Pergamon

Tetrahedron Letters, Vol. 37, No. 36, pp. 6547-6550, 1996
Copyright © 1996 Published by Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01395-0

An Efficient Stereocontrolled Synthesis of Functionalized Chlorodienes and Chlorotrienes

Margarita Mladenova*[b], Mouâd Alami[a] and Gérard Linstrumelle[a]

a: Ecole Normale Supérieure, Département de Chimie, URA 1679, 24 rue Lhomond, 75231 Paris Cedex 05, France
*Fax: (+33) 1 47 07 68 56

b: Institute of Organic Chemistry, Bulgarian Academy of Sciences, BG-1113 Sofia, Bulgaria
*Fax: (+359) 2 70 02 25

Key Words: palladium, chlorodienes, chlorotrienes, ω-chlorodienal and trienal, ω-chlorodienones and trienones

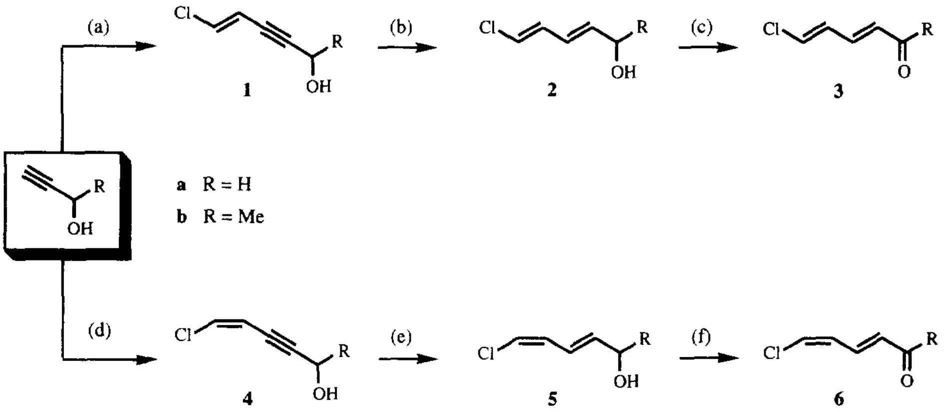
Abstract: A stereoselective synthesis of ω-chlorodienals and ω-chlorodienones was described. Conjugated ω-chlorotrienals and trienones were also easily prepared via an efficient palladium-catalyzed rearrangement of allylic acetates. Copyright © 1996 Published by Elsevier Science Ltd

There has been great interest in recent years in polyene synthesis. Functionalized halogenopolyenes were shown to be useful intermediates for the stereocontrolled construction of polyunsaturated compounds.[1] However, the access to the different (*E*) or (*Z*)-isomers generally display little stereoselectivity. We report herein a short and stereocontrolled synthesis of:

- (i) (*E*,*E*) or (*E*,*Z*) ω-chloropentadienal and the corresponding ω-chlorodienones.

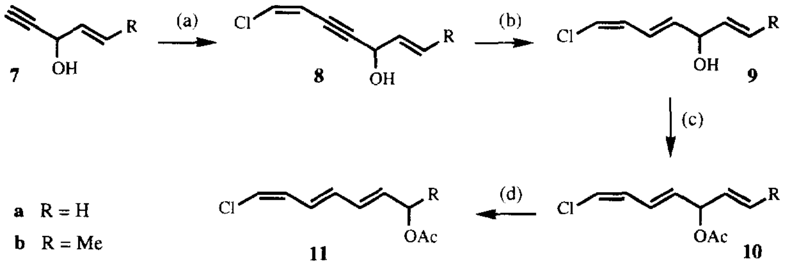
- (ii) (*E*,*E*,*E*) or (*E*,*E*,*Z*) ω-chloroheptatrienal and the corresponding ω-chlorotrienones.

