

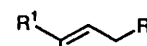
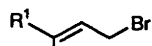
## Selective Alkylation and Allylation of Allylic Halides by Tetraorganoindates: Regio- and Stereo-selective Synthesis of Rosefuran and Sesquirosefuran

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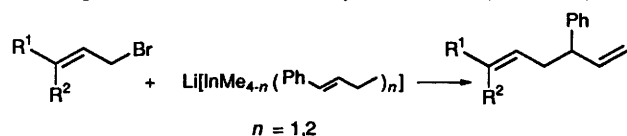
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Tetraalkylindates regioselectively alkylate allylic bromides at the  $\alpha$ -carbon. In this way, 1,5-dienes have been regio- and stereo-selectively synthesized by the allyl-allyl coupling of allylic bromides and allylic indates, including rosefuran **1** and sesquirosefuran **3**.

We have reported that organoindium reagents are readily available and versatile reagents for organic transformations.<sup>1</sup> In



methyl-substituted indate gives a higher product yield than the corresponding butyl compound probably because it is sterically less bulky. Methylindium was, therefore, used as the complexing reagent. Cinnamyl chloride is much less reactive than the corresponding bromide. (Cinnamyl)methylindate also gave 1,5-dienes upon the treatment with allylic bromides (Scheme 4), in a



Allylic bromide		Yield (%)
R <sup>1</sup>	R <sup>2</sup>	
Me	H	100
Ph	H	100
Pr	H	84
H	Pr	84

good yields by the  $\gamma,\alpha$ -coupling of allylic indates and allylic bromides. Only the reaction of methyl(prenyl)indate with cinnamyl bromide yielded two isomeric products, although the  $\gamma,\alpha$ - vs.  $\alpha,\alpha$ -ratio is still large (65:35). Although a similar  $\gamma,\alpha$ -coupling of allylic borate-allylic halide is known,<sup>6b</sup> our indate-based procedure is superior in terms of both regio- and stereo-selectivity and ease of preparation of the allylic organometallic reagents.

*Synthesis of Rosefuran and Sesquirosefuran.*—The high regio- and stereo-selectivity of the present indium-based allyl-allyl coupling provides an easy and efficient access to 1,5-dienes. For a demonstration of the usefulness of the coupling, we synthesized two furanoid terpenes possessing a 1,5-diene moiety. Rosefuran **1**, a component of Bulgarian rose oil, *Rosa damascena* Mill.,<sup>7</sup> has, until now, been prepared by a variety of methods,<sup>8</sup> of which copper(I)-catalysed prenylation of 3-furylmethylmagnesium bromide with prenyl phosphate is one of the most straightforward.<sup>9</sup> (3-Furylmethyl)indate, necessary

In summary, efficient and convenient methods for alkyl-allyl and allyl-allyl couplings have been developed based on the reaction of tetraorganoindates and allylic halides.

### Experimental

Mass spectra were measured on a Hitachi M-2000 spectrometer at 70 eV. IR spectra were recorded for neat oils on a JASCO IRA-102 spectrophotometer.  $^1\text{H}$  NMR spectra were obtained for solutions in  $\text{CDCl}_3$  on a Hitachi R-90 spectrometer (90 MHz) or a Varian XL-200 spectrometer (200 MHz) with  $\text{Me}_4\text{Si}$  as internal standard;  $J$  values are given in Hz.  $^{13}\text{C}$  NMR spectra were measured for solutions in  $\text{CDCl}_3$  with a Varian XL-200 spectrometer (50 MHz). Methylolithium ( $1.08 \text{ mol dm}^{-3}$  in diethyl ether) and butyllithium ( $1.63 \text{ mol dm}^{-3}$  in hexane) were commercially obtained. All reactions were carried out under argon.

