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ω-BROMOALKAPOLYENYLMETHYL KETONES—II

USE OF 5-BROMO-3-PENTEN-2-ONE ETHYLENE KETAL AS A C_5-SYNTHON

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Abstract—The preparation of the phosphonium salt and the dimethyl-phosphonate of (*E*)-5-bromo-3-penten-2-one ethylene ketal, **6** and **7**, is described. These C_5-isoprenoid synthons were condensed with several aldehydes and ketones giving mixtures of the corresponding *E* and *Z*-olefination products. Reaction of the anion of the phosphonate derivative with β-ionone gave 9-*cis* and 9-*trans*-β-C_{18}-tetraenone ketals, **13** and **14**, which by subsequent hydrolysis afforded 9-*cis* and 9-*trans*-β-C_{18}-tetraenones, **15** and **16**. A C_6-isoprenoid synthon is also described.

Wittig and Wittig–Horner reactions are the most general approaches towards the synthesis of olefins. Both reactions have special interest when applied to the synthesis of isoprenoid compounds, where the number of examples of the use of these reactions is very large.[1] Many natural products are even synthesized in industrial scale by these olefination reactions.[2] In the last years several papers have been published on the synthesis of polyene isoprenoids by the Wittig–Horner reaction[3] and some C_5-isoprenoid synthons, none of them of the phosphorous-derivative type, have also been described.[4] Liu and coworkers[5] have prepared many derivatives in the vitamin A series utilizing Wittig or Wittig–Horner derivatives in some steps.

We report now the preparation and utility of a phosphorous C_5-synthon. In the preceding paper[6] we have shown that the first member of ω-bromoalkapolyenylmethyl ketones, i.e. 5-bromo-3-penten-2-one **1**, cannot be used directly as a C_5-synthon through its conversion to Wittig or Wittig–Horner derivatives. Therefore, we have tried to mask the carbonyl group in order to prevent abnormal reactions trigged by its presence. Since the most frequent and useful method to protect a carbonyl group is its transformation to a ketal group, we attempted to synthesize first the ethylene ketal of **1** and this proved to be fruitful as shown in the results reported herein.

Synthesis of (E)-5-*bromo*-3-*penten*-2-*one ethylene ketal* (**2**)

Due to the great instability of **1** its direct ketalization was not essayed and the synthesis of **2** was reduced to the synthesis of (*E*)-3-penten-2-one ethylene ketal[7] **3**, and its allylic bromination.

Ketal **3** could be prepared by Wittig or Wittig–Horner reaction through the corresponding derivatives of a halogenopropanone ethylene ketal and acetaldehyde. Nevertheless, while bromo- and chloropropanone ethylene ketals are well known,[8] their conversion to phosphonium salts or phosphonates has never been reported and in fact we were unable to prepare them. Thus, bromo- or chloropropanone ethylene ketal was refluxed in various conditions in the presence of triphenylphosphine or trialkylphosphites and the products were always recovered unaltered: steric hindrance should be the cause of this unreactivitity.

An alternative route to ketal **3** would be the direct ketalization of 3-penten-2-one **4**, the difficulty being the possible migration of the double bond as frequently encountered, although this can be prevented using a weak acid catalyst.[9] Treatment of **4** with ethylene glycol in the presence of adipic acid gives a mixture of products from which 2-methyl-2-[(*E*)-1-propenyl]-1,3-dioxolane, i.e. ketal **3**, and 2-(2*RS*)-2-(2-hydroxyethoxy)propyl-2-methyl-1,3-dioxolane (**5**) were isolated by distillation and preparative GLC.

Dioxolane **5** derives formally from a Michael addition of ethylene glycol to ketone **4** followed by ketalization, and was identified by the presence of a hydroxyl stretching band at 3510 cm^{-1} and by ^1H NMR data, in particular the absence of olefinic protons. It is worthwhile to mention the absorption of the diastereotopic protons of the methylene linked to the dioxolane ring at δ 1.85, that in the presence of the chemical shift reagent Eu(fod)$_3$ can be well resolved.

The formation of dioxolane **5** did not represent an important loss of material since heating it at 180°C in the presence of adipic acid gave 78% yield of ketal **3**. Therefore, the total yield for the ketalization of **4** was 58%.

The structural assignment of ketal **3** was based on ^1H NMR, showing an olefinic absorption of two protons, AB system centered at δ 5.57 (J_{AB} = 16 Hz), and IR spectroscopy with a weak carbon-carbon double bond stretching band at 1675 cm^{-1}.

Allylic bromination of ketal **3** with NBS in the presence of calcium oxide, sodium hydrogenocarbonate[10] and benzoyl peroxide gave in a 70% yield ketal **2**, i.e. 2-[(*E*)-3-bromo-1-propenyl]-2-methyl-1,3-dioxolane, which is significantly more stable than the corresponding bromoketone **1**. The structure was characterised by ^1H NMR, olefinic absorption centered at δ 5.85 (J_{AB} = 15 Hz), mass spectrometry and IR in which spectrum the carbon-carbon double bond stretching band is almost not observed.