Thus, selective reduction with Red-Al®[2] of chloroenynols **1** and **4**, obtained by coupling of propargyl alcohols with (*E*) and (*Z*)-1,2-dichloroethylene,[3] followed by manganese oxide oxydation[4] led to a stereocontrolled preparation of (2*E*,4*E*)-5-chloro-2,4-pentadienal **3a**, (2*E*,4*Z*)-5-chloro-2,4-pentadienal **6a**[1i,5,6] and the corresponding (*E*) and (*Z*) ω-chlorodienones **3b** and **6b** in high yield[7] (Scheme 1).



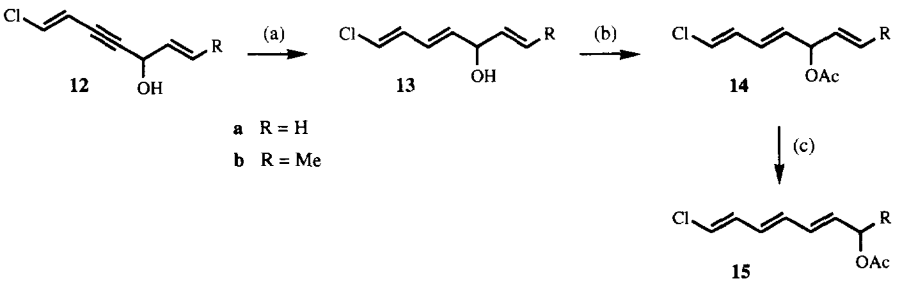
Scheme 1: (a) (*E*)-ClCH=CHCl, piperidine, 5% $PdCl_2(PPh_3)_2$, 10% CuI (R = H: 88%, R = Me: 86%); (b) Red-Al, THF, -30° to 20°C, 2h (R = H: 67%, R = Me: 80%); (c) MnO_2, CH_2Cl_2 (R = H: 87%, R = Me: 81%); (d) (*Z*)-ClCH=CHCl, $BuNH_2$, 5% $PdCl_2(PPh_3)_2$, 10%, CuI, Et_2O (R = H: 92%, R = Me: 88%); (e) Red-Al, THF (R = H: 79%, R = Me: 91%); (f) MnO_2, CH_2Cl_2 (R = H: 92%, R = Me: 98%).

When coupled with (*Z*)-1,2-dichloroethylene under palladium-copper catalysis, the enynols **7a** and **7b** gave the chloroalcohols **8a** and **8b**. These compounds were reduced by Red-Al® into the trienols **9a** and **9b** in 80 and 90% yield. A rapid Pd(II)-catalyzed rearrangement[8] of the corresponding acetates **10a** and **10b** in THF at room temperature for a few hours led regio and stereoselectively to the pure conjugated (*E,E,Z*)-chloroacetates **11a**[9] and **11b** in 96 and 91% yield respectively[10] (Scheme 2).



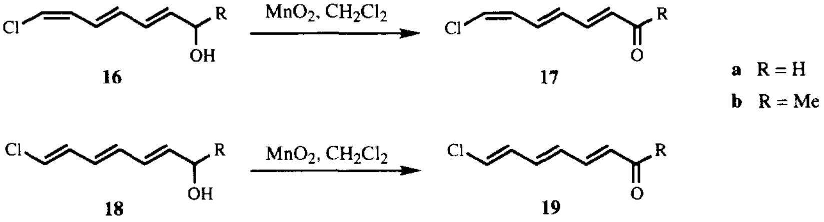
Scheme 2: (a) (*Z*)-ClCH=CHCl, $BuNH_2$, 5% $PdCl_2(PPh_3)_2$, 10%, CuI, Et_2O (R = H: 82%, R = Me: 80%); (b) Red-Al, THF, -30° to 20°C, 2h (R = H: 80%, R = Me: 90%); (c) Ac_2O, Et_3N, CH_2Cl_2; (d) 5% $PdCl_2(MeCN)_2$, THF, 20°C, 2 to 5 h (R = H: 96%, R = Me: 91%).

The same strategy using (*E*)-1,2-dichloroethylene instead of the (*Z*)-isomer, gave the (*E,E,E*)-chlorotrienes **15a** and **15b** by a four-step sequence in good yields (Scheme 3).