*Alkylation of Allylic Bromides with Tetraalkylindates.—Typical experimental procedure.* To a stirred solution of indium(III) iodide (846 mg, 1.7 mmol) in diethyl ether ( $20 \text{ cm}^3$ ) at  $0^\circ\text{C}$  was added butyllithium ( $3.2 \text{ cm}^3$  in hexane, 5.1 mmol) over a period of 5 min. The mixture was stirred at  $0^\circ\text{C}$  for 10 min and then at room temperature for 40 min. To the resulting solution of tributylindium, further butyllithium ( $0.94 \text{ cm}^3$  in hexane, 1.5 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. Cinnamyl bromide (256 mg, 1.3 mmol) in diethyl ether ( $2 \text{ cm}^3$ ) was then added to the mixture which was then stirred at room temperature for 3 h. The reaction was quenched by the addition of dilute hydrochloric acid to the mixture which was then extracted with diethyl ether. The extracts were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated under reduced pressure. The residue was column chromatographed (silica gel, hexane) to give 1-phenylhept-1-ene (198 mg, 88%) as a colourless oil. All other reactions were carried out and worked up similarly. The structures of the products were determined by MS, IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR, and, in the cases of new compounds, by elemental analyses.

*Allylation of Allylic Bromides with Allylic Indates.—Typical experimental procedure.* To a stirred solution of allylindium sesquiodide, prepared from indium powder (230 mg, 2 mmol) and allyl iodide ( $0.274 \text{ cm}^3$ , 3 mmol) in tetrahydrofuran ( $5 \text{ cm}^3$ ), was slowly added butyllithium ( $2.8 \text{ cm}^3$  in hexane, 4.3 mmol) at  $0^\circ\text{C}$ . The mixture was stirred at  $0^\circ\text{C}$  for 10 min and then at room temperature for 2 h. To the resulting solution of lithium allyl(methyl)indate, cinnamyl bromide (256 mg, 1.3 mmol) in diethyl ether ( $2 \text{ cm}^3$ ) was added and the whole mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of dilute hydrochloric acid to the mixture, which was then extracted with diethyl ether. The extracts were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated under reduced pressure. The residue was column chromatographed (silica gel, hexane) to give 1-phenylhexa-1,5-diene (146 mg, 80%). All other reactions were carried out and worked up similarly.

1,1-Diphenylhexa-1,5-diene. Colourless oil (Found: C, 92.2; H, 7.8.  $\text{C}_{18}\text{H}_{18}$  requires C, 92.26; H, 7.74);  $m/z$  234 ( $\text{M}^+$ , 93%) and 115 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3090, 3060, 3030, 2960, 2920, 1625, 1595, 1480, 1443, 988, 963, 910, 763, 742 and 690;  $\delta_{\text{H}}$ (90 MHz) 2.20 (4 H, m,  $\text{CH}_2$ ), 4.90–5.10 (2 H, m, olefinic H), 5.60–6.00 (1 H, m, olefinic H), 6.05 (1 H, t,  $J$  7, olefinic H) and 7.15–7.40 (10 H, m, Ph);  $\delta_{\text{C}}$  29.1 (t), 34.0 (t), 114.9 (t), 126.8 (d), 126.9 (d), 127.2 (d), 128.0 (d), 128.1 (d), 129.2 (d), 129.9 (d), 138.1 (d), 140.2 (s), 141.9 (s) and 142.8 (s).

(E)-3-Phenylnona-1,5-diene. Colourless oil (Found: C, 89.9; H, 10.3.  $\text{C}_{15}\text{H}_{20}$  requires C, 89.93; H, 10.07%);  $m/z$  200 ( $\text{M}^+$ , 38%) and 117 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3080, 3075, 2950, 2900, 2890, 2854, 1640, 1600, 1490, 1450, 1406, 1375, 960, 915, 750 and

700;  $\delta_{\text{H}}$ (200 MHz) 0.82 (3 H, t,  $J$  7, Me), 1.31 (2 H, hex,  $J$  7,  $\text{CH}_2$ ), 1.92 (2 H, q,  $J$  7,  $\text{CH}_2$ ), 2.42 (2 H, t,  $J$  6,  $\text{CH}_2$ ), 3.24–3.40 (1 H, q,  $J$  7, CH), 5.04 (1 H, d,  $J$  17, olefinic H), 5.06 (1 H, d,  $J$  10, olefinic H), 5.24–5.50 (2 H, m, olefinic H), 6.00 (1 H, ddd,  $J$  17, 10 and 6, olefinic H) and 7.12–7.40 (5 H, m, Ph);  $\delta_{\text{C}}$  13.5 (q), 22.5 (t), 34.5 (t), 38.6 (t), 50.0 (d), 114.1 (t), 126.0 (d), 127.6 (d), 127.8 (d), 128.2 (d), 132.1 (d), 141.7 (d) and 143.9 (s).