Synthesis of Wittig and Wittig–Horner derivatives of ketal **2**

Ketal **2** was converted, cleanly and in high yield, into its phosphonium salt **6** by reaction with triphenylphosphine without the problems observed in the analogous reaction with the bromoketone **1**.[6] Its structure was confirmed by ^1H NMR data that allow the assignment of

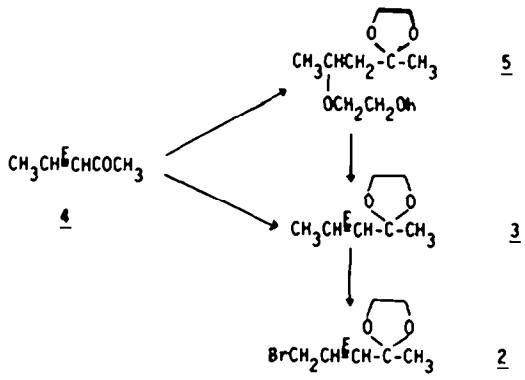


Fig. 1.

all the protons including the allylic system which presents a complex absorption due to virtual coupling[11] among the methylene protons (also coupled with phosphorous, $J_{PH} = 14$ Hz) at δ 4.77 and their β olefinic proton that absorbs jointly with the other one in an almost collapsed AB system at δ 5.8. Note that in the phosphonium salt **6** no tautomerism takes place in contrast with the behaviour of the phosphonium salt produced from bromoketone **1**.[6]

Ketal **2** also was made to react with trimethyl phosphite giving the corresponding phosphonate **7** in 86% yield, its structure being confirmed by mass spectrometry, IR and ^{1}H NMR. In this spectrum also the protons of the allylic system linked to the phosphorous atom show a complex absorption: methylene protons at δ 2.45 ($J_{PH} = 22$ Hz measured by a decoupling experiment by irradiaiton at δ 5.5, olefinic protons).

The configuration of the double bond, not derivable from spectral data since the olefinic protons are almost synchronous in both compounds, is assumed to be *E* due to the configuration of the initial bromoketone and the stereochemistry of the condensation products (*vide infra*).

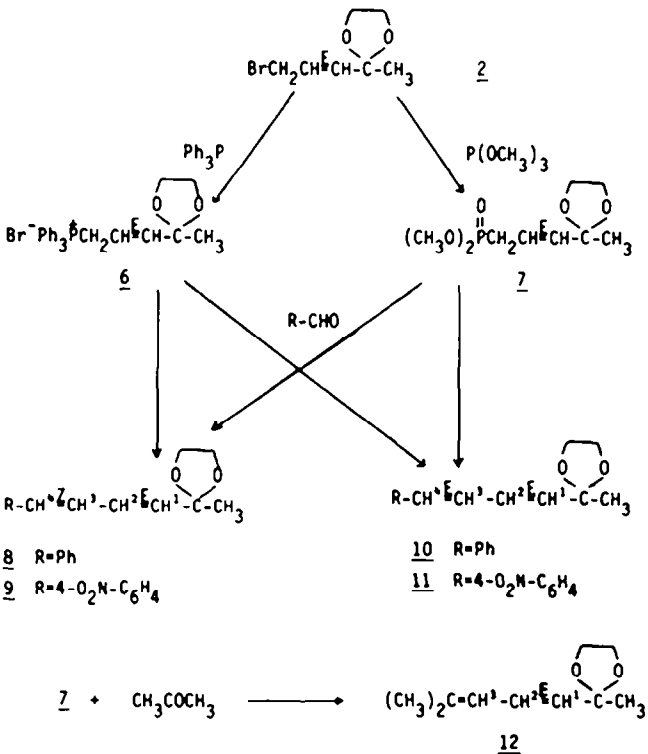
Use of compounds **6** *and* **7** *as* C_5*-synthons*

The utility of phosphonium salt **6** and phosphonate **7** was proved in a series of Wittig and Wittig–Horner condensations. (i) Condensations with benzaldehyde and 4-nitrobenzaldehyde are summarized in Scheme 1 and Table 1.

In all the hexadienone derivatives the double bond initially present into the C_5-synthon has been shown to have *E* configuration by ^{1}H NMR data: H^1 proton absorbs in all four products cleanly separated upfield from the other olefinic bands and in all cases J = 15–16 Hz; i.e. no isomerization of this double bond occurs through the corresponding anion formation.

On the condensation with the phosphonium salt **6** the configuration of the new created double bond varies depending on the base and cation used for the formation of the ylide being the ratio *Z*:*E* from equimolar (presence of Li^+) to 9:1 (absence of Li^+). This behaviour is the normal for nonstabilized ylides.[12] This fact seems to indicate that in the ylide the canonic form "b" contributes very little to the resonance hybrid perhaps because the negative charge would interact with the non-bonding pairs of electrons of the oxygen atoms. Accordingly, the phosphorane deriving from phosphonium salt **6** should be considered as a non-stabilized ylide.

Very little experience exists on non-stabilized phosphonates. Thomas[13] in a review on phosphonates indicates



Scheme 1.

Table 1.

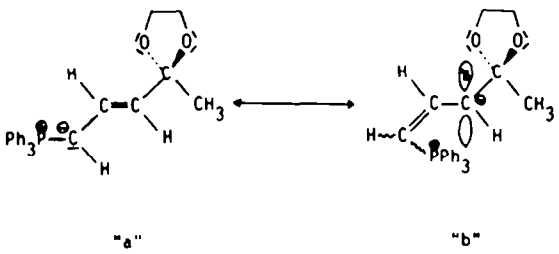
C_5-synthon	Base	Solvent	Aldehyde	Products	Z:E ratio[a]	Yield (%)[b]
6	PhLi	ether	benzaldehyde	8 and 10	1:1	35
6	NaH	DMF	benzaldehyde	8 and 10	9:1[c]	40
6	PhLi	ether	4-nitrobenzaldehyde	9 and 11	1:1	34
6	NaH	DMF	4-nitrobenzaldehyde	9 and 11	2:1[d]	63
7	NaH	DMF	benzaldehyde	8 and 10	1:9[c]	59
7	NaH	DMF	4-nitrobenzaldehyde	9 and 11	1:7	35

a) Isomeric ratio was determined by ^{1}H-nmr.

b) Yields correspond to isolated mixture of isomers.

c) The major isomer was separated by distillation.

d) Both isomers were isolated by column chromatography on silica gel.



