Pergamon

Tetrahedron Vol. 50, No. 11, pp. 3389-3396, 1994

0040-4020/94 $6.00+0.00

0040-4020(94)E0093-9

Palladium-Catalysed Vinylation of tertiary Allylic Alcohols : a New Protocol for the Synthesis of Isoprenoid Aldehydes.

Hugues BIENAYME* and Catherine YEZEGUELIAN

Rhône-Poulenc, Centre de Recherches des Carrières,
BP 62, 69192, SAINT-FONS cedex, France

Key Words : Prenylation, Isoprenoid Aldehydes, Vitamin A, Retinal, Heck Vinylation, Palladium.

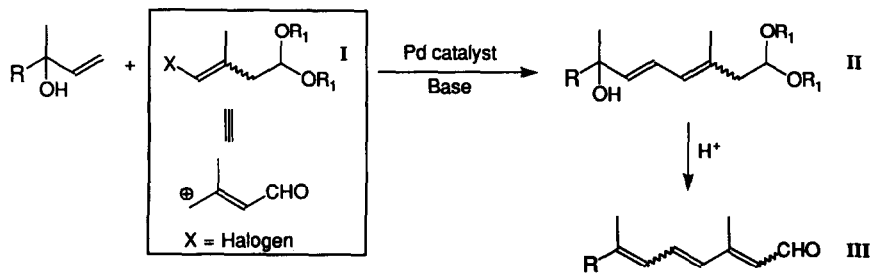
Abstract : Heck vinylation of tertiary allylic alcohols with iodo-acetal **Ic**, *followed by an acid catalysed acetal hydrolysis-dehydration reaction, furnished isoprenoid aldehydes regioselectively in high yields.*

INTRODUCTION

The palladium-catalysed arylation and vinylation of olefins (Heck reaction) has become an increasingly used carbon-carbon bond forming reaction over the past two decades[1]. We envisioned that this methodology could be extremely useful in retinoids synthesis where chemoselectivity, regioselectivity and mild reaction conditions are needed[2].

We describe here a new prenylation method based on a two reaction sequence : Heck vinylation of a tertiary allylic alcohol by an acetal of type **I** followed by acidic hydrolysis/dehydration of the adduct **II** to deliver the polyunsaturated aldehydes **III** possessing five more carbon atoms (See scheme 1). Key compounds **I** have been designed as prenal cation equivalents[3] which would regioselectively add on the less substituted β-position of allylic alcohols[4], yielding dienol acetals **II** with the correct isoprenoid skeleton.

This prenylation method is illustrated here by the synthesis of several aldehydes including retinal **IIIe**, an intermediate of industrial importance in the manufacture of vitamin A and β-carotene[5].

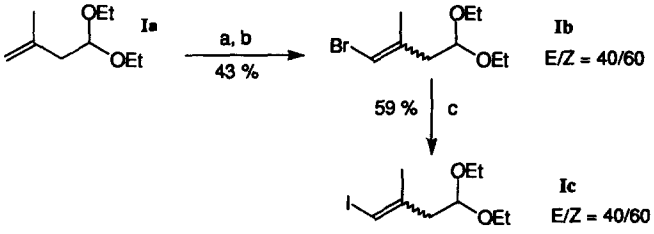


Scheme 1

RESULTS AND DISCUSSION

Acetal **Ib** (X = Br, R = Et) was prepared from the known acetal[6] **Ia** (X = H, R = Et) by a bromination-dehydrobromination reaction sequence [3] (scheme 2).

The new acetal **Ic** (X = I, R = Et) was easily obtained from **Ib** by a nickel catalysed iodine-bromine exchange reaction[7]. Both compounds are reasonably stable and showed no decomposition after several months of storage in an ice-cold freezer.



Scheme 2

a) Br_2, Na_2CO_3, CCl_4, -20°C ; b) tBuOK, Et_2O, 0°C ; c) KI (3 eq), $NiBr_2$ (0,1 eq), Zn (0,2 eq) DMF, 60 - 90°C, ultrasound.