Scheme 3: (a) Red-Al, THF, -30° to 20°C, 2h (R = H: 93%, R = Me: 90%); (b) Ac_2O, Et_3N, CH_2Cl_2; (c) 5% $PdCl_2(MeCN)_2$, THF, 20°C, 2 to 5h (R = H: 95%, R = Me: 40%)

These functionnalized chlorotrienes **11** and **15** can be transformed into other polyenes by further elaboration at the carbon-halogen or carbon-acetoxy bond. Thus, hydrolysis of the acetoxy trienes **11** (**a** or **b**) and **15** (**a** or **b**) into the alcohols **16** (**a** or **b**) and **18** (**a** or **b**) followed by manganese oxidation gave the pure (*E,E,Z*) and (*E,E,E*) ω-chlorotrienals **17a**[11] (46% yield), **19a**[12] (79% yield) and ω-chlorotrienones in good yields (**17b**: 73% yield; **19b**: 66% yield).



In conclusion, ω-chlorodienals and trienals and the corresponding ketones were prepared stereoselectively in good yield. Owing to the presence of the two reactive terminal functions, they can be considered as useful intermediates for the synthesis of polyenes. Additional developments will be reported in due course.

Typical procedure: To a stirred solution of (1,4*E*,6*Z*)-3-acetoxy-7-chloro-hepta-1,4,6-triene **10a** (2.86 mmol, 534 mg) in dry THF (6 mL) was added $PdCl_2(MeCN)_2$ (37 mg, 5 mol %) and the reaction was stirred at room temperature and monitored by TLC analysis until complete consumption of the starting material (2 to 5 h). After evaporation of the solvent *in vacuo*, the crude material was purified by filtration through silica gel (eluent: petroleum ether) and gave 512 mg (96%) of pure chlorotriene **11a**.[9]

Acknowledgement: The CNRS is gratefully acknowledged for financial support.

References and notes:

1. (**a**) Uenishi, J.I.; Beau, J.M.; Armstrong, R.W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756-4758. (**b**) Duhamel, L.; Ple, G.; Ramondenc, Y. *Tetrahedron Lett.* **1989**, *30*, 7377-7380. (**c**) Chemin, D.; Linstrumelle, G. *Tetrahedron* **1992**, *48*, 1943-1952. (**d**) Alami, M.; Crousse, B.;

Linstrumelle, G.; Mambu, L.; Larchevêque, M. *SynLett* **1993**, 217-218. (**e**) Yokokawa, F.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett.* **1993**, *34*, 6559-6562. (**f**) Lipshutz, B.H.; Alami, M.; Susfalk, R.B. *Synlett* **1993**, 693-695. (**g**) Babudri, F.; Fiandanese, V.; Naso, F.; Punzi, A. *Tetrahedron Lett.* **1994**, *35*, 2067-2070. (**h**) Smith, III, A.B.; Maleczka, Jr., R.E.; Leazer, Jr., J.L.; Leahy, J.W.; McCauley, J.A.; Condon, S.M. *Tetrahedron Lett.* **1994**, *35*, 4911-4914. (**i**) Soullez, D.; Ple, G.; Duhamel, L.; Duhamel, P. *J. Chem. Soc. Chem. Commun* **1995**, 563-564. (**j**) Torrado, A.; Iglesias, B.; Lopez, S.; De Lera, A.R. *Tetrahedron* **1995**, *51*, 2435-2454.

2. Denmark, S.E.; Jones, T.K. *J. Org. Chem.* **1982**, *47*, 4595-4597.
3. (**a**) Chemin, D.; Linstrumelle, G. *Tetrahedron* **1994**, *50*, 5335-5344. (**b**) Alami, M.; Gueugnot, S.; Domingues, E.; Linstrumelle, G. *Tetrahedron* **1995**, *51*, 1209-1220.(**c**) Crousse, B.; Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1995**, *36*, 4245-4248.
4. Cahiez, G.; Alami, M. Manganese dioxide in *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L.; Ed. Wiley, Chichester **1995**, *5*, 3229-3235.
5. Arnold, Z.; Zemlica, *J. Coll. Czech. Chem. Comm.* **1959**, *24*, 2378-2386.
6. Soullez, D. Ph. D. *Thesis*, Rouen University, **1994**.
7. All new compounds reported herein exhibited spectral data in full accord with assigned structures and gave satisfactory elemental analyses.

