Synthesis of the First Natural Host Germination Stimulant for *Striga asiatica*

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The germination stimulant, 5-methoxy-3-[(8′*Z*,11′*Z*)-pentadeca-8′,11′,14′-trienyl]benzene-1,2,4-triol, exuded by *Sorghum bicolor* for the seeds of *Striga asiatica* (witchweed) has been synthesized.

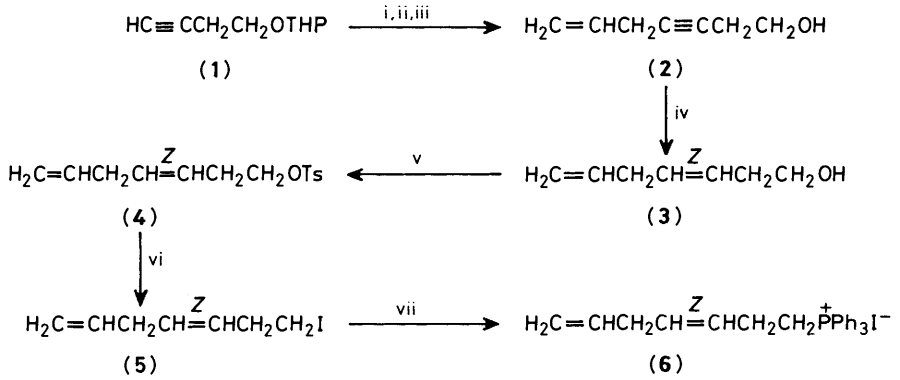
A little understood feature of parasitism in plants is that the host may exude a stimulant which causes the germination of the parasite. Some of the host plants involved constitute food crops of vast economic and social importance. These include the legumes sorghum, maize, and millett which are staple foods in many tropical areas of the world where the plants are parasitized by various species of the genus *Striga*.[1] A potent germination stimulant for *Striga* species, the sesquiterpene strigol, was isolated from cotton which is not a natural host for *Striga*.[2] According to a recent report, however, the first germination stimulant for *Striga asiatica* seeds, 5-methoxy-3-[(8′*Z*,11′*Z*)-pentadeca-8′,11′,14′-trienyl]benzene-1,2,4-triol (**17**), was isolated in minute quantity from a natural host, *Sorghum bicolor*.[3] This compound is active at 10^{-7} M concentration and is capable of defining the distance away from the host root at which *Striga* germinates. We now describe an efficient synthesis of this compound and the related biologically inactive quinone (**18**).

We chose to adopt a convergent synthetic route to the target molecule (**17**) in which the (*Z*) double bond at the 8′-position in the side chain would be constructed by a Wittig reaction at a late stage in the synthesis. For this purpose we therefore required the phosphonium salt (**6**) (Scheme 1) and the protected aldehyde (**15**) (Scheme 2).

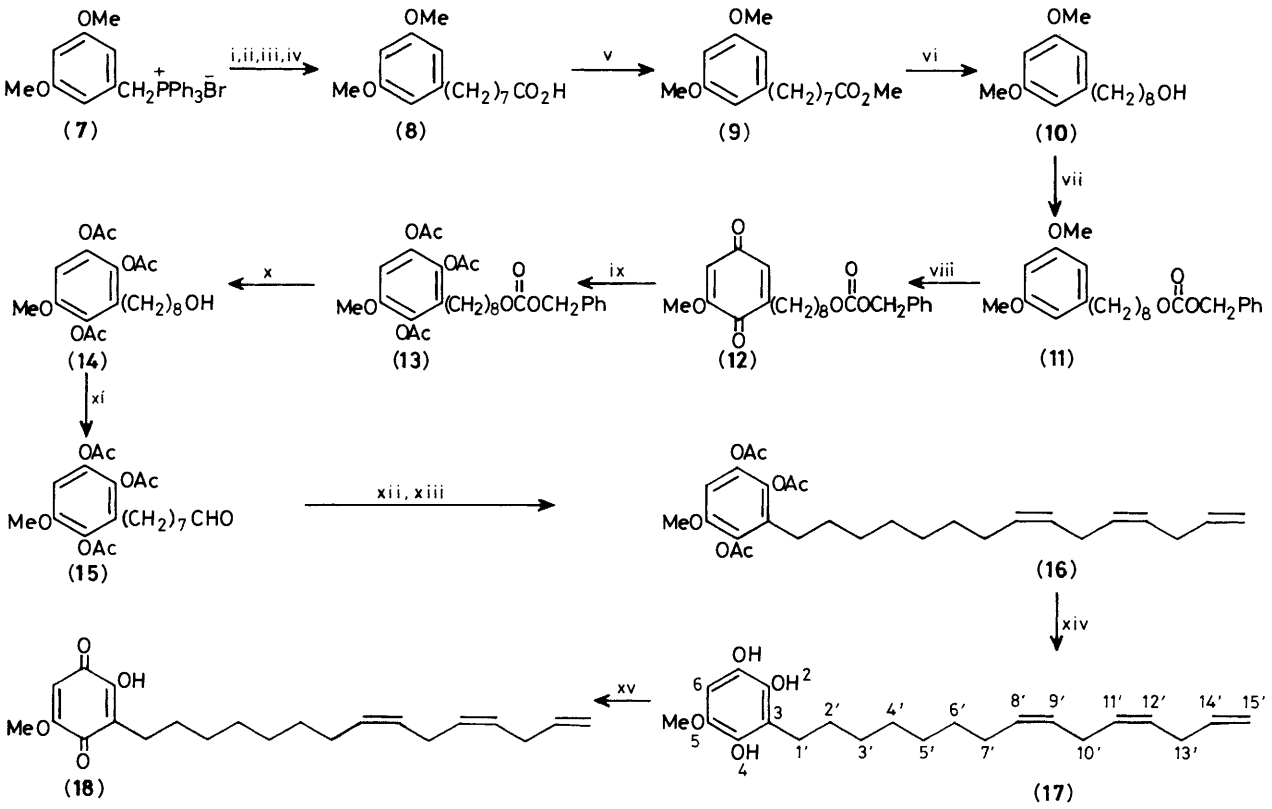
The starting material for the synthesis of the phosphonium salt (**6**) was the known tetrahydropyranyl ether (**1**) of but-3-yn-1-ol[4] which was allowed to react as its Grignard reagent with allyl bromide in the presence of copper(I) chloride. Deprotection of the crude product gave the eneynol (**2**) as an oil (67%), b.p. 45 °C at 0.01 mmHg. Partial reduction now gave pure (*Z*)-dienol (**3**) (89%), b.p. 60 °C at 0.5 mmHg.[5] This compound was now converted sequentially into the tosylate (**4**) (82%), the iodo compound (**5**) (100%), and finally into the phosphonium iodide (**6**) (96%), m.p. 145—147 °C.