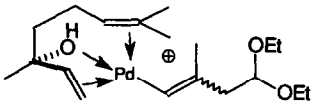
Acetal **Ic** was chosen for this study since very mild Heck - type reactions were expected between vinylic iodides and allylic alcohols[8].

As shown from table 1, acetal **Ic** reacted smoothly with tertiary allylic alcohols in the presence of a catalytic amount of palladium acetate and a stoechiometric amount of either a silver or a thallium salt [9,10,19]. The corresponding condensation adducts **II** were isolated in good to excellent yields after silica gel chromatography.

These compounds proved to be stereoisomer mixtures roughly reflecting the isomer ratio of the starting iodide, but free from any regioisomer[11]. This outstanding regioselectivity is best illustrated with the polyunsaturated vinyl-ψ-ionol and vinyl-β-ionol examples. These two sensitive substrates gave unambigously the very labile tetraenol acetals **IId** and **IIe** in good yields (entries 6 and 10).

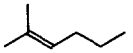
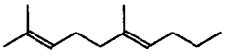
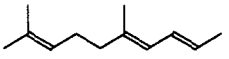
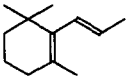
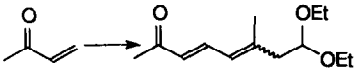
Surprisingly, this vinylation reaction was found to be quite substrate dependent. For instance, linalol and nerolidol (entries 3 and 5) reacted quickly with **Ic** in the presence of palladium acetate and thallium (I) acetate whereas 2-methyl-butene-2-ol and vinyl-β-ionol (entries 1 and 7) were rather sluggish under the same reaction conditions and needed the more reactive palladium acetate/silver acetate or carbonate catalytic systems (entries 2,9 and 10).

This marked behaviour difference of structurally similar substrates found when using the thallium acetate base might be due to internal olefin coordination to palladium at one stage of the reaction with linalol or nerolidol (but not with 2-methyl-buten-2-ol or vinyl-β-ionol). If we assume that addition of the vinyl palladium species to the allylic alcohol double bond is the rate determining step, then additional coordination might explain the observed rate enhancement, as depicted below.



In the vinyl-β-ionol case (entries 7-10), catalytic efficiency was found in the order TlOAc < Tl_2CO_3 < AgOAc < Ag_2CO_3, showing that apparently the nature of both metal and counterion are important to achieve high yields. Similar observations have recently been made on a intramolecular Heck-arylation[19].

Table 1

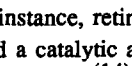
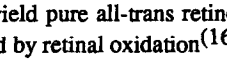
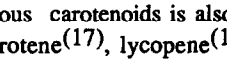
Entry[a]	Alcohols → Acetals (II)		Base (eq)	Temperature/Time	Yield[b]	Isomer ratio Z / E
1	R = CH_3	IIa	TlOAc (1,10)	65°C / 31 h	33 % (65 %)	51 / 49
2	id		Ag_2CO_3 (0,52)	67°C / 8 h	82 %	60 / 40
3	R = 	IIb	TlOAc (1,02)	65°C / 4 h	75 %	65 /35
4	id		Ag_2CO_3 (0,60)	65°C / 0,5 h	70 % (82 %)	60 / 40
5	R = 	IIc	TlOAc (1,02)	58°C / 5 h	77% (85 %)	63 / 37
6	R = 	IId	Ag_2CO_3 (0,59)	67°C / 2 h	70 %	55 / 45
7	R = 	IIe	TlOAc (1,05)	65°C / 48 h	38 %	52 / 48
8	id		Tl_2CO_3 (0,53)	67°C / 22 h	57 % (76 %)	55 / 45
9	id		AgOAc (1,03)	67°C / 2 h	69 %	50 / 50
10	id		Ag_2CO_3 (0,54)	65°C / 3 h	82 %	60 / 40
11[c]			K_2CO_3 (2,4)	22°C / 4 h	86 %	62 / 38

a) Conditions : allylic alcohol (3 eq), Pd $(OAc)_2$ (0,05 eq), DMF ; b) In brackets : yields based on recovered starting material ; c) Conditions : Ketone (5 eq), Pd $(OAc)_2$ (0,05 eq), Bu_4NCl (1,3 eq), DMF.