"a" "b"

Fig. 2.

that the anions corresponding to these compounds attack aldehydes or ketones giving anionic intermediates that decompose with difficulty to the olefins. However, in an article from Corey[14] quoted by Thomas some condensations are described from non-stabilized phosphonates. The anion of our phosphonate 7 should be non-stabilized for the same reasons as exposed above, but reacts efficiently with aldehydes and (*vide infra*) with ketones. Nothing is known on the stereospecificity of the condensations of non-stabilized phosphonates. In our case an *E* configuration predominates on the created double bond. This can be due to the difficult decomposition of the anionic intermediates shifting the equilibrium between the carbonyl compound and the phosphonate anion to that intermediate which results in the olefin thermodynamically more stable. However, the observed ratio of products can also be explained through kinetic control and this possibility can not be excluded.

The assignment of configuration of the considered double bond was made by ^{1}H NMR. Compound **8** shows a straightforward first order ethylenic absorption, with $J_{H^4\text{-}H^5} = 10$ Hz, which points to the *Z* configuration. Compounds **9** and **11** were assigned by the width of the aromatic AA'BB' system: *E* configuration with completely coplanar conjugation of the benzene ring with the olefinic system must have the smaller width since the electron-withdrawing effect of the nitro group is more compensated: **9** has a width of 47 Hz and **11** a width of 41 Hz.[15]

(ii) The phosphonate **7**, unlike phosphonium salt **6**, could react with ketones *via* its anion. The reaction with propanone, a saturated ketone, afforded a 50% yield of (*E*)-6-methyl-3,5-heptadien-2-one ethylene ketal **12**. Configuration of the double bond coming from the phosphonate was deduced unambiguously by ^{1}H NMR data: the three olefinic protons are well resolved and $J_{H^2\text{-}H^3} = 15.3$ Hz can be measured directly.

With α,β-unsaturated ketones, phosphonates react poorly due to the smaller electrophilicity of the carbonyl carbon atom and to the competitive Michael addition, among other possibilities.[16] All our attempts to condense the anion of the phosphonate **7** with the α,β-unsaturated ketones 3-buten-2-one and 4-methyl-3-penten-2-one were negative. Better results were obtained in the Wittig-Horner condensation of phosphonate **7** with β-ionone in the presence of sodium hydride. This result is another example that indicates that β-ionone reacts easier with nucleophiles at the carbon atom of the carbonyl group than other α,β-unsaturated ketones. The number of examples that demonstrate this exceptional reactivity of β-ionone is large.[1] From the crude of the mentioned reaction, in addition to unreacted β-ionone and deconjugated (*E*)-and (*Z*)-retroionone, two condensation products were isolated: 2-methyl - 2 - [1*E*,3*Z*,5*E*) - 4 - methyl - 6 - (2,6,6 - trimethyl - 1 - cyclohexyl) - 1,3,5 - hexatrienyl]-1, 3-dioxolane **13** and its 3*E* isomer **14**.

The total yield of this condensation was 36% based on the initially present β-ionone. The ratio of stereoisomers 3*Z*:3*E* was approx. 3:2, isomer *Z* being the thermodynamically more stable (CH_3–: 1.70 kcal/mol; CH_2=CH–: 1.35 kcal/mol)[17]

Ketals **13** and **14**, partially separated by column chromatography, were identified by UV (λ_{max} = 286 and 290 nm respectively), mass spectrometry (M^+ = 302) and analysis of the olefinic systems in their ^{1}H NMR spectra: stereoisomer 9*Z* gave a straightforward, first order spectrum. Moreover, careful hydrolysis with aqueous oxalic acid of these ketals afforded quantitatively the known β-C_{18}-tetraenones **15** and **16**, identified by comparison of their spectral data.[1,18]

Since these β-C_{18}-tetraenones have been converted to vitamin A methyl ester stereoisomers, the route herein described using our C_5-synthon phosphonate of (*E*)-5-bromo-3-penten-2-one ethylene ketal- is formally a new and facile synthesis of carotenoid compounds, specially vitamin A.

Homologation to a C_8-synthon. The described C_5-synthon can be homologated to an ω-bromoalkapolyenylmethyl ketone with eight carbon atoms, one

