The Use of an Arsorane as Isoprenoid Reagent: Synthesis of 5-Substituted 3-Methyl-2,4-pentadienoic Esters (ABA Ester Analogs)[1]

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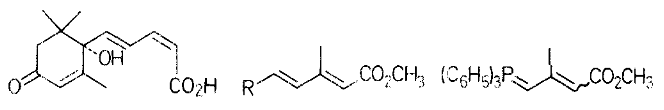
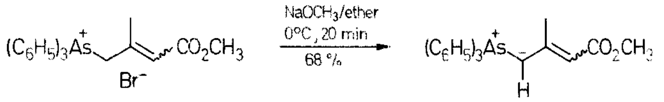
By using of 3-methoxycarbonyl-2-methyl-2-propenylidenetriphenylarsorane (4) as isoprenoid reagent, 5-substituted 3-methyl-2,4-pentadienoic esters 6A and 6B (ABA ester analogs) were synthesized in 88–98% yields under mild conditions.

The preparation of 5-substituted 3-methyl-2,4-pentadienoic esters 1 has attracted considerable attention, because it is related to the carotenoids, to the important plant hormone abscisic acid (ABA), etc. Many uses of ABA in modern agriculture have been suggested, but its high cost resulting from a long and difficult synthesis with a low overall yield[2,3] makes its wide use impractical. Therefore many chemists have focused on the synthesis of its analogs. Milborow et al.[4] indicated that the configuration of the side chain, (2*Z*, 4*E*)-2,4-pentadienoic acid, might be a prerequisite for high activity. Bittner et al.[5] reported, however, that 3-methyl-5-*p*-chlorophenyl-(2*E*, 4*E*)-2,4-pentadienoic acid exhibited high ABA-like activity. Therefore, the 4*E* configuration in 1 might be necessary for the biological activity. However, four geometric isomers of 1 were obtained *via* pure *Z* or *E* Wittig reagent 2,[6-8] the newly formed double bond being in either *Z* or *E* configuration. Gedye et al.[8] reported that the corresponding *Z* and *E* phosphonate ester reacted with aldehydes with extensive stereomutation of the original double bond.

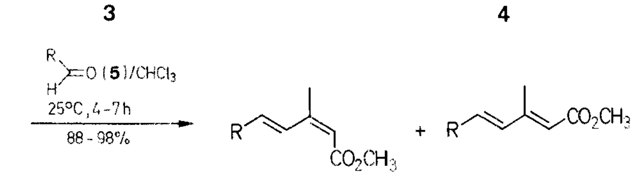


ABA 1 2

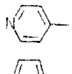
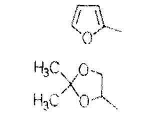
We would like to report here the use of highly reactive arsorane 4 (generated from a 1:1 mixture of *Z* and *E* arsonium bromide 3) as isoprenoid reagent to synthesize ABA ester analogs.



3 4



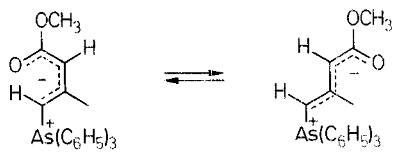
6A (a-g) 6B (a-g)

6A, 6B	R	6A, 6B	R
a	*p*-$NO_2C_6H_4$	e	
b	*p*-ClC_6H_4		
c	*p*-$CH_3OC_6H_4$	f	
d	C_6H_5		
		g	

Our method gave only two isomeric products 6A and 6B). The newly formed double bond is exclusive in the *E* configuration and excellent yields (88–98%) were obtained.

The experimental procedure is convenient. Treatment of a 1:1 mixture of *Z*- and *E*- arsonium salt 3 with sodium methoxide afforded 3-methoxycarbonyl-2-methyl-2-propenylidene triphenylarsorane 4, which reacted with a variety of aldehydes to give only the two isomers 6A and 6B.

In our method, the product 6 consisted of about 50–60% of 6A, which is usually hard to prepare. The reason for the formation of 6A might be due to the existence of arsorane 4 as two conformers (*Z*)-4 and (*E*)-4 in rapid equilibrium, as in the case of phosphonium ylides.[6]



Z-4 *E*-4

3-Methoxycarbonyl-2-methyl-2-propenyltriphenylarsonium Bromide (3): Triphenylarsine (33 g, 0.11 mol) and a 1:1 mixture of methyl (*E*)- and (*Z*)-4-bromo-3-methyl-2-butenoate[9] (19 g, 0.1 mol) are stirred at 60–70°C under nitrogen in a capped thick-wall tube for 3 h. The white solid is collected and washed with benzene to afford 3 (*E*:*Z*, 1:1), which is recrystallized from chloroform/ethyl acetate; yield: 43 g (85%); m.p. 139–140°C.