Another acces to dienol acetal **IIa** is shown in the last entry. Vinylation of methyl vinyl ketone with **Ic** according to ref. 12 furnished the condensation adduct in good yield . Methylation with methyl lithium in ether gave **IIa** in 87 % yield.

Finally the known polyunsaturated aldehydes **III** were easily obtained from dienol acetals **II** by treatment with dilute hydrobromic acid in hot aqueous acetone[13] (table 2). Mixtures of stereoisomers on double bonds at C_2 and C_6 were formed in this acetal hydrolysis/dehydration reaction, with the all-trans usually predominating (the double bond at C_4 was always trans).

Table 2

Entry (a)	Acetals (II) ⟶ Aldehydes (III)		Yield	Isomer ratio(b) E / Z
1	R = CH_3	IIIa	85 %	74 / 26
2	R = 	IIIb	72 %	72 / 28 (c)
3	R = 	IIIc	87,5 %	76 / 24 (d)
4	R = 	IIId	78 %	70 / 30
5	R =	IIIe	75 %	74 / 26 (e)

a) Conditions : Acetal (0,5 mmol), 1 % HBr/acetone (0,1 mL), 0,5 % H_2O/acetone (12 mL), reflux ; b) E/Z ratio of terminal (C_2) double bond ; c) exact ratio C_2-C_6 (EE/EZ/ZE/ZZ) = 45/27/18/10 ; d) exact ratio C_2-C_6 (EE/EZ/ZE/ZZ) = 48/28/14/10 ; e) exact ratio C_2-C_6 (EE/EZ/ZE/ZZ) = 46/28/16/10.

The aldehydes **III** thus obtained are pivotal intermediates in the synthesis of retinoids and carotenoids (scheme 3). For instance, retinal **IIIe** (stereoisomer mixture) may be crystallized in the presence of hydroquinone and a catalytic amount of iodine, to give the all-trans retinal-hydroquinone complex in virtually quantitative yield [14]. Borohydride reduction, or better catalytic reduction with Ru H_2 $(TPP)_2$, of this complex yield pure all-trans retinol (vitamin A)[15]. Alternatively, the important retinoic acid is smoothly obtained by retinal oxidation[16].

Access to various carotenoids is also straightforward by reductive McMurry dimerization of these aldehydes : β-carotene[17], lycopene[18] could be obtained from retinal **IIIe** and ψ –retinal **IIId**, respectively.

Scheme 3

In summary, we have developed a new short route to carotenoid aldehydes featuring a Heck vinylation of tertiary allylic alcohols and a hydrolysis/dehydration reaction. This methodology was used in a short and high yielding synthesis of retinal.

ACKNOWLEDGEMENT

The authors would like to thank the Analytical Service at CRC, and Rhône-Poulenc for permission to publish these results.

EXPERIMENTAL SECTION

General methods :

^{1}H-NMR Spectra were recorded at 360 MHz on a Bruker WH-360 instrument. Chemical shifts are expressed relative to Me_4Si as internal standard. IR Spectra were recorded on a Perkin-Elmer 1750 spectrophotometer (neat or in CCl_4 solutions). MS Spectra were obtained on a VG-ZAB instrument. A varian 3400 gas chromatograph with DB1 column was used for analysis, and 20-45 µm Amicon silica gel for preparative flash chromatography.

4-iodo-3-methyl-3-buten-1-al, diethylacetal (Ic)

A 15-mL Schott flask is charged with Zn (90,7 mg ; 1,39 mmol), KI (3,020 g ; 18,2 mmol), $NiBr_2$ (3,98 mL of a 0,17 M solution in DMF ; 0,67 mmol) ; **Ib**[3a] (1,414 g, 5,96 mmol), and DMF (7,5 mL). The mixture is sonicated for 2 h 30 (20 kHz, P = 40 W, undatim ultrasonics immersion horn) under an argon atmosphere, the temperature being maintained in the range of 60 - 95 °C.