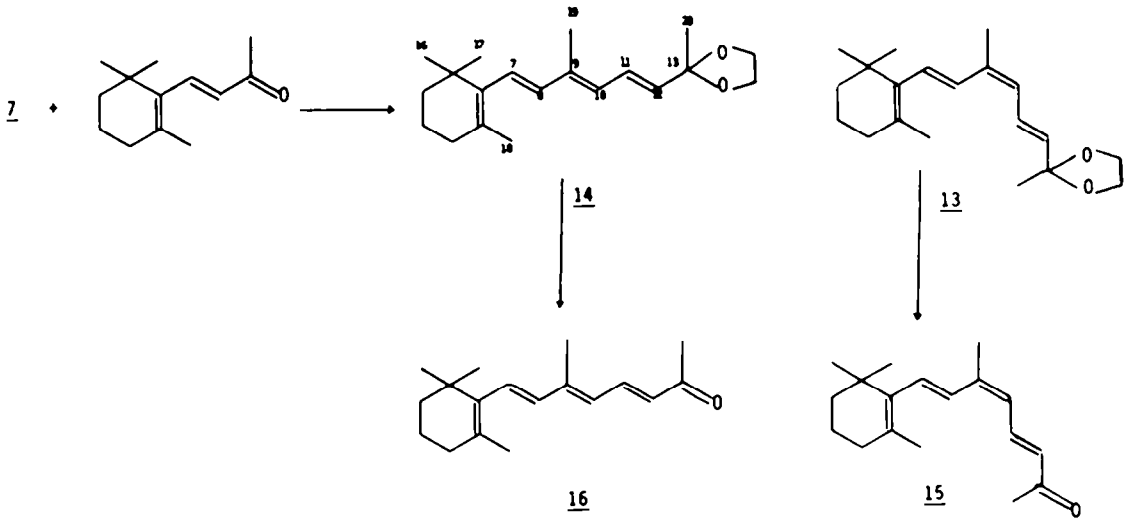


Fig. 3.

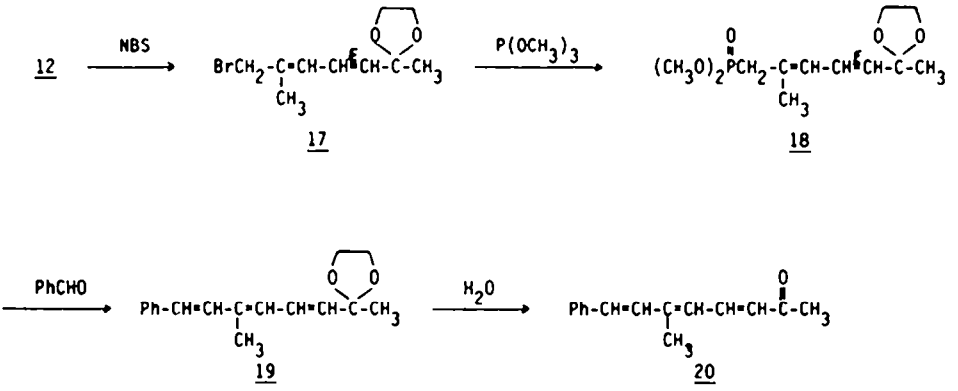


Fig. 4.

of them as a branched methyl group, mimicking the isoprene rules.

Ketal **12** was brominated with NBS affording only allylic bromination products, i.e. the two possible isomers 2-[(1*E*, 3*Z*)- and 2-[(1*E*, 3*E*)-5-bromo-4-methyl-1, 3-pentadienyl]-2-methyl-1,3-dioxolane **17**, that were identified by ^{1}H NMR of the crude, which presents two singlets at δ 4.05 and 3.95 for the bromomethyl groups.

Conversion of the crude mixture to the corresponding Wittig–Horner derivatives was performed through reaction with trimethyl phosphite giving a 82% yield of the phosphorous compound **18**, which was identified by ^{1}H NMR and mass spectrometry.

Condensation of **18** with benzaldehyde to prove its capability was positive giving a 66% of a crude product identified as 2-methyl-2-(4-methyl-6-phenyl-1,3,5-hexatrienyl)-1,3-dioxolane **19** by its ^{1}H NMR spectrum and mass spectrometry of the hydrolyzed product, 6-methyl-8-phenyl-3, 5, 7-octatrien-2-one **20**.

EXPERIMENTAL

^{1}H NMR spectra were recorded in $CDCl_3$ or CCl_4 (TMS as an internal standard) on a Perkin–Elmer R-12 spectrometer (60 MHz). IR spectra were recorded on a Perkin–Elmer Infracord 720 spectrophotometer. Mass spectra were registered on a Hewlett–Packard 5930 A spectrometer at 70 eV. UV spectra were recorded on a Perkin–Elmer 550 spectrophotometer.

(E)-*3-penten-2-one* (**4**). This ketone was obtained by Wittig condensation or by preparative GLC as described in the preceding paper.[6]

2-Methyl-2-[(E)-1-propenyl]-1, 3-dioxolane (**3**) *and* 2-[(2RS)-2-(2-*hydroxyethoxy)propyl*]-2-*methyl*-1, 3-*dioxolane* (**5**)

A solution of 42.0 g (0.5 mol) of (*E*)-3-penten-2-one, 31.0 g (0.5 mol) of ethylene glycol and 100 mg of adipic acid in 150 ml of benzene was refluxed in a Dean-Stark assembly for 5 days. During this time 6.0 ml of water were separated. After addition of 100 mg of sodium carbonate the benzene was distilled off and the following fractions were collected: (i) b.p. 80–126°/760 torr, 35.6 g; 73% in weight of benzene, 22% of pentenone and 5% of 1,3-dioxolane (**3**) (NMR). (ii) b.p. 126–155°/760 torr, 28.2 g; 40% in weight of pentenone, 58% of 1,3-dioxolane (**3**) and traces of benzene and glycol (NMR). (iii) b.p. 50–90°/0.3 torr, ethylene glycol. (iv) b.p. 90–105°/0.3 torr, 9.3 g of 1,3-dioxolane (**5**).

