J = 6.9 Hz, 3 H), 1.07 (s, 3 H), 1.79 (bs, 1 H), 1.82 (septet, J = 6.9 Hz, 1 H), 2.46 (s, 3 H), 3.89 and 3.95 (AB, J = 9.6 Hz, 2 H), 7.36 and 7.80 (AB, J = 8.4 Hz, 2 H); ^{13}C NMR δ 16.3 (CH_3), 17.3 (CH_3), 19.3 (CH_3), 21.6 (CH_3), 34.0 (CH), 73.5 (C), 75.3 (CH_2), 127.9 (CH), 129.9 (CH), 132.6 (C), 144.9 (C).

Racemic **8** was similarly prepared from (±)-**7**.

Acetone Dimethylhydrazone (9).[17] A mixture of 12 mL (0.16 mmol) of acetone (99.5%) and 12 mL (0.16 mmol) of *N,N*-dimethylhydrazine (98%) was refluxed overnight. NaOH (5 g) was added; then the upper layer was decanted, dried with CaH_2 overnight, and distilled to give 10.61 g (68%) of pure product **9** (bp 92–94 °C; lit.[17] bp 94–94.5 °C); ^1H NMR δ 1.88 (s, 3 H), 1.91 (s, 3 H), 2.39 (s, 6 H).

(*R*)-5-Hydroxy-5,6-dimethyl-2-heptanone Dimethylhydrazone (10). To 484 mg (4.84 mmol) of **9** in 8 mL of dry THF at 0 °C under nitrogen was added 3.9 mL (6.29 mmol) of 1.6 M of butyllithium in hexanes dropwise, and the solution was stirred for 30 min. Tosylated diol (*S*)-**8** (659 mg, 2.42 mmol) in 7 mL of THF was added dropwise, and the mixture was stirred for 20 h at 0–10 °C. The reaction mixture was quenched with 5 mL of saturated aqueous NH_4Cl and 5 mL of water. The aqueous layer was extracted 3 times with diethyl ether (8 mL each). The combined organic layers were washed with 5 mL of saturated aqueous NaCl, dried ($MgSO_4$), and concentrated to yield 557 mg of crude product, which was converted to (*R*)-**3** without purification. (Partial hydrolysis of **10** occurs spontaneously on standing.) ^1H NMR: δ 0.90 (d, J = 6.9 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 1.06 (s, 3 H), 1.97 (s, 3 H), 2.44 (s, 6 H), and others.

The racemate was similarly prepared from (±)-**8**.

(*R*)-5-Hydroxy-5,6-dimethyl-2-heptanone (3). A mixture of 557 mg (2.79 mmol) of (*R*)-**10**, 523 mg (3.07 mmol) of $CuCl_2(H_2O)_2$ in 42 mL of THF, 8 mL of 0.05 N phosphate buffer (pH 7), and 14 mL of water was stirred for 1.5 h at ambient temperature. Saturated aqueous NH_4Cl (10 mL) and added with brief stirring; then the organic layer was separated and the aqueous layer was extracted 3 times with diethyl ether (15 mL each). The combined organic layers were dried ($MgSO_4$) and concentrated to yield 353 mg of crude product, which was chromatographed on silica gel with 10–20% diethyl ether in pentane to give 281 mg (74% overall from (*S*)~**8**) of pure product identified as an equilibrium mixture of three tautomers **2**, **2'**, and **3** by NMR. The ee was determined as 96 ± 4% by the integration of the signals at 82.9 (major) and 82.7 ppm (minor) in the ^{13}C NMR spectrum in the presence of $Pr(hfc)_3$: GC-MS analysis (column, 12 m NB HP-1 capillary; solvent, EtAc. CI: gas, isobutane; flow, 1.5 mL/min; inj, temp, 250 °C; temp profile, 50 °C/5 min then 50–250 °C, 15 °C/min) gave two fractions: the first one (t_R 2.8 min) was analyzed as 1 and the second (t_R 5.3 min) as **2**/**2'**/**3**: ^1H NMR (C_6D_6) δ 0.76 (d, J = 6.8 Hz), 0.79 (d, J = 6.9 Hz), 0.83 (d, J = 6.9 Hz), 0.84 (s), 0.85 (d, J = 6.8 Hz), 0.89 (d, J = 6.8 Hz), 0.93 (s), 1.03 (d, J = 6.8 Hz), 1.29 (s), 1.36 (s), 1.39 (s), 1.68 (s), and others; ^{13}C NMR (C_6D_6) δ 17.1 (CH_3), 17.7 (2 CH_3), 18.0 (CH_3), 18.2 (CH_3), 18.5 (CH_3), 20.9 (CH_3), 22.5 (CH_3), 25.3 (CH_3), 28.2 (CH_3), 28.7 (CH_3), 29.4 (CH_3), 32.9 (CH_2), 34.3 (CH_2), 35.4 (CH_2), 37.7 (CH), 37.9 (CH_2), 37.9 (CH), 38.1 (CH_2), 38.9 (CH_2), 39.4 (CH), 73.5 (C), 87.1 (C), 87.5 (C), 104.7 (C), 105.2 (C), 207.8 (C); $[\alpha]^{20}_D$ +1.95° (c = 2, pentane); MS (EI) m/e 143 (5), 125 (4), 115 (100), 97 (54), 87 (41), 83 (20), 70 (30), 55 (33); MS (CI) m/e 159 (MH^+) [lit.[4] ^{13}C NMR δ 74.06, 87.70, 87.99, 104.8, 105.4, 209.9, and others; $[\alpha]^{22}_D$ 4.16 (pentane, c = 0.77)].