After cooling, the reaction mixture is filtered on florisil, extracted with Et_2O, washed twice with water, and dried ($MgSO_4$).
The residue is purified by flash-chromatography (silica gel, 40/1 pentane/Et_2O), giving 1,035 g of a Z/E = 60/40 mixture of iodoacetal Ic (59 %).

^{1}H-NMR (ppm) : 1,20 (t, 6H, J = 7 Hz) ; 3,4 - 3,8 (m, 4H).

Z isomer : 1,97 (d, 1,8H, J = 1 Hz) ; 2,55 (d, 1,2H, J = 6 Hz) ; 4,65 (t, 0,6H, J = 6 Hz) ; 5,97 (m, 0,6H).

E isomer : 1,89 (d, 1,2H, J = 1 Hz) ; 2,52 (d, 0,8H, J = 6 Hz) ; 4,59 (t, 0,4H, J = 6 Hz) ; 6,02 (m, 0,4H).

IR (cm^{-1}) : 3060, 1616, 1125, 1064. **MS** (m/e) : 239 (-EtOH), 103. **HRMS** for m/e = 239 : $C_7H_{12}OI$.

Anal. Calc. for $C_9H_{17}O_2I$: C = 38,04 ; H = 6,03 ; O = 11,26. Found : C : 38,00 ; H = 6,00 ; O = 11,36.

General procedure for the vinylation of allylic alcohols

To a mixture of **Ic** (0,270 g ; 0,95 mmol) and an allylic alcohol (2,85 mmol) in anhydrous DMF (2 mL) is added Pd $(OAc)_2$ (10,7 mg ; 0,048 mmol), and the base (see table I).

The vigorously stirred suspension is heated under argon for the indicated period.
After cooling, and filtration over florisil, the clear yellow solution is diluted with Et_2O, washed twice with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Chromatographic purification (silica, gel, 50/1, CH_2Cl_2/ Acetone) gives the desired hydroxyacetals **IIa-c**. In the case of acetals **IId** and **IIe** silica is neutralized with 1 % Et_3N / CH_2Cl_2 prior to use.

7-hydroxy-3,7-dimethyl-octa-3,5-dien-1-al, diethylacetal (IIa)

^{1}H-NMR (ppm) : 1,20 (t, 6H, J = 7 Hz) ; 1,34 (s, 3H) ; 1,36 (s, 3H) ; 1,84 (m, 3H) ; 3,4 - 3,8 (m, 4H) ; 5,89 (m, 1H)

Z isomer : 2,51 (d, 1H, J = 6 Hz) ; 4,58 (t, J = 6 Hz) ; 5,73 (d, J = 15,5 Hz) ; 6,48 (dd, J = 10,5 Hz, 16 Hz).

E isomer : 2,38 (d, 1H, J = 6 Hz) ; 4,61 (t, J = 6 Hz) ; 5,75 (d, J = 15,5 Hz) ; 6,46 (dd, J = 10,5 Hz, 16 Hz).

IR (cm^{-1}) : 3609, 1635, 1123, 1060. **MS** (m/e) : 197, (-EtO), 103. **HRMS** for m/e = 197 : $C_{12}H_{21}O_2$.

Anal. Calc. for $C_{14}H_{26}O_3$: C = 69,38 ; H = 10,81 ; O = 19,80. Found : C = 69,25 ; H = 11,04 ; O = 19,53.

8-prenyl-7-hydroxy-3,7-dimethyl-octa-3,5-dien-1-al, diethylacetal (IIb)

^{1}H-NMR (ppm) : 1,20 (t, 6H, J = 7 Hz) ; 1,29 (s, 3H) ; 1,60 (m, 5H) ; 1,79 (s, 3H) ; 1,84 (m, 3H) ; 2,10 (m, 2H) ; 3,4 - 3,8 (m, 4H) ; 5,11 (m, 1H) ; 5,65 (d, 1H, J = 15 Hz) ; 5,92 (m, 1H).

