## A HIGHLY STEREOSELECTIVE SYNTHESIS OF E-11-HEXADECEN-1-OL ACETATE: PURE TRANS PHEROMONES FROM ACYLSILANE/YLIDE CHEMISTRY

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**Abstract:** The preparation of E-11-hexadecen-1-ol acetate, a sex attractant of the sweet potato leaf folder moth, *Brachmia macroscopa* (and other related species, *eg. Mamestra brassicae* and *Sceliodes cordalis*) in >99% isomeric purity is described.

For some time, there has been an immense interest in the preparation of alkenes of very high isomeric purity with many of these new methods being applied to the synthesis of pheromones, where even minor amounts of isomeric impurities can diminish or even negate the bioactivity of the compound of interest.<sup>2</sup> The potential of vinylsilanes to function as precursors to long chain pheromones was recognized over a decade ago.<sup>3</sup> Unfortunately, in these cases, the isomeric purities of **2** were sufficiently low (*ie. ca.* 90% *Z* or *E*) so as to limit their applications to such natural products. Wittig chemistry has been extensively applied to such products, and the Schlossermodified process results in the formation of *trans*-alkenol pheromone components which are normally of 90-96% isomeric purity.<sup>2,4,5</sup>

Recently, we described the preparation of Z-1,2-disubstituted vinylsilanes in high isomeric purity from the reaction of non-stabilized ylides and aliphatic acylsilanes under soluble lithium salt conditions.<sup>6</sup> The reaction exhibits a remarkable sensitivity to the precise nature of the substitution pattern on both the acylsilane and ylide portions of the combining partners and on the reaction conditions in general. Thus, our acylsilane/ylide methodology appeared particularly well-suited to the synthesis of straight chain pheromones in that *n*-alkyl groups on both of the combining partners could be tolerated and extremely high Z-selectivities can be obtained in an operationally-simple procedure. To demonstrate the value of such an approach, we chose to prepare the  $C_{16}$  alkenol acetate (*ie.* **4E**), a true pheromone component of the sweet potato leaf folder moth, *Brachmia macroscopa* and related species.<sup>2</sup> Our reaction sequence is shown in Scheme 1 below.

While other excellent methods to both vinylsilanes<sup>3</sup> and *trans* alkenyl acetate pheromones are available,<sup>2</sup> our strategy clearly demonstrates for the first time, that acylsilanes<sup>7</sup> can be effectively used to orchestrate the Wittig olefination to provide vinylsilane precursors to such compounds in moderate yield (48%), but with truly exceptional isomeric purity (>99%)! This selectivity combined with operational ease in the approach, counterbalance the modest yield, where the deprotonation of **1** by the ylide is a competing side reaction.<sup>6</sup> Moreover, all of the other steps

SCHEME 1



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from the commercially available 10-undecen-1-ol give over 90% product yields in each case. Several points should be mentioned in the above Scheme. For one, it is critical to isolate the phosphonium salt precursor to the above yilde as a pure crystalline compound.<sup>4</sup> Also, the terminal alkenyl functionality in **2** is selectively hydroborated with 9-BBN giving, after oxidation, the primary alcohol, exclusively, with absolutely no detectable dihydroboration.<sup>8</sup> Acetylation of **3** in aceto-nitrile at room temperature produces hydrogen chloride which desilylates the vinylsilane with complete retention of configuration.<sup>9</sup> that is, from pure **3** to pure **4***E*, in one step!

To ascertain the configuration of **2**, it was photoisomerized to an E/Z (*ie.* 80:20) mixture employing Zweifel's procedure<sup>10</sup> which enabled us to quantitatively analyze the product composition by capillary GC as well as by <sup>13</sup>C NMR.<sup>11</sup> The isomeric Z pheromone (*viz.* Z-11-hexadecen-1-ol acetate<sup>2,8</sup>) of Sesamia inferens (purple stem borer) and related species was prepared under similar conditions from our ylide and pentanal to give Z-1,11-hexadecadiene (Z/E = 96:4) (78%) followed by the hydroboration-oxidation and acetylation method of Bestmann.<sup>8</sup> Combining limits of detection capillary GC data (50m x 0.25mm 3-cyanopropyl silicone) with the differing <sup>13</sup>C NMR allylic carbon resonances for the isomeric pheromones, we were able to determine that **4E** is >99% of the *E* isomer. This development should add to the existing legion of synthetic applications of the Wittig olefination.

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11. All products exhibited spectroscopic and analytical data which were wholly consistent with the assigned structures. 10-Undecen-1-yltriphenylphosphonium iodide was prepared from PPh<sub>3</sub> (0.886 mol, 233 g) in THF (1 L) and 11-iodoundec-1-ene (0.886 mol, 248 g) (48h reflux). Concentration and recrystallization from EtOAc gave 448 g (93%) of the desired salt (mp 91-92°). <sup>31</sup>P;  $\delta$  24.3 ppm. To the ylide from the above salt (0.071 mol, 38.41 g), in dry THF (300 mL), and n-BuLi (45.6 mL 1.6 M; 0.071 mol) (-78° to 0° then -110°), was added 1 (0.071 mol, 11.2 g) and, after warming to rt (2h), quenching with NH<sub>4</sub>Cl (sat) gave. after drying (MgSO<sub>4</sub>) and concentration *in vacuo*, filtering (C<sub>5</sub>H<sub>12</sub>) through alumina (Fresh, dry, neutral alumina is essential to avoid partial desilylation!), concentration and distillation, 10.1 g (48%) of 2Z (bp 132-133°C, 1 torr). **3** was prepared from 2Z and 9-BBN (24 mmol each) in dry THF (2h, rt) followed by oxidation (8.3 mL, 3 M NaOH; 8.3 mL, 30% H<sub>2</sub>O<sub>2</sub> dropwise). After 1.5h at reflux, workup gave 6.71 g (91%) of 3 (bp 143-8°C, 0.4 torr) <sup>29</sup>Si (TMS); -7.9 ppm. Stirring **3** in dry acetonitrile (0.5 M) with AcCl (10% excess, added dropwise) at room temperature gives, after 30 min and quenching (NH<sub>4</sub>Cl (sat)), drying (K<sub>2</sub>CO<sub>3</sub>), concentration at reduced pressure, and distillation at 0.4 torr, 90% of **4E** (bp 134°C). <sup>13</sup>C NMR (CDCl<sub>3</sub>);  $\delta$ .0.4 (TMS); 114.1, 139.1, 33.9 (C-1,2,3); 28.9, 29.1, 29.4, 30.2 (C-4 thru C-9); 32.1 C-10); 142.9 (C-11); 139.1 (C-12); 38.2 (C-13); 33.3 (C-14); 22.4 (C-15); 14.0 (C-16) ppm (vs. 2E:  $\delta$  -1.1 (TMS); 140.3 (C-11); 140.8 (C-12) ppm.) **4E**<sup>2d</sup>;  $\delta$  20.6; 171.0 (OAc); 64.5, 28.6, 25.9 (C-1,2,3); 29.1, 29.2, 29.4 (3C), 29.6 (C-4 thru -9); 32.5 (C-10); 130.2 (2C) (C-11,12); 32.2 (C-13); 31.8 (C-14); 22.1 (C-15); 13.8 (C-6) ppm. **4Z**:  $\delta$  20.7; 170.8 (OAc); 64.4, 28.6, 25.8 (C-1,2,3); 29.4 (3C), 29.7 (C-4 thru -9); 27.1 (C-10); 129.7 (2C) (C-11,12); 26.8 (C-13); 31.9 (C-14); 22.2 (C-15); 13.8 (C-6) ppm.