The compounds of fraction 2 were separated by preparative GLC on a 1 m × 1/4 in. column, 20% SE-30 on Chromosorb A 60/80 mesh, T_C: 90°C, flux of N_2 175 ml/min, t_r(**4**): 210 s, t_r(**3**): 500 s. Pure pentenone (7.9 g) and 18.6 g of pure 1,3-dioxolane (**3**) were collected. These two products could also be separated by distillation in a spinning band column. Analytical samples of the dioxolanes **3** and **5** were obtained by distillation of the chromatographed product (b.p. 139–140°/760 torr) and redistillation of a sample of fraction 4 (b.p. 94–96°/0.3 torr) respectively.

1,3-Dioxolane **3**: ^{1}H NMR (CCl_4): δ 5.80 (dq, CH_3CH=CH, J = 16 Hz, J' = 6 Hz); 5.35 (d, CH_3CH=CH); 3.80 (s, OCH_2); 1.70 (d, CH_3); 1.33 (s, CH_3). IR (CCl_4): 3010, 2960, 2910, 1675, 1445,

1375, 1210, 1040, 970 cm^{-1}. MS (%): 113 (M-15, 94), 87 (100), 69 (86), 43 (36). *Anal.* Calc for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.60; H, 9.59%.

1,3-Dioxolane 5: ^{1}H NMR (CCl_4): δ 3.90 (s, OCH_2 dioxolan ring); 3.84–3.20 (m, 5 OCH and OH); 1.97 (dd, CH_2, 1 H, J = 14.6 Hz, J' = 7.3 Hz); 1.68 (dd, CH_2, 1 H, J = 14.6 Hz, J' = 4.6 Hz); 1.38 (s, CH_3); 1.20 (d, CH_3, J = 7 Hz). IR (CCl_4): 3700–3200 (OH) cm^{-1}. MS (%): 175 (M-15, 4), 87 (100), 43 (33). *Anal.* Calc for $C_9H_{18}O_4$: C, 56.82; H, 9.54. Found: C, 56.73; H, 9.74%.

Transformation of 5 to 3. Adipic acid (100 mg) was added to the product of fraction 4 (9.0 g) and the mixture was distilled at 190°C for 8 hr collecting 4.8 g (78%) of 1,3-dioxolane 3 with traces of ethylene glycol. Taking into account this transformation and the recovered pentenone, the total yield of ketalization was 58%.

2-[(E)-3-*Bromo-1-propenyl*]-2-*methyl*-1, 3-*dioxolane* (2)

A mixture of 1.29 g (10 mmol) of dioxolane 3, 1.90 g (11 mmol) of NBS (Merck), 1.10 g (13 mmol) of sodium bicarbonate, 0.85 g (15 mmol) of CaO and 100 mg of $(BzO)_2$ in 12 ml of anhydrous CCl_4 was irradiated for 12 min with a 500 W sunlamp. Filtration of the crude mixture, elimination of the solvent under vacuum and distillation (b.p. 60–65°/0.2 torr) afforded 1.48 g (7 mmol; 70%) of 2 as a colourless liquid. The product was unstable after standing at room temperature, and was immediately used. ^{1}H NMR (CCl_4): δ 6.07 (dt, $BrCH_2CH$=CH, J = 15 Hz, J' = 16 Hz); 5.63 (d, $BrCH_2CH$=CH, J = 15 Hz); 3.92 (d, $BrCH_2$); 3.88 (s, OCH_2); 1.40 (s, CH_3). IR (CCl_4).: 3010, 2960, 2900, 1375, 1285, 1200, 1040, 970 cm^{-1}. MS (%): 193–191 (M-15, 5), 149-147 (3), 127 (13), 121–119 (3), 112 (31), 87 (100), 43 (39), 39 (20). *Anal.* Calc for $C_7H_{11}BrO_2$: C, 40.60; H, 5.36; Br, 38.59. Found: C, 40.71; H, 5.34; Br, 38.18%.

(E)-4,4-*Ethylenedioxy-2-pentenyltriphenylphosphonium bromide* (6)

Dry triphenylphosphine (5.08 g; 19 mmol) was dissolved in 50 ml of anhydrous ether and 4.00 g (19 mmol) of bromo-derivative 2 were added. The mixture was left under inert atmosphere at room temperature for two months. The precipitate was filtered, washed several times with anhydrous ether and dried to afford 7.55 g (17 mmol; 83%) of the phosphonium salt 6 (m.p. 152–155°). Recrystallization did not enhance the purity. The product was unstable to moisture and above 40°C. ^{1}H NMR ($CDCl_3$): δ 8.2–7.6 (m, Ph); 6.15–5.40 (m, CH=CH); 4.77 (m, CH_2, J_{P-H} = 14 Hz); 3.9–3.6 (m, OCH_2); 1.25 (s, CH_3). IR (KBr): 3050, 3000, 2900, 2800, 1665, 1620, 1580, 1485, 1440, 1220, 1115, 1030, 980 cm^{-1}. *Anal.* Calc for $C_{25}H_{26}BrO_2P$: C, 63.98; H, 5.58; Br, 17.02; P, 6.60. Found: C, 63.74; H, 5.79; Br, 16.84; P, 6.56%.