Z isomer : 2,52 (d, 1,3H, J = 5,5 Hz) ; 4,58 (t, J = 6 Hz) ; 6,46 (dd, J = 11 Hz, 15 Hz)

E isomer : 2,38 (d, 0,7H, J = 5,5 Hz) ; 4,61 (t, J = 6 Hz) ; 6,45 (dd, J = 11 Hz, 15 Hz).

IR (cm^{-1}) : 3611, 1163, 1123, 1061, 970.

MS (m/e) : 292 ($-H_2O$), 247 ($-H_2O$/-EtO), 201. **HRMS** for m/e = 292 : $C_{19}H_{32}O_2$.

Anal. Calc. for $C_{19}H_{34}O_3$: C = 73,50 ; H = 11,04 ; O = 15,46. Found : C = 72,55 ; H = 10,44 ; O = 15,27.

8-geranyl-7-hydroxy-3,7-dimethyl-octa-3,5-dien-1-al, diethylacetal (IIc)

^{1}H-NMR (ppm) : 1,19 (t, 3H, J = 7 Hz) ; 1,24 (s, 3H) ; 1,53 (s, 3H) ; 1,62 (s, 3H) ; 1,96 (m, 4H) ; 3,4 - 3,8 (m, 4H) ; 5,00 (m, 1H) ; 5,06 (m, 1H) ; 5,59 (d, 1H, J = 15 Hz) ; 6,40 (dd, 1H, J = 10,5 Hz, 15 Hz).

Z isomer : 1,62 (s, 1,8H) ; 1,78 (s, 1,8H) ; 2,45 (d, 1,2H, J = 5,5 Hz) ; 4,51 (t, 0,6H, J = 5,5 Hz) ; 5,86 (m, 0,6H).

E isomer : 1,53 (s, 1,2H) ; 1,76 (s, 1,2 H) ; 2,31 (d, 0,8H, J = 5,5 Hz) ; 4,53 (t, 0,4H, J = 5,5 Hz) ; 5,83 (m, 0,4H).

IR (cm^{-1}) : 3610, 1656, 1125, 1064. **MS** (m/e) : 314 ($-H_2O$; -EtO). **HRMS** for m/e = 314 : $C_{22}H_{34}O$.

Anal. Calc. for $C_{24}H_{42}O_3$: C = 76,14 ; H = 11,18 ; O = 12,68. Found : C = 76,67 ; H = 11,40 ; O = 12,56.

8-geranylidene-7-hydroxy-3,7-dimethyl-octa-3,5-dien-1-al, diethylacetal (IId)

^{1}H-NMR (ppm) : 1,20 (t, 6H, J = 7 Hz) ; 1,43 (s, 3H) ; 1,60 (s, 3H) ; 1,68 (s, 3H) ; 1,75 - 2,20 (m, 10H) ; 3,4 - 3,8 (m, 4H) ; 4,56 (t, 0,5H, J = 6 Hz) ; 4,59 (t, 0,5H, J = 6 Hz) ; 5,11 (m, 1H) ; 5,60 - 6,27 (m, 4H) ; 6,37 - 6,68 (m, 2H).

Z isomer : 2,51 (d, 1,1H, J = 6 Hz).

E isomer : 2,38 (d, 0,9H, J = 6 Hz).

IR (cm^{-1}) : 3450, 1677, 1654, 1628, 1600, 1125, 1060, 970.

MS (m/e) : 376, 358 ($-H_2O$), 312 ($-H_2O$; -EtOH), 103 **HRMS** for m/e = 376 : $C_{24}H_{40}O_3$.