(Z)-3-Phenylnona-1,5-diene. Colourless oil (Found: C, 89.9; H, 10.3.  $\text{C}_{15}\text{H}_{20}$  requires C, 89.93; H, 10.07%);  $m/z$  200 ( $\text{M}^+$ , 3%) and 117 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3050, 3000, 2950, 2900, 2850, 2834, 1635, 1600, 1490, 1450, 1406, 1375, 960, 915, 750 and 698;  $\delta_{\text{H}}$ (200 MHz) 0.87 (3 H, t,  $J$  7, Me), 1.30 (2 H, m,  $\text{CH}_2$ ), 1.93 (2 H, m,  $\text{CH}_2$ ), 2.48 (2 H, t,  $J$  6,  $\text{CH}_2$ ), 3.32 (1 H, m, CH), 5.05 (1 H, d,  $J$  17, olefinic H), 5.07 (1 H, d,  $J$  11, olefinic H), 5.38 (2 H, m, olefinic H), 6.00 (1 H, ddd,  $J$  17, 10 and 6, olefinic H) and 7.16–7.40 (5 H, m, Ph);  $\delta_{\text{C}}$  13.7 (q), 22.6 (t), 29.4 (t), 33.1 (t), 49.8 (d), 114.2 (t), 126.1 (d), 127.3 (d), 127.6 (d), 128.3 (d), 130.9 (d), 141.6 (d) and 143.9 (s).

(E)-6,10-Dimethyl-3-phenylundeca-1,5,9-triene. Colourless oil (Found: C, 89.6; H, 10.6.  $\text{C}_{19}\text{H}_{26}$  requires C, 89.34; H, 10.66%);  $m/z$  254 ( $\text{M}^+$ , 39%) and 117 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3109, 3100, 3075, 2975, 2925, 2850, 1640, 1600, 1490, 1440, 1430, 1370, 970 and 910;  $\delta_{\text{H}}$ (200 MHz) 1.53 (3 H, s, Me), 1.58 (3 H, s, Me), 1.67 (3 H, s, Me), 1.80–2.10 (4 H, m,  $\text{CH}_2$ ), 2.41 (2 H, t,  $J$  7,  $\text{CH}_2$ ), 3.30 (1 H, q,  $J$  7, CH), 4.99–5.30 (4 H, m, olefinic H), 6.00 (1 H, ddd,  $J$  17, 10 and 7, olefinic H) and 7.15–7.40 (5 H, m, Ph);  $\delta_{\text{C}}$  16.1 (q), 17.7 (q), 25.7 (q), 26.6 (t), 34.0 (t), 39.7 (t), 50.0 (d), 114.2 (t), 122.2 (d), 124.3 (d), 126.1 (d), 127.7 (d), 128.3 (d), 131.3 (s), 136.2 (s), 141.9 (d) and 144.3 (s).