The racemate was similarly prepared from the racemic precursor.

(*R*)-2,3-Dihydro-2,5-dimethyl-2-isopropylfuran (1). When the above ketone–hemiketal mixture was injected into a GC instrument (column, Carbowax A 20 M; carrier gas, He) at an injection temperature of 300 °C and a column temperature of 110 °C, only the desired product (*R*)-**1** and water were observed. Thus a pure sample was obtained: ^1H NMR (C_6D_6) δ 0.87 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 1.20 (s, 3 H), 1.67 (bs, 3 H), 1.82 (septet, J = 6.8 Hz, 1 H), 2.07 (A of $ABXY_3$, $J_{AX} = J_{AY}$ = 2.1 Hz, J_{AB} = 14.6 Hz, 1 H), 2.47 (B of $ABXY_3$, $J_{BX} = J_{BY}$ = 2.2 Hz, J_{AB} = 14.6 Hz, 1 H), 4.34 (bs, 1 H); ^{13}C NMR δ 13.7, 17.1, 17.2, 24.0, 37.0, 38.9, 89.5, 93.3, 153.0; MS (EI) m/e 140 (21), 125 (11), 97 (100), 83 (12), 70 (30), 55 (37); MS (CI, isobutane) m/e

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141 (MH^+) [lit.[4] ^1H NMR δ 0.86 (3 H, d, J = 7 Hz), 0.88 (3 H, d, J = 7 Hz), 1.17 (3 H, s), 1.66 (3 H, bs), 1.58–2.70 (3 H, m), 4.33 (1 H, bs); ^{13}C NMR δ (C_6D_6) 13.87, 17.38, 23.81, 37.44, 39.75, 89.27, 93.14, 153.69.

Acknowledgment. This work was supported by NSF grant CHE-8703060.

Supplementary Material Available: ^1H NMR spectra of compounds (*R*)-1, α-(*R*)-6, α-(*S*)-6, (*S*)-8, and (*RS*)-2/2′/3 (6 pages). Ordering information is given on any current masthead page.

Solid Superacid-Catalyzed Organic Synthesis. 4.[1a] Perfluorinated Resinsulfonic Acid (Nafion-H) Catalyzed Friedel–Crafts Benzylation of Benzene and Substituted Benzenes

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Nafion-H, a perfluorinated resinsulfonic acid, catalyzes Friedel–Crafts benzylation of benzene and substituted benzenes with benzyl alcohols under relatively mild experimental conditions. Reactions are clean, and water formed as a byproduct does not deactivate the catalyst. It was also found that this method is applicable to the intramolecular cycloalkylation and oligomerization of methoxybenzyl alcohols.