8-cyclogeranylidene-7-hydroxy-3,7-dimethyl-octa-3,5-dien-1-al, diethylacetal (IIe)

^{1}H-NMR (ppm) : 1,00 (s, 6H) ; 1,20 (t, 6H, J = 7 Hz) ; 1,40 - 1,70 (m, 10H) ; 1,80 (s, 1,5H) ; 1,85 (s, 1,5H) ; 1,98 (m, 2H) ; 3,4 - 3,8 (m, 4H) ; 5,93 (m, 1H) ; 6,09 (m, 1H) ; 6,50 (dd, 1H, J = 11 Hz, 15 Hz).

Z isomer : 2,50 (d, 0,5H, J = 6 Hz) ; 4,57 (t, J = 6 Hz) ; 5,54 (d, J = 16 Hz) ; 5,74 (d, J = 15 Hz).

E isomer : 2,38 (d, 0,5H, J = 6 Hz) ; 4,62 (t, J = 6 Hz) ; 5,55 (d, J = 16 Hz) ; 5,75 (d, J = 15 Hz).

IR (cm^{-1}) : 3606, 1658, 1125, 1060.

MS (m/e) : 358 ($-H_2O$), 330 (-EtOH), 103. **HRMS** for m/e = 358 : $C_{24}H_{38}O_2$.

Anal. Calc. for $C_{24}H_{40}O_3$: C = 76,55 ; H = 10,71. Found : C = 76,81 ; H = 10,16 ;

8,8-diethoxy-3,7-methyl-octa-3,5-dien-2-one

^{1}H-NMR (ppm) : 1,16 (t, 6H, J = 7 Hz) ; 1,93 (s, 3H) ; 2,25 (s, 3H) ; 3,40 - 3,80 (m, 4H) ; 5,96 - 6,11(m, 2H)

Z isomer : 2,60 (d, 1,2H, J = 5 Hz) ; 4,56 (t, J = 5 Hz) ; 7,42 (dd, J = 11,5 Hz, 15 Hz).

E isomer : 2,44 (d, 0,8H, J = 5 Hz) ; 4,60 (t, J = 5 Hz) ; 7,40 (dd, J = 11,5 Hz, 15 Hz).

IR (cm^{-1}) : 1686, 1667, 1634, 1589, 1364, 1123, 1063.

MS (m/e) : 181 (-EtOH), 103. **HRMS** for m/e = 181 : $C_{11}H_7O_2$.

Preparation of acetal IIa from 8,8-diethoxy-6-methyl-octa-3,5-dien-2-one.

To a solution of the ketone (0,124g ; 0,549 mmol) in dry THF (4 mL) is added at -78°C under argon a 1,6M solution of MeLi in Et_2O (0,875 mL ; 1,4 mmol).
The solution is stirred for 1,5 h, then quenched with a mixture of water (0,5 mL) and THF (4 mL), warmed up, diluted with Et_2O, washed twice with brine, dried ($MgSO_4$), and concentrated in vacuo.
The residue (0,132 g) is purified by flash-chromatography (10/1 pentane/Et_2O) to give **Ic** (0,116 g ; 0,478 mmol, 87 %).

General procedure for the preparation of aldehydes IIIa-e from acetals IIa-e

An acetal **II** (0,5 mmol) and 12 mL of aqueous acetone (made from acetone 192 mL and water 1 mL) are charged in a 10 mL flask equipped with a condenser.
The solution is heated to reflux, then 0,1 mL of dilute hydrobromic acid (made from acetone 5 mL and 47 % HBr 0,1 mL) is added. Reflux is maintained until disappearance of the acetal and formation of the strongly U.V. active spot of the unsaturated aldehyde (TLC, 10/1 pentane/ Et_2O).
The orange-red solution is diluted with Et_2O (50 mL), washed twice with water, dried ($MgSO_4$) and evaporated in vacuo.
Chromatography (silica gel, 10/1 pentane - Et_2O) yields the pure aldehydes **IIIa-e** identical to authentic samples.