Dimethyl (E)-4, 4-*ethylenedioxy-2-pentenylphosphonate* (7)

A mxture of 1.32 g (6.4 mmol) of bromo compound 2 and 1.50 g (12 mmol) of trimethyl phosphite was heated at 115° during 30 min. Distillation of the crude afforded a first fraction (b.p. 105-115°/15 torr) of dimethyl methylphosphonate and a second fraction (b.p. 125–130°/0.1 torr) of the phosphonate 7 (1.30 g; 5.5 mmol; 86%). ^{1}H NMR (CCl_4): δ 6.00–5.25 (m, CH=CH); 3.80 (s, OCH_2); 3.63 (d, OCH_3, J_{P-H} = 10 Hz); 2.75–2.20 (m, CH_2, J_{P-H} = 22 Hz); 1.35 (s, CH_3). IR (CCl_4): 3000, 2960, 2900, 1250, 1030, 970, 940 cm^{-1}. MS (%): 221 (M-15, 43), 177 (7), 149 (10), 127 (10), 109 (33), 96 (15), 87 (100), 79 (22). *Anal.* Calc for $C_9H_{17}O_5P$: C, 45.76; H, 7.26; P, 13.11. Found: C, 45.90; H, 7.30; P, 12.97%.

Generation of (E)-4, 4-*ethylenedioxy-2-pentenylidenephosphorane* (21), *and its reaction with benzaldehyde*

(i) *Using PhLi as base.* To a suspension of 2.35 g (5 mmol) of the phosphonium salt 6 in 30 ml of anhydrous ether were added 5 mmol of phenyllithium under argon atmosphere. After a few minutes 0.56 g (5 mmol) of benzaldehyde were dropped. The mixture was stirred at room temperature overnight and afterwards was filtered. The filtrate was washed with water, dried over Na_2SO_4 and the solvent was removed under vacuum obtaining a crude (1.25 g), which contained equimolar amounts of 2-[(1*E*, 3*Z*)-4-phenyl-1, 3-butadienyl]-2-methyl-1, 3-dioxolane (8) and 2-[(1*E*, 3*E*)-4-phenyl-1, 3-butadienyl]-2-methyl-1, 3-dioxolane (10) (NMR). This crude material was filtered through 12 g of SiO_2 with hexane–ether (4–1) as eluent giving a first fraction (242 mg) of a yellow liquid, which contained as a major isomer 8 and a second fraction (134 mg) of a yellow liquid, which contained as a major isomer 10. Yield 35%. MS (%): 216 (M, 49), 201 (100), 157 (41), 129 (82), 128 (61), 127 (25), 115 (42), 87 (37), 77 (22), 51 (22), 43 (73). *Anal.* Calc for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.67; H, 7.68%.

(ii) *Using NaH as base.* In 5 ml of anhydrous DMF were dissolved 0.35 g (0.73 mmol) of the phosphonium salt 6 and 0.16 g (1.5 mmol) of benzaldehyde. Then, 0.73 mmol of NaH were added under inert atmosphere at room temperature and an evolution of hydrogen was immediately observed. The reaction mixture was left 4 h at ambient temperature and afterwards was poured over pentane–water. The aqueous phase was washed three times with pentane; the organic layer was dried over Na_2SO_4 and the solvent was removed under vacuum giving a residue of 123 mg of 8 and 10 in a 9:1 ratio (NMR). Distillation (b.p. 90–105°/0.4 torr) of this crude afforded 64 mg (0.29 mmol; 40%) of 8. ^{1}H NMR (CCl_4): δ PhCH^4=CH^3–CH^2=CH^1 system: 7.3 (s, Ph); 6.8 (dd, H^2, J = 16 Hz, J' = 10 Hz); 6.45 (d, H^4, J = 10 Hz); 6.10 (t, H^3, J = J' = 10 Hz); 5.70 (d, H^1, J = 16 Hz); 3.85 (s, OCH_2); 1.43 (s, CH_3).

Reaction of the phosphonate 7 with benzaldehyde in the presence of NaH

To a solution of 0.28 g (1.2 mmol) of 7 and 0.16 g (1.5 mmol) of benzaldehyde in 5 ml of DMF were added under inert atmosphere at room temperature 12 mmol of NaH observing hydrogen evolution. After 4 hr at 20° the mixture was poured over pentane–water. The same working up as in the preceding operation afforded a pale yellow liquid (224 mg), in which the isomers 8 and 10 were observed in a 1:9 ratio (NMR). Distillation of this crude afforded 153 mg (0.7 mmol; 59%) of pure 10 (b.p. 120–125°/0.2 torr). ^{1}H NMR (CCl_4): δ PhCH^4=CH^3–CH^2=CH^1 system: 7.4–7.0 (m, Ph); 6.7–6.1 (H^2, H^3, H^4 complex absorption); 5.58 (d, H^1, J = 16 Hz); 3.80 (s, OCH_2); 1.40 (s, CH_3).

Reaction of the phosphorane 21 *with 4-nitrobenzaldehyde*

(i) *Using PhLi as base.* The reaction was carried out with 4.77 g (10 mmol) of the phosphonium salt 6 under the above conditions obtaining a crude (2.61 g), which contained equimolar amounts of 2-methyl-2-[(1*E*,3*Z*)-4-(4-nitrophenyl)-1,3-butadienyl]-1, 3-dioxolane 9 and 2-methyl-2-[(1*E*, 3*E*)-4-(4-nitrophenyl)-1, 3-butadienyl]-1, 3-dioxolane 11 (NMR). This crude was filtered through 55 g of SiO_2 with hexane–ether (1-1) as eluent affording 0.90 g (3.4 mmol; 34%) of a mixture of both isomers. MS (%): 261 (M, 26), 246 (100), 202 (23), 128 (51), 115 (18), 87 (18), 43 (19). *Anal.* Calc for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.45; H, 5.62; N, 5.17%.