Introduction

Friedel–Crafts alkylation reactions in solution generally give complex reaction mixtures. The formation of reactant (and product) catalyst complexes, the increased tendency of alkylated products toward further alkylation and isomerization, coupled with the long contact of the reactant with the catalyst, result in complex mixtures of products. Polyalkylation, isomerization, transalkylation, dealkylation, and polymerization all occur under the reaction conditions.

There is, therefore, of substantial interest to catalyze alkylation reactions with solid acids which decrease these side reactions.[2] Gas-phase alkylation performed over catalysts such as sulfonated polystyrene resins allows for short contact time and weak complexation of the reactants with the catalyst, thus resulting in much cleaner and less complex product mixtures.[3] These beneficial results are due to the high acidity of the resin.

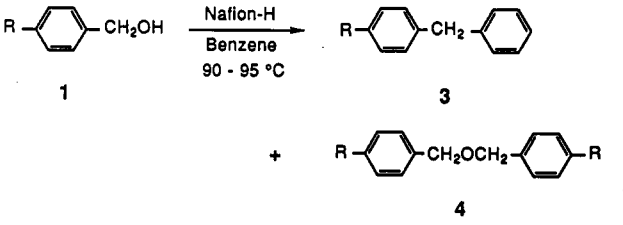
We now describe a convenient and efficient method of Nafion-H[4] (a solid perfluorinated resinsulfonic acid) catalyzed benzylation of benzene and substituted benzenes with benzyl alcohols.

Results and Discussion

The benzylation reactions were carried out by heating a stirred mixture of the corresponding benzyl alcohols (1), aromatics (2), and the solid Nafion-H catalyst at 95–100 °C. Product diphenylmethanes (3) were simply isolated by filtering the hot reaction mixture and distilling off the solvent. The reactions are very clean; water is the only byproduct of the reaction.

The reaction is general for benzyl alcohols (see Table I) and aromatics that normally undergo Friedel–Crafts benzylations. Benzene with benzyl alcohols (1) gave the corresponding diphenylmethanes (3) in >50% yields. As shown in Table I, the present method provides excellent yields of diphenylmethanes (3), and no concomitant trans-*tert*-butylation and transbromination were observed under the reaction conditions (runs 3, 4). The amount of the catalyst used relative to the benzyl alcohol was between 5% and 10% by weight. Optimum yields were obtained with 10% of catalyst (Table I), whereas 5% gave only slightly lower yields.

Table I. Nafion-H-Catalyzed Benzylation of Benzene with Substituted Benzyl Alcohols (1)[a]



run	R in 1	reaction time (h)	products yields (%)[b] 3	4
1	H	4	69 (54)[c]	22 (16)[c]
2	4-CH_3	1	97 (81)[c]	3
3	4-*t*-Bu	1	90 (85)[c]	2
4	4-Br	12	91 (70)[c]	6
5	4-NO_2[d]	24	60 (52)[c]	22 (19)[c]

[a] [Benzene]/[benzyl alcohol] = 30:1; catalyst 10 wt %. [b] The yields were determined by GLC analyses unless otherwise indicated. [c] Isolated yields are shown in parentheses. [d] The starting compound was recovered in 15% yield.

The benzylation reaction was further studied by reacting various substituted benzenes (2) with benzyl alcohol (1) under similar conditions (Table II). The yields of 3 are comparable for toluene, ethylbenzene, *o*-xylene, *m*-xylene, *p*-xylene, and mesitylene, and somewhat lower for benzene because of formation of the dehydration products, dibenzyl ethers (4).

The isomeric composition of the diphenylmethanes (3) resulting from alkylbenzenes were determined by GLC. The results (Table III) show that the reactions give predominantly ortho–para substitution, in accordance with

(1) (a) Solid Superacids Catalyzed Organic Synthesis. 4. Part 2: Yamato, T.; Hideshima, C.; Prakash, G. K. S.; Olah, G. A. *Catalysis Lett.*, in press. (b) Saga University. (c) University of Southern California.
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(4) Olah, G. A.; Iyer, P. S.; Prakash, G. K. S. *Synthesis* **1986**, 513.

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