(E)-1-Phenyl-4-propylhexa-1,5-diene. Colourless oil (Found: C, 89.65; H, 10.2.  $\text{C}_{15}\text{H}_{20}$  requires C, 89.94; H, 10.06%);  $m/z$  200 ( $\text{M}^+$ , 77%) and 117 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3050, 3025, 2950, 2850, 1635, 1600, 1490, 1450, 1414, 1375, 990 and 910;  $\delta_{\text{H}}$ (200 MHz) 0.89 (3 H, t,  $J$  7 Me), 1.18–1.48 (4 H, m,  $\text{CH}_2$ ), 2.00–2.38 (3 H, m, CH and  $\text{CH}_2$ ), 5.01 (1 H, d,  $J$  17, olefinic H), 5.02 (1 H, d,  $J$  11, olefinic H), 5.66 (1 H, m, olefinic H), 6.22 (1 H, dt,  $J$  16 and 6, olefinic H), 6.40 (1 H, d,  $J$  16, olefinic H) and 7.16–7.44 (5 H, m, Ph);  $\delta_{\text{C}}$  14.0 (q), 20.1 (t), 36.4 (t), 38.6 (t), 43.8 (d), 114.2 (t), 125.9 (d), 126.7 (d), 128.3 (d), 129.0 (d), 130.8 (d), 137.7 (s) and 142.6 (d).

(E)-2,6-Dimethyl-9-vinylododeca-2,6-diene. Colourless oil (Found: C, 86.7; H, 12.7.  $\text{C}_{16}\text{H}_{28}$  requires C, 87.19; H, 12.81%);  $m/z$  220 ( $\text{M}^+$ , 48%) and 123 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3076, 2975, 2925, 2850, 1638, 1440, 1378, 1100, 990 and 912;  $\delta_{\text{H}}$ (200 MHz) 0.88 (3 H, t,  $J$  6 Hz, Me), 1.18–1.40 (4 H, m,  $\text{CH}_2$ ), 1.59 (3 H, s, Me), 1.61 (3 H, s, Me), 1.68 (3 H, s, Me), 1.90–2.18 (7 H, m,  $\text{CH}_2$  and CH), 4.89–5.20 (2 H, m, olefinic H), 5.20–5.23 (2 H, m, olefinic H) and 5.50–5.76 (1 H, m, olefinic H);  $\delta_{\text{C}}$  14.1 (q), 16.1 (q), 17.6 (q), 20.2 (t), 25.6 (q), 26.6 (t), 33.3 (t), 36.4 (t), 39.7 (t), 44.0 (d), 113.6 (t), 122.7 (d), 124.3 (d), 131.1 (s), 135.4 (s) and 143.2 (d).

3-Benzylhex-1-ene. Colourless oil (Found: C, 89.3; H, 10.5.  $\text{C}_{13}\text{H}_{18}$  requires C, 89.59; H, 10.41%);  $m/z$  174 ( $\text{M}^+$ , 16%) and 149 (100);  $\nu_{\text{max}}/\text{cm}^{-1}$  3050, 3025, 2950, 2850, 1635, 1600, 1490, 1450, 1414, 1375, 990 and 910;  $\delta_{\text{H}}$ (200 MHz) 0.84 (3 H, t,  $J$  6 Hz, Me), 1.15–1.48 (4 H, m,  $\text{CH}_2$ ), 2.30 (1 H, m, CH), 2.62 (2 H, dd,  $J$  8 and 4,  $\text{CH}_2$ ), 4.86 (1 H, d,  $J$  17, olefinic H), 4.94 (1 H, d,  $J$  10, olefinic H), 5.59 (1 H, ddd,  $J$  17, 10 and 8, olefinic H) and 7.01–7.35 (5 H, m, Ph);  $\delta_{\text{C}}$  14.0 (q), 20.2 (t), 36.3 (t), 41.8 (t), 45.3 (d), 114.3 (t), 125.6 (d), 127.9 (d), 129.2 (d), 140.6 (s) and 142.4 (d).

(E)-4,4-Dimethyl-1-phenylhexa-1,5-diene. Colourless oil (Found: C, 90.3; H, 9.9.  $\text{C}_{14}\text{H}_{18}$  requires C, 90.26; H, 9.74%);  $m/z$  186 ( $\text{M}^+$ , 8%) and 117 (100);  $\delta_{\text{H}}$ (200 MHz) 1.05 (6 H, s, Me), 2.22 (2 H, d,  $J$  8,  $\text{CH}_2$ ), 4.93–5.60 (2 H, m, olefinic H), 5.89 (1 H, dd,  $J$  17 and 10, olefinic H), 6.24 (1 H, dt,  $J$  16 and 7, olefinic H), 6.38 (1 H, d,  $J$  16, olefinic H) and 7.20–7.44 (5 H, m, Ph);  $\delta_{\text{C}}$  26.6 (q), 26.6 (q), 37.1 (s), 46.0 (t), 110.5 (t), 125.9 (d), 126.8 (d), 127.5 (d), 128.4 (d), 131.9 (d), 137.7 (s) and 148.0 (d).