(ii) *Using NaH as base.* To a solution of 0.55 g (1.2 mmol) of the phosphonium salt 6 and 0.18 g (1.2 mmol) of 4-nitrobenzaldehyde in 5 ml of anhydrous DMF were added, under inert atmosphere at 20°, 1.2 mmol of NaH, observing evolution of hydrogen. The mixture was poured over chloroform–water and after the usual working up afforded a residue of 0.52 g, which was filtered through 5.5 g of SiO_2 with hexane–ether (5-1) as eluent. The first collected fractions (59 mg; m.p. 64–80°) corresponded to the isomer 9. The next fractions (106 mg) corresponded to mixtures of both isomers, and the last fractions (26 mg; m.p. 105–112°) corresponded to the isomer 11. Yield 63%. Isomer 9: ^{1}H NMR ($CDCl_3$): δ ArCH^4=CH^3–CH^2=CH^1 system: 7.85 (AA'BB' system, Δν = 47 Hz, J = 8 Hz); 7.0–6.3 (m, H^4, H^3, H^2); 5.90 (d, H^1, J = 15 Hz); 3.88 (d, OCH_2, J = 1.8 Hz); 1.43 (s, CH_3). Isomer 11: ^{1}H NMR ($CDCl_3$): δ ArCH^4=CH^3–CH^2=CH^1 system: 7.85 (AA'BB' system, Δν = 41 Hz, J = 8 Hz); 6.95–6.25 (m, H^4, H^3, H^2); 5.90 (d, H^1, J = 15 Hz); 3.92 (d, OCH_2, J = 1.3 Hz); 1.50 (s, CH_3).

Reaction of the phosphonate 7 with 4-nitrobenzaldehyde in the presence of NaH

The reaction was carried out with 283 mg (1.2 mmol) of the phosphonate 7 under analogous conditions as with benzaldehyde (changing pentane-water for chloroform-water) obtaining 360 mg

of a crude product with an isomer ratio 9: 11 of 1:7 (NMR). This crude was filtered through 4 g of SiO_2 with hexane–ether (5–1) as eluent to afford several mixtures of the isomers (109 mg; 0.4 mmol; 35%).

2-Methyl-2-[(E)-4-methyl-1, 3-pentadienyl]-1, 3-dioxolane (12)

To a solution of 1.06 g (4.5 mmol) of the phosphonate 7 and 0.70 g (12 mmol) of propanone in 4 ml of anhydrous DMF were added, under inert atmosphere at 20°, 4.6 mmol of NaH observing evolution of hydrogen. The same working up as in the case of benzaldehyde afforded a yellow oil (0.55 g), which by distillation (b.p. 55–60°/0.2 torr) gave 366 mg (2.2 mmol; 49%) of the dioxolane 12 as a colourless liquid. ^{1}H NMR (CCl_4): δ $(CH_3)_2C{=}CH^3$–$CH^2{=}CH^1$ olefinic system: 6.48 (dd, H^2, J = 15 Hz, J' = 11 Hz); 5.78 (dm, H^3, J = 11 Hz); 5.38 (d, H^1, J = 15 Hz); 3.75 (s, OCH_2); 1.78 ($(CH_3)_2C$=); 1.38 (s, CH_3). IR (CCl_4): 3010, 2950, 2900, 1690, 1660, 1640, 1450, 1380, 1200, 1040, 980, 960 cm^{-1}. MS (%): 1.68 (M, 18), 153 (100), 109 (35), 87 (29), 81 (57), 79 (18), 53 (18), 43 (73), 41 (24), 39 (22). *Anal.* Calc for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.15; H, 9.66%.

2 - Methyl - 2 - [(1E,3Z,5E) - 4 - methyl - 6 - (2,6,6 - trimethyl - 1 - cyclohexenyl) - 1,3,5 - hexatrienyl] - 1,3 - dioxolane (13) *and its* 3E *isomer* (14)

Under dark conditions, to a solution of 0.62 g (2.6 mmol) of the phosphonate 7 and 0.24 g (1.3 mmol) of β-ionone in 1.8 ml of anhydrous DMF were added, at −30° under inert atmosphere, 2.6 mmol of NaH observing after a few minutes evolution of hydrogen. The mixture was kept at this temperature for one hour and then it was left at 20° overnight. The reaction mixture was chromatographied on 80 g of SiO_2 with hexane–ether (100–8) as eluent. From the fractions of this chromatography the following pure products were identified (among others as unreacted β-ionone, (*E*)- and (*Z*)-retroionone): Isomer 13 (60 mg): ^{1}H NMR ($CDCl_3$): δ 6.88 (dd, H_{11}, J = 15 Hz, J' = 11 Hz); 6.76 (d, H_8, J = 15 Hz); 6.25 (d, H_7, J = 15 Hz); 6.00 (d, H_{10}, J = 11 Hz); 5.63 (d, H_{12}, J = 15 Hz); 3.97 (s, OCH_2); 2.15–2.20 (CH_2); 1.95 (CH_3-19); 1.73 (CH_3-18); 1.49 (CH_3-20); 1.25 (CH_2); 1.03 (CH_3-16, 17). IR (CCl_4): 3000, 2960, 2900, 1450, 1370, 1200, 1040, 970 cm^{-1}. MS (%): 302 (M, 0.5), 287 (0.6), 105 (10), 99 (10), 91 (17), 87 (100). UV (EtOH): λ_{max} = 204 and 286 nm. Isomer 14 (40 mg): ^{1}H NMR ($CDCl_3$): δ 6.72 (dd, H_{11}, J = 15 Hz, J' = 11 Hz); 6.10 (s, H_7 and H_8); 6.00 (d, H_{10}, J = 10 Hz); 5.58 (d, H_{12}, J = 15 Hz); 3.92 (s, OCH_2); 2.1–1.9 (CH_2); 1.92 (CH_3-19); 1.67 (CH_3-18); 1.49 (CH_3-20); 1.4–1.2 (CH_2); 1.00 (CH_3-16, 17). IR (CCl_4): 3000, 2960, 2900, 1450, 1370, 1200, 1040, 970 cm^{-1}. MS (%): 302 (M, 3.5), 287 (4), 215 (4), 107 (21), 105 (25), 99 (21), 91 (33), 87 (100). UV (EtOH): λ_{max} = 290 nm.

