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A FACILE SYNTHESIS OF ω-SUBSTITUTED CONJUGATED POLYENONES VIA ARSONIUM SALT AND ITS APPLICATION TOWARDS THE SYNTHESIS OF NAVENONE A[1]

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Abstract: In the presence of K_2CO_3, a variety of aldehydes condensed with the arsonium bromide **8** at 0-3°C to give exclusively ω-substituted polyenones **1** in good yields, and the synthesis of navenone A was achieved by this procedure.

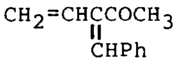
The synthesis of ω-substituted conjugated polyenones **1**, such as naturally occurring navenones,[2] a trail-breaking alarm pheromone of sea slug, has attracted considerable attention of synthetic organic chemists. The Wittig or Wittig-Horner reaction is the most general approach towards the synthesis of olefins. However, it has been shown that the triphenylphosphine reacts with 5-bromo-3-penten-2-one to give a mixture of bromides which, in turn, on treating with potassium t-butoxide reacts with benzaldehyde to give a mixture of desired (3E, 5E)-6-phenyl-3,5-hexadien-2-one **2** and undesired 3-benzylidene-4-penten-2-one **3** in very low yield.[3]

$R(CH=CH)_nCOCH_3$

1

$PhCH=CH-CH=CHCOCH_3$

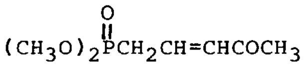
2



$CH_2=CH\underset{\overset{\|}{CHPh}}{C}COCH_3$

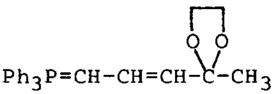
3

The abnormal Arbuzov reaction of γ-halogeno-α,β-unsaturated ketone prevents the preparation of corresponding phosphonate **4**.[3] Phosphorane **5** or phosphonate **6** with a masked carbonyl group reacted with aldehydes to give a mixture of E and Z olefination products. The subsequent hydrolysis of the resulting dioxalane products should be carried out for several days and the overall yield was very low. Furthermore, the starting material (E)-5-bromo-3-penten-2-one ethylene acetal was rather difficult to prepare.[4]



$(CH_3O)_2\overset{\overset{O}{\|}}{P}CH_2CH=CHCOCH_3$

4



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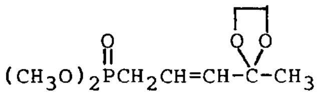


6

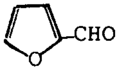
In contrast to triphenylphosphine, we found that triphenylarsine reacted with 5-bromo-3-penten-2-one smoothly to give a pure arsonium bromide **8**, which was confirmed by ^1H NMR.[5] Herein we wish to describe a facile synthesis of ω-

substituted polyenones **1** featured by the direct use of arsonium bromide **8** in the presence of K_2CO_3 at low temperature in good yields.

$$\underset{\substack{n=0,1\\ \mathbf{7}}}{R(CH{=}CH)_nCHO} + \underset{\mathbf{8}}{[Ph_3\overset{+}{As}CH_2CH{=}CHCOCH_3]Br^-} \xrightarrow[0\text{-}3°C,\ -Ph_3AsO]{K_2CO_3,\ Et_2O(\text{trace } H_2O)} \underset{\substack{n=0,1\\ \mathbf{1}}}{R(CH{=}CH)_{n+2}COCH_3}$$

The results are shown in the following Table.

Table Synthesis of Conjugated Polyenones

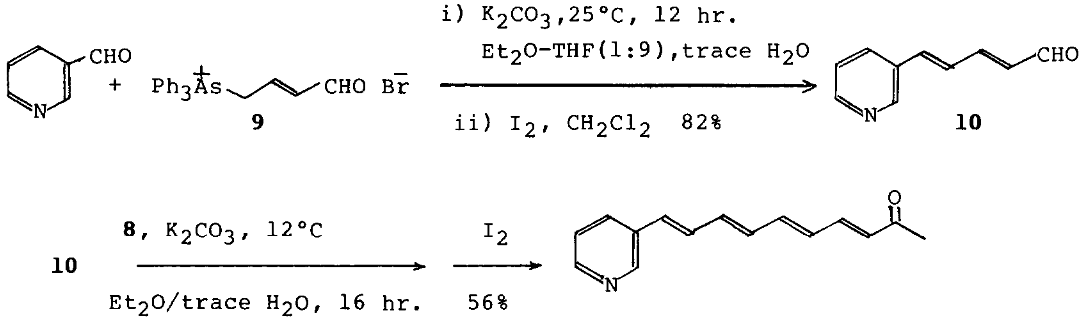
Entry	RCHO **7**	Temp.(°C)/Time(h)	Yield of **1** (%)	(3E,5E):(3E,5Z)
1	C_6H_5CHO	0-3/36	81	77:23
2	$p\text{-}O_2N\text{-}C_6H_4CHO$	0-3/8	91	74:26
3	$p\text{-}Cl\text{-}C_6H_4CHO$	25/16	87	84:16
4	$C_6H_5CH{=}CHCHO$	0-3/28	84	85:15
5	$n\text{-}C_5H_{11}CHO$	0-3/20	56	78:22
6	$n\text{-}C_8H_{17}CHO$	0-3/6.5	67	79:21
7		0-3/19	71	74:26