REFERENCES AND NOTES

1. a) Heck, R. F. Org. React. **1982**, *27*, 345 ; b) Heck, R. F. Palladium reagents in organic syntheses ; *Academic Press : London*, **1985**.
2. For recent retinoids syntheses involving palladium catalysis see :
   Negishi, E.I. ; Ay, M. ; Gulevich, Y. V. ; Noda, Y. *Tetrahedron Lett.*, **1993**, *34*, 1437. De Lera, A. R. ; Torrado, A. ; Iglesias, B. ; Lopez, S. *Tetrahedron Lett.* **1992**, *33*, 6205. Negishi, E. I. ; Owczarczyk, Z. *Tetrahedron Lett.* **1991**, *32*, 6683. Trost, B.M. ; Fortunak J.M.D. *Tetrahedron Lett.*, **1981**, *22*, 3459
3. This kind of acetal has recently been used by L. Duhamel and coworkers, but as a prenal *anion* equivalent : a) Duhamel. L. ; Ancel, J. E. *Tetrahedron*, **1992**, *48*, 9237 see also ; b) Duhamel, L. ; Ancel, J. E., J. *Chem. Research*, **1990**, 154. c) Duhamel, L. ; Duhamel, P. ; Lecouve, J. P. *Tetrahedron*, **1987**, *43*, 4339 and 4349.
4. For Heck arylation and vinylation of allylic alcohols see :
   Bernocchi, E. ; Cacchi, S. ; Ciattini, P. G. ; Morera, E. ; Ortar, G. *Tetrahedron Lett.*, **1992**, *33*, 3073. Gaudin, J. M. *Tetrahedron Lett.* **1991**, *32*, 6113. Arcadi, A. ; Bernocchi, E. ; Cacchi, S. ; Marinelli, F. *Tetrahedron*, **1991**, *47*, 1525. Mandai, T. ; Hasegawa, S. I. ; Fujimoto, T ; Kawada, U. ; Nokami, J. ; Tsuji, J. *Synlett*, **1989**, *85*. Torii, S. ; Okumoto, H. ; Akahoshi, F. ; Kotani, T. *J. Am. Chem. Soc. 1989*,

111, 8932. Aslam, M. ; Elango, V. ; Davenport, K.G. *Synthesis*, **1989**, 869. Larock, R.C. ; Leung, W-Y. ; Stolz-Dunn, S. *Tetrahedron Lett.* *1989*, 30, *6629*. Benhaddou, R. ; Czernecki, S. ; Ville, G. ; Zegar, A. *Organometallics* **1988**, *7*, 2435. Smadja, W. ; Czernecki, S. ; Ville, G., Georgoulis, C. *Organometallics*, **1987**, *6*, 166. Smadja, W. ; Ville, G. ; Cahiez, G. *Tetrahedron Lett.*, **1984**, *25*, 1793. Kao, L-C ; Stakem, G. ; Patel, B. A. ; Heck, R. F. *J. Org. Chem.* **1982**, *47*, 1267. Tamaru, Y. ; Yamada, Y. ; Yoshida, Z. *J. Org. Chem.* **1978**, *43*, 3396. Chalk, A. J. ; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273 and 1206. Melpolder, J. B. ; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265.