The total yield of condensation products was 36% (140 mg) based on the initially present β-ionone.

(3E,5Z,7E) - 6 - Methyl - 8 - (2,6,6 - trimethyl - 1 - cyclohexenyl) - 3,5,7-octatrien-2-one (15) *and its* 5E *isomer* (16)

In 1.5 ml of ethanol were dissolved 60 mg of 13 and a few drops of water and 50 mg of oxalic acid were added. After one week of standing at 20° under inert atmosphere and protected from the light the hydrolysis was complete (TLC). The mixture was extracted (in absence of light) with hexane and the solvent was eliminated under vacuum obtaining a yellow liquid (49 mg; 96%), that was identified as 15 by their ^{1}H NMR and UV spectra, that showed identical to the ones described by Mousseron-Canet[17] and Liu.[5]

The same procedure performed with 40 mg of 14 afforded 32 mg (94%) of a yellow liquid, that was identified as 16 through their ^{1}H NMR and UV spectra, that showed identical to the ones described by Mousseron-Canet[17] and Liu.[5]

2-[(1E,3Z-E)-6-Bromo-4-methyl-1,3-pentadienyl]-2-methyl-1,3-dioxolane (17)

A mixture of 0.37 g (2.2 mmol) of dioxolane 12, 0.38 g (2.1 mmol) of NBS (Merck), 0.25 g (3.0 mmol) of $NaHCO_3$ and 0.10 g (1.8 mmol) of CaO in 4 ml of anhydrous CCl_4 was irradiated 150 min with a 500 W sunlamp. A ^{1}H NMR spectrum of a sample showed that the reaction had taken place in a 75%. Longer irradiation resulted in partial decomposition and the reaction mixture became black. Distillation of the dioxolane 12 gave a residue of a yellow oil (0.46 g; 85%) consisting of a 1:2 mixture of the bromo derivative (1*E*, 3*Z*)-17 and (1*E*, 3*E*)-17 in high purity, that was directly used for the next step. All attempts to distill this crude resulted in decomposition of the product. ^{1}H NMR (CCl_4): δ 6.70–5.50 (olefinic protons, at 5.60 H_6, d, J = 15 Hz); 4.05 (s, $BrCH_2$); 3.95 (s, $BrCH_2$); 3.80 (s, OCH_2); 2.0 (s, CH_3); 1.35 (s, CH_3). MS (%): 231–233 (M-15, 1), 167 (2.5), 153 (11), 109 (14), 87 (100), 43 (67).

Dimethyl (2Z-E,4E) - 6,6 - ethylenedioxy - 2 - methyl - 2,4 - heptadienyl-phosphonate (18)

A mixture of 0.46 g (1.9 mmol) of the bromodioxolane 17 and 1.00 g (8 mmol) of trimethylphosphite was heated under inert atmosphere at 115–120° for 30 min. Distillation of volatiles at 115°/0.2 torr left a pale yellow residue (0.42 g; 82%), that was identified as the phosphonate 18 (NMR). ^{1}H NMR (CCl_4): δ 6.6–5.2 (olefinic protons); 3.85 (s, OCH_2); 3.65 (d, OCH_3, J = 10 Hz); 2.90–2.30 (CH_2-P); 1.93 (dd, CH_3, J = 4 Hz), J' = 1.5 Hz); 1.40 (s, CH_3). MS (%): 276 (M, 20), 261 (25), 217 (33), 214 (30), 189 (50), 166 (33), 151 (43), 133 (19), 122 (39), 118 (36), 109 (56), 107 (44), 105 (28), 94 (30), 93 (39), 91 (30), 87 (84), 79 (100), 77 (31), 43 (71).

6-Methyl-8-phenyl-3, 5, 7-octatrien-2-one (20)

To a solution of 195 mg (0.7 mmol) of the phosphonate 18 and 200 mg (1.9 mmol) of benzaldehyde in 3 ml of anhydrous DMF were added, at 20° under inert atmosphere, 0.8 mmol of NaH. The same working up as in the reaction of the phosphonate 7 with benzaldehyde gave a residue of 120 mg (0.47 mmol; 66%), that was identified as the condensation product 2-methyl-2-(4-methyl - 6 - phenyl - 1,3,5 - hexatrienyl) - 1,3 - dioxolane 19 by its NMR spectrum: ^{1}H NMR (CCl_4): δ 7.5–7.0 (Ph); 6.8–5.4 (=CH–); 3.85 (s, OCH_2); 2.0 (s, CH_3); 1.40 (s, CH_3). After several days at ambient conditions, hydrolysis of this dioxolane was complete. Chromatography on 0.5 g of SiO_2 with hexane–ether (5–1) as eluent afforded 36 mg of the ketone 20. MS (%): 212 (M, 11), 169 (31), 154 (19), 141 (17), 128 (19), 115 (22), 105 (38), 91 (42), 77 (47), 65 (18), 51 (29), 43 (100).

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