   3b: ^{1}H-NMR (250 MHz): δ 6.99 (dd, 1H, J = 15.6 and 10.3 Hz), 6.63 to 6.46 (m, 2H), 6.10 (d, 1H, J = 15.6 Hz), 2.21 (s, 3H); ^{13}C-NMR (62.9 MHz): δ 197.75, 138.30, 131.90, 130.65, 129.65, 27.55.

   6b: ^{1}H-NMR (250 MHz): δ 7.51 (dd, 1H, J = 15.8 and 9.7 Hz), 6.52 to 6.39 (m, 2H), 6.24 (d, 1H, J = 15.8 Hz), 2.34 (s, 3H); ^{13}C-NMR (62.9 MHz): δ 198.50, 135.35, 133.25, 128.25, 127.00, 27.30.
8. (**a**) Overman, L.E.; Knoll, F.M. *Tetrahedron Lett.* **1979**, 321-324. (**b**) Oehlschlager, A.C.; Mishra, P.; Dhami, S. *Can. J. Chem.* **1984**, *62*, 791-797.
9. **11a**: ^{1}H-NMR (250 MHz): δ 6.68 (dd, 1H, J = 14.4 and 10.3 Hz), 6.45 to 6.26 (m, 3H), 6.07 (d, 1H, J = 7.5 Hz), 5.88 (dt, 1H, J = 14.4 and 6.4 Hz), 4.65 (d, 2H, J = 6.4 Hz), 2.1 (s, 3H); ^{13}C-NMR (62.9 MHz): δ 170.60, 134.15, 133.55, 129.35, 128.65, 126.80, 119.20, 64.35, 20.85. UV: (EtOH) λ = 273 nm (ε_{max} = 30400).
10. A non-stereoselective synthesis of unfunctionalized conjugated chlorotrienes has been published, see: (a) Kiehl, A.; Eberhardt, A.; Müllen, K. *Liebigs Ann.* **1995**, 223-230. (**b**) Charoenying, P.; Davies, P.H.; McKerrecher, D.; Taylor, R.J.K. *Tetrahedron Lett.* **1996**, *37*, 1913-1916.
11. **17a:** ^{1}H-NMR (250 MHz): δ 9.62 (d, 1H, J = 7.9 Hz), 7.20 (dd, 1H, J = 15.3 and 11.1 Hz), 7.08 (dd, 1H, J = 15.1 and 10.7 Hz), 6.57 (dd, 1H, J = 15.1 and 11.1 Hz), 6.46 (dd, 1H, J = 10.7 and 7.2 Hz), 6.30 (d, 1H, J = 7.2 Hz), 6.23 (dd, 1H, J = 15.3 and 7.9 Hz); ^{13}C-NMR (62.9 MHz): δ 193.45, 150.85, 134.70, 132.85, 132.60, 128.95, 124.15; UV: (EtOH) λ = 310 nm (ε_{max} = 36200).
12. **19a:** ^{1}H-NMR (250 MHz): δ 9.56 (d, 1H, J = 7.9), 7.17 (dd, 1H, J = 15.3 and 10.3 Hz), 6.68 to 6.48 (m, 4H), 6.23 (dd, 1H, J = 15.3 and 7.9 Hz); ^{13}C-NMR (62.9 MHz): δ 193.20, 150.50, 137.40, 132.80, 132.20, 130.40, 126.75; UV: (EtOH) λ = 311 nm (ε_{max} = 38600).

(*Received in France* 21 *June* 1996; *accepted* 15 *July* 1996)