Reaction conditions: The solvent used was Et_2O(trace H_2O) except Et_2O/THF (1:1)-trace H_2O in **Entry 3**. All compounds were characterized by elemental analysis (except for the known compounds in **Entry 1,3,4**), MS, IR and ^1H NMR. The ratio of the isomers was estimated by GC or TLC scanning and ^1H NMR.

E-5-Bromo-3-penten-2-one[3] reacted with triphenylarsine without solvent at 50 °C for 4 hrs to form arsonium bromide **8** in 43% yield.[5]

The typical procedure for the synthesis of polyenones: **8** (2.4 mmol), C_6H_5CHO(2 mmol), K_2CO_3(2.4 mmol) and Et_2O(12 ml)/trace H_2O(60 μl) were mixed under N_2 and stirred at 0-3°C. After the reaction was complete (monitored by G.C.), most of triphenylarsine oxide was removed by a short silica gel column chromatography. The crude product was shown by GC to be a mixture of two isomers (77:23). The pure E,E- , E,Z-isomers and a mixture of two isomers were obtained in 56%, 18% and 7% yields respectively by flash chromatography . They were characterized by ^1H NMR according to the data reported in literature[6] and mass spectra. The (3E,5Z) isomer was isomerized to (3E,5E) isomer on treating with I_2 under daylight.

The synthesis of navenone A[2] **11** was conveniently achieved by utilizing this reaction. Condensation of 3-pyridinecarbaldehyde with formylallyltriphenylarsonium bromide[7] **9** in Et_2O-THF(1:9)-trace H_2O in the presence of potassium carbonate at 25°C for 12 h gave a mixture of (2E,4E)- and (2E,4Z)- 5-(3-pyridyl)-pentadienal and the (2E,4Z) isomer was isomerized to the desired (2E,4E) isomer **10** on treating with I_2 under daylight. The yield of **10** was 82%. **10** reacted with **8** to afford a mixture of two isomers (9:1) in favor of the desired all trans isomer **11**, which was obtained in 56% yield by flash chromatography and identified as navenone A by its spectra.[8] The undesired isomer could be isomerized to **11** by treating with I_2 under daylight. It is noteworthy **11** has been synthesized by Sakakibara et al.[2] by a seven step reaction in 1% overall yield.



navenone A **11**

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Referances and Notes:

(1) This paper is the 55th report on the application of elemento-organic compounds of fifth and sixth groups in organic syntheses.
(2) M. Sakakibara, M. Matsui, Agric. Biol. Chem., 43 117(1979).
(3) J. Font, P.de March, Tetrahedron, 37, 2391(1981).
(4) J.Camps, J.Font, P.de March, Tetrahedron, 37, 2493(1981).

(5) The reagent **8** gave satisfactory elemental analysis (Found: C% 58.78, H% 4.59, Br% 17.10; Calc.: C% 58.87, H% 4.72, Br% 17.03). m.p. 127-128°C. ^{1}H NMR (60 MHz TMS/ $CDCl_3$ δ): 2.10(s, 3H), 5.20(d, 2H), 6.68(m, 2H), 7.70(m, 15H); IR: 1620, 1670, 1695cm^{-1},

(6) A.F. Kluge, C.P Lillya, J.Org.Chem., 36, 1971(1977).

(7) Y.Z. Huang, L.L. Shi and J.H. Yang, Facile Formyl-enyl-olefination of Aldehydes by Means of Arsonium Salt, to be published.

(8) Navenone A: mp 138-140°C, UV λ_{max}^{MeOH}367 nm(ε 59,930) and 378 nm(ε 58,003), IR ν_{max}^{KCl} 1675(C=O),1570(C=C) cm^{-1}; ^{1}H NMR($CDCl_3$, 200 MHz, δ): 2.28(s, 3H), 6.18(d,J=15Hz 1H for 3-H), 6.36-7.17(m,7H), 7.26(1H, for 5'-H), 7.72(1H for 4'-H), 8.45(1H, for 6'-H), 8.62(1H, for 2'-H); MS (m/e): 225(M^+), 210 (M^+-Me),182(M^+-Ac).

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