Table. 5-Substituted 3-Methyl-2,4-pentadinoic Esters **6A** and **6B** Prepared

6	Reaction Time (25°C)	Yield (%)	A : B[a]	m.p. (°C) or b.p. (°C)/torr[b]	Molecular Formula[c] or Lit. Data	IR (KCl or film)[d] (cm^{-1})	MS[e] m/e (%)	^{1}H-NMR (CCl_4 or $CDCl_3$/TMS)[f] δ (ppm)
a	4 h	98	2 : 1	88–90	$C_{13}H_{13}NO_4$ (247.2)	1710, 1610, 1170	247 (M^+, 31)	2.36 (*E, E*); 2.10 (*Z, E*) (s, 3H); 3.68 (s, 3H); 5.91 (*E, E*), 5.78 (*Z, E*) (s, 1H); 6.84 (*E, E*), 8.50 (*Z, E*) (d, 1H, *J* = 16 Hz); 6.87 (d, 1H, *J* = 2.5 Hz); 7.5–8.2 (m, 4H)
b	7 h	98	1 : 1	97–98	$C_{13}H_{13}ClO_2$ (236.7)	1710, 1618, 1170	236 (M^+, 34)	2.34 (*E, E*), 2.16 (*Z, E*) (s, 3H); 3.64 (s, 3H); 5.78 (*E, E*), 5.65 (*Z, E*) (s, 1H); 6.70 (*E, E*), 8.35 (*Z, E*) (d, 1H, *J* = 16 Hz); 6.73 (d, 1H, *J* = 2.5 Hz); 7.2–7.5 (m, 4H)
c	7 h	88	1 : 1	57–59 68–70	$C_{14}H_{14}O_3$ (232.3)	1710, 1600, 1160	232 (M^+, 36)	2.32 (*E, E*), 2.05 (*Z, E*) (s, 3H); 3.60 (s, 3H); 3.72 (s, 3H); 5.72 (*E, E*), 5.55 (*Z, E*) (s, 1H); 6.71 (*E, E*), 8.35 (*Z, E*) (d, 1H, *J* = 16 Hz); 6.8–7.5 (m, 5H)
d	4 h	98	3 : 2	108/1	b.p. 110–114/1 torr[5]	1725, 1620, 1170	202 (M^+, 38)	2.33 (*E, E*), 2.03 (*Z, E*) (s, 3H); 3.63 (s, 3H); 5.78 (*E, E*), 5.62 (*Z, E*) (s, 1H); 6.71 (*E, E*), 8.38 (*Z, E*) (d, 1H, *J* = 16 Hz); 6.75 (d, 1H, *J* = 2.5 Hz); 7.2–7.5 (m, 5H)
e	5 h	98	3 : 2	160/6	$C_{12}H_{13}NO_2$ (203.2)	1710, 1600, 1160	203 (M^+, 24)	2.33 (*E, E*), 2.07 (*Z, E*) (s, 3H); 3.65 (s, 3H); 5.83 (*E, E*), 5.71 (*Z, E*) (s, 1H); 6.66 (*E, F*), 8.63 (*Z, E*) (d, 1H, *J* = 16 Hz); 7.15 (d, 2H, *J* = 6 Hz); 8.45 (d, 2H, *J* = 6 Hz)
f	4 h	98	1 : 1	120/2	$C_{11}H_{12}O_3$ (192.2)	1710, 1600, 1160	192 (M^+, 100)	2.29 (*E, E*), 2.01 (*Z, E*) (s, 3H); 3.62 (s, 3H); 5.74 (*E, E*), 5.57 (*Z, E*) (s, 1H); 6.28–6.60 (m), 8.16 (d, *J* = 16 Hz) (together 4H); 7.31 (d, 1H, *J* = 2.5 Hz)
g	4 h	89	1 : 1	100/4	$C_{12}H_{18}O_4$ (226.3)	1720, 1620, 1160	226 (M^+, 34)	1.33 (s, 6H); 2.22 (*E, E*), 2.00 (*Z, E*) (s, 3H); 3.45–3.98 (m, 2H); 3.61 (s, 3H); 4.5 (m, 1H); 5.5 (m, 1H); 6.00–7.20 (m), 7.67 (d, *J* = 16 Hz) (together 2H)

[a] The ratio of isomers was estimated by the integrated intensities of the ^{1}H-NMR peaks.
[b] Boiling point of bulb-to-bulb, short-path distillation; bath temperature given.
[c] Satisfactory microanalyses obtained: C ±0.20, H ±0.26, N ±0.13, exception: **6g** (C −0.60).
[d] The IR spectra were recorded with a Specord 75-IR spectrophotometer.
[e] The mass spectra were recorded with a Finnigan 4021 spectrometer.
[f] The ^{1}H-NMR spectra were recorded at 60 MHz with a Varian EM 360 spectrometer or at 200 MHz with a Varian XL-200 spectrometer.

$C_{24}H_{24}AsBrO_2$	calc.:	C 57.73	H 4.85	Br 16.00
(499.3)	found:	57.60	5.04	15.92

IR (KCl): ν = 1700, 1640, 1150 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 2.05 (*E*), 2.16 (*Z*) (s, 3H); 3.58 (*E*), 3.36 (*Z*) (s, 3H); 5.14 (*E*), 5.38 (*Z*) (s, 2H): 6.05 (*E*), 5.77 (*Z*) (b d, 1H); 7.73 ppm (m, 15H).

3-Methoxycarbonyl-2-methyl-2-propenylidenetriphenylarsorane (4):
To a suspension of sodium methoxide (20 mmol) in absolute ether (20 ml) is added arsonium bromide **3** (10 g, 20 mmol) at 0°C under nitrogen. The mixture is stirred for 20 min. The solid is collected under nitrogen, washed with ice water until neutral, and vacuum dried to give **4**, yield: 5.7 g (68%); m.p. 108–111°C.

$C_{24}H_{23}AsO_2$	calc.:	C 68.90	H 5.54
(418.4)	found:	68.39	5.38

5-Substituted 3-Methyl-2,4-pentadienoic esters 6A and 6B; General Procedure:
3-Methoxycarbonyl-2-methyl-2-propenylidene triphenylarsorane (**4**; 1.26 g, 3 mmol), aldehyde **5** (20 mmol) and chloroform (10 ml) are placed in a reaction tube under nitrogen. The mixture is stirred at 25°C for 4–7 h. The solvent is removed under vacuum, and the residue is purified by flash chromatography on silica gel (petroleum ether (b.p. 60–90°C)/ethyl acetate as eluent). The products thus obtained are further purified by recrystallization or distillation.

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(1) This paper is the 48th report on the application of elemento-organic compounds of the fifth and sixth groups in organic syntheses.
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