The starting material for the synthesis of the aldehyde (**15**) was the phosphonium bromide (**7**)[6] which as its derived ylide was caused to undergo a Wittig reaction with ethyl 7-oxoheptanoate.[7] The crude product was converted by hydrolysis and reduction into the acid (**8**) (100%), m.p. 60—62 °C. Methylation now gave the ester (**9**) (95%), b.p. 200 °C at 0.01 mmHg, which on reduction afforded the alcohol (**10**) (100%), b.p. 230 °C at 0.01 mmHg. This latter compound was protected as its benzyloxycarbonyl derivative (**11**) (100%) which on oxidation with chromium trioxide under mild conditions supplied the quinone (**12**) (90%) as yellow needles, m.p. 40—41 °C. Thiele acetylation of the quinone gave the triacetoxy compound (**13**) (91%). The structure of this compound, and hence the regiospecifity of the Thiele reaction, was confirmed by a NOESY experiment. In the spectrum of compound (**13**) there was a strong off-diagonal interaction between the resonance of the aromatic proton and that of the methoxy group. Deprotection of compound (**13**) by hydrogenolysis gave the alcohol (**14**) (77%) which on oxidation with pyridinium chlorochromate supplied the required aldehyde (**15**) (100%).

Wittig reaction between the aldehyde (**15**) and an excess of the ylide derived from the phosphonium iodide (**6**) gave the triene (**16**) (56%) which on deprotection by treatment with lithium aluminium hydride gave the germination stimulant (**17**) (100%) as an unstable oil the spectroscopic properties of which were in accord with the literature.[3] The stereochemical



Scheme 1. *Reagents and conditions:* i, EtMgBr, THF, Ar, 60 °C, 45 min; ii, CuCl, CH_2=$CHCH_2Br$, Ar, 60 °C, 45 min; iii, PPTS, MeOH, Ar, 55 °C, 18 h; iv, H_2, 5% Pd/$BaSO_4$, C_5H_5N; v, $CHCl_3$, *p*-$MeC_6H_4SO_2Cl$, C_5H_5N, 0 °C, 6 h; vi, NaI, Me_2CO, 25 °C, 2 d; vii, Ph_3P, MeCN, reflux, Ar, 2 d.



Scheme 2. *Reagents and conditions:* i, BuLi, THF, Ar, 25 °C; ii, $OHC(CH_2)_5CO_2Et$, Ar, 25 °C; iii, NaOH, H_2O, MeOH, reflux, 5 h; iv, H_2, 10% Pd/C, EtAc; v, MeOH, H_2SO_4, reflux, 16 h; vi, $LiAlH_4$, Et_2O, 25 °C, 3 h; vii, $ClOCOCH_2Ph$, C_5H_5N, PhMe, 0—60 °C, 3 h; viii, 4 equiv. CrO_3, AcOH, H_2O, 0—25 °C, 1.5 h; ix, Ac_2O, H_2SO_4, 25 °C, 12 h; x, H_2, 10% Pd/C, EtAc, 2 h; xi, PCC, NaOAc, CH_2Cl_2, 0—25 °C, 3 h; xii, 4 equiv. (**6**), BuLi, THF, −78 °C, Ar, 0.5 h; xiii, HMPA, THF, −78 °C, Ar, 2 h; xiv, THF, $LiAlH_4$, Ar, 25 °C, 10 min; xv, PhH, 1% aq. $FeCl_3$, 15 min.

homogeneity of this material was confirmed by the ^{13}C n.m.r. spectrum.[8] Mild oxidation of the stimulant provided the quinone (**17**) as yellow plates (100%), m.p. 37—39 °C. Again the spectroscopic data for this compound were in accord with the literature.[3]

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8 ^{13}C N.m.r. spectrum: δ_C(75.5 MHz; $CDCl_3$) 23.83 (C-1′), 25.56 (C-10′), 27.22 (C-7′), 29.06, 29.25. 29.44, 29.63, and 29.66 (each CH_2), 31.51 (C-13′), 56.56 (OMe), 97.95 (C-6), 114.67 (C-15′), 116.69 (C-3), 126.78, 127.51, and 129.31 (C-9′, C-11′, and C-12′), 130.46 (C-8′), 135.82, 135.99, 137.70, and 139.88 (C-1, C-2, C-4, and C-5), and 136.83 (C-14′).

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