5. Isler, O. Carotenoids, Birkhauser Verlag, Basel, **1971**. Sporn, M. B. ; Roberts, A. B. ; Goodman, D. S. The Retinoids, *Academic Press*, New-York, **1984**. Paust, J. *Pure and Appl. Chem.* **1991**, *63*, 45. Liu. R. S. H. ; Asato, A. E. *Tetrahedron*, **1984**, *40*, 1931. Kienzle, F. *Pure and Appl. Chem.* **1976**, *47*, 183.
6. Picotin, G. ; Miginiac, P. *Chem. Ber.* **1986**, *119*, 1725.
7. Tanaki, K. ; Hayama, N. ; Ivokawa, S. I., *Chem. Lett.*, **1978**, 1435. The published procedure was improved by using a sonicated reactor (see experimental part) and DMF instead of HMPA.
8. a) Jeffery, T. *Tetrahedron Lett.* **1991**, *32*, 2121. b) Jeffery, T. *Tetrahedron Lett.* **1990**, *31*, 6641. c) Jeffery, T. *J. Chem. Soc. Chem. Commun.* **1991**, 324. d) Jeffery, *J. Chem. Soc. Chem. Commun.*. **1984**, 1287. Somewhat lower yields and selectivities were observed when using bromoacetal **Ib**.
9. No reaction took place in the absence of these salts or in the presence of Bu_4NCl (see 8d).
10. For the use of thallium or silver salts in Heck-type reactions see : Jeffery, T. *Tetrahedron Lett.* **1993**, *34*, 1133. Grigg, R. ; Kennewell, P. ; Teasdale, A. J. *Tetrahedron Lett.* **1992**, *33*, 7789. Madin, A. Overman, L. E., *Tetrahedron Lett.*, **1992**, *33*, 4859. Jeffery, T. *Tetrahedron Lett.* **1992**, *33*, 1989. Cabri, W. ; Candiani, I. ; Bedeschi, A. ; Santi, R. *Tetrahedron Lett.* **1991**, 32 , 1753. Larock, R.C. ; Gong, W. H. *J. Org. Chem.* **1989**, *54*, 2047. Sato, Y. ; Sodeoka, M. ; Shibasaki, M. *Chem. Lett.* **1990**, 1953. Abelman, M. M. ; Overman, L. E. ; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959. Grigg, R. ; Loganathan, V. ; Sukirthanlingam, S. *Tetrahedron Lett.* **1990**, *31*, 6573. Larock, R. C. ; Gong, W. H. ; Baker, B. E. ; *Tetrahedron Lett.* **1989**, *30*, 2603. Larock, R. C. ; Song, H. ; Baker, B. E. ; Gong, W. H. *Tetrahedron Lett.*. **1988**, *29*, 2919. Abelman, M. M. ; Overman, L. E. *J. Am. Chem. Soc.*, **1988**, *110*, 2328. Abelman, M. M. ; Oh, T. ; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130. Karabelas, K. ; Hallberg, A. *J. Org. Chem.*, **1988**, *53*, 4909. Karabelas, K. ; Hallberg, A. *J. Org. Chem.*, **1986**, *51*, 5286. Karabelas, K. ; Hallberg, A. *J. Org. Chem.*, **1985**, *50*, 3896. Karabelas, K. ; Hallberg, A. *Tetrahedron Lett.* **1985**, *26*, 3131.
11. Determined by 360 MHz ^1H NMR.
12. Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667
13. Brunie, J. C. ; Raymond, L. Ger. Pat 2,933,996 (1980) to Rhône-Poulenc. See also, ref. 3b.
14. Redel, J. ; Nicolaux, G. Fr. Pat. 1,288,975 and 1,291,622 (1961) to Rhône-Poulenc. US Pat. 3,013,080 (1961) to Eastman Kodac.
15. Allmang, G. ; Grass, F. ; Grosselin, J. M. ; Mercier, C. *J. Mol. Catal.* **1991**, *66*, L 27 and references cited.
16. Takeda, J.P. Patent 60,15862 (1960) Futterman, S. *J. Biol. Chem.* **1962**, *237*, 677. Elder, T. D. ; Topper, Y. *J. Biochim. Biophys. Acta* **1962**, *64*,430. Barva, R. K. ; Barva, A. B. *Biochem. J.* **1964**, *92*, 21c. Barva, A. B. ; Ghosh, M. C. ; Goswami, K. *Biochem. J.* **1969**, *113*, 447.
17. McMurry J. E. US Patent 4,225,734 (1978). McMurry, J. E. ; Fleming, M. P. *J. Am. Chem. Soc.* **1974**, *96*, 4708.
18. Straub, O. Key to carotenoids, Birkhauser Verlag ; Basel, 1987.
19. Grigg, R. ; Loganathan, V. ; Santhakumar, V. ; Sridharan, V. ; Teasdale, A. *Tetrahedron Lett.* **1991**, *32*, 687.

(*Received in Belgium* 17 *August* 1993; *accepted* 10 *January* 1994)