(E)-6-Methyl-1-phenylhepta-1,5-diene. Colourless oil (Found: C, 90.0; H, 10.0.  $C_{14}H_{18}$  requires C, 90.26; H, 9.74%);  $m/z$  186 ( $M^+$ , 12%) and 117 (100);  $\delta_H$ (200 MHz) 1.64 (3 H, s, Me), 1.72 (3 H, s, Me), 2.14–2.36 (4 H, m,  $CH_2$ ), 5.21 (1 H, t,  $J$  6, olefinic H), 6.28 (1 H, dt,  $J$  16 and 7, olefinic H), 6.42 (1 H, d,  $J$  16, olefinic H) and 7.18–7.46 (5 H, m, Ph);  $\delta_C$  17.7 (q), 25.6 (q), 27.9 (t), 33.2 (t), 123.7 (d), 125.8 (d), 126.7 (d), 128.4 (d), 129.8 (d), 130.6 (d), 131.9 (s) and 137.8 (s).

(E)-4,8-Dimethyl-1-phenyl-4-vinylnona-1,7-diene. Colourless oil (Found: C, 89.7; H, 10.3.  $C_{19}H_{26}$  requires C, 89.70; H, 10.30%);  $m/z$  254 ( $M^+$ , 69%) and 117 (100);  $\nu_{max}/cm^{-1}$  3109, 3100, 3075, 3025, 2975, 2925, 2895, 1638, 1600, 1490, 1440, 1410, 1375, 990, 910, 740 and 690;  $\delta_H$ (200 MHz) 1.01 (3 H, s, Me), 1.30 (2 H, m,  $CH_2$ ), 1.59 (3 H, s, Me), 1.67 (3 H, s, Me), 1.82–2.10 (2 H, m,  $CH_2$ ), 2.22 (2 H, d,  $J$  7,  $CH_2$ ), 4.90–5.18 (3 H, m, olefinic H), 5.80 (1 H, dd,  $J$  17 and 11, olefinic H), 6.12–6.40 (2 H, m, olefinic H) and 7.16–7.39 (5 H, m, Ph).

**Synthesis of Rosefuran 1 and Sesquirosefuran 3.**—A solution of lithium (3-furylmethyl)methylindate in 1,4-dioxane (2  $cm^3$ ) was prepared in a similar manner to that described above from indium powder (230 mg, 2 mmol), 3-furylmethyl bromide (483 mg, 3 mmol), and methyl lithium (4.0  $cm^3$ , 3 mmol). Prenyl bromide (194 mg, 1.3 mmol) in 1,4-dioxane (1  $cm^3$ ) was added slowly at 0 °C to the mixture which was then stirred at 0 °C for 1 h and then at room temperature for a further 1 h. The reaction was worked up and the products were purified by column chromatography on silica gel (hexane) to give an oil (172 mg, 88%).  $^1H$  NMR and GLC analyses revealed the oil to be a mixture of rosefuran 1 and perillene 2 (90:10), by direct comparison with the authentic samples.<sup>9</sup> By using geranyl bromide in place of prenyl bromide, a mixture of sesquirosefuran 3 and dendrolasin 4 (95:5) was obtained in 68% total yield.

(3-Thienylmethyl)indate was similarly prepared and allowed to react with prenyl bromide. Aqueous work-up and column chromatography gave an oil, which was analysed by GLC to

be a mixture of compounds 5–7 in yields of 37, 41 and 14%, respectively. Authentic samples of compounds 5–7 were prepared according to the literature.<sup>9</sup>

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