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Recent advances in double bond formation

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Abstract - This review is presented in five sections dealing respectively with the Wittig and related reactions, sulfone chemistry, allylic rearrangements, acetylene chemistry and miscellaneous.

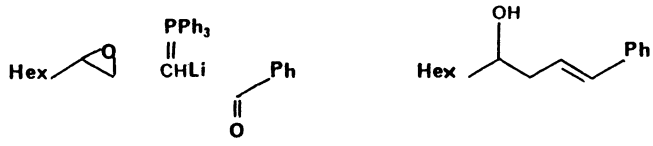
INTRODUCTION

The formation of double bonds, preferably in a stereoselective way is of central interest not only in the carotenoid field but also for the synthesis of insects pheromones, leucotrienes, antibiotics etc. This short survey will present some part of the progress which has been accomplished since this field was extensively reviewed (1).

WITTIG AND RELATED REACTIONS

Phosphorous ylids

The synthesis of polyenes via phosphonium ylids was discussed by Bestmann (2) at a recent carotenoid symposium. NMR (particularly at high field) proved exceedingly useful in elucidating the nature of the Wittig intermediates (3). Treatment of butyl triphenyl phosphonium bromide with sodium hexamethyl disilazide in THF at 20°C and reaction with benzaldehyde at -78°C showed the formation of the cis oxaphosphetane. Work up gave β-propyl styrene (E/Z = 4/96). The same reaction with lithium showed a mixture of the cis-oxaphosphetane and the trans isomer (3.8/1). On warming to -25°C, the disappearance of both oxaphosphetanes and the appearance of triphenylphosphine oxide occurred in a monotonous relationship. The ratio of the cis/trans oxaphosphetanes gradually changed to 1/1. The isomeric olefins were formed in a ratio Z/E = 1.5/1. When the lithium ylid was treated with hexanal, the oxaphosphetanes were formed in a ratio of 5.8/1 which gradually changed to 1/1. The olefins however were formed in the ratio E/Z = 5.8/1. Thus the cis-oxaphosphetane decomposes faster than the trans. With aliphatic aldehydes equilibration of the oxaphosphetanes does not take place whereas, with aromatic ones, it does.
The oxaphosphetanes react with anhydrous HBr or LiBr to give stereospecifically the hydroxy (lithioxy) phosphonium bromides which, in turn, can be converted back into the oxaphosphetanes by HK or NaHMDS. Treatment of a mixture (c/t=2.6/1) of oxaphosphetanes with BuLi followed by HBr gave a majority of the hydroxy phosphonium corresponding to compound which is formed in the "Schlosser modification". Thus the oxaphosphetanes must now be considered as the true intermediates in the Wittig reactions particularly under the "salt-free conditions".
Another puzzling question has been to understand the preferred formation of the Z-olefin. Following up on some work of Meyers, Schlosser observed that cis-oxaphosphetanes were formed at a "normal" rate whereas the rate for the trans isomer was much slower. Molecular models show that in the transition state the alkyl group R in the ylid forces the neighbouring phenyl group out of the plane by roughly 50°. The other equatorial phenyl points with an ortho hydrogen towards one of the substituents of the carbonyl group. If this interaction is stronger than that with the R group the formation of the cis-oxaphosphetane will be favoured. This analysis was confirmed by the finding that triethylphosphonium ylids led indeed to a high proportion of E olefins. The same model could explain why branching in the ylid decreased the cis selectivity whereas branching in the aldehyde increased it.
β-Or γ-oxido-ylids have recently been formed in the reaction of doubly deprotonated phosphonium salts (with s-BuLi in ether or t-BuLi in THF) "lithiated ylids" with carbonyl compounds (6) or epoxides. E-olefinic compounds are thus produced in a three components assembly.



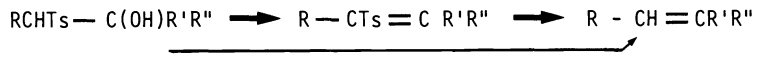
The selective formation of E double bonds from a γ-oxido ylid could be considered as an intramolecular Schlosser modification (5a). Investigation of a serie of oxido ylids $Ph_3P{=}CH{-}(CH_2)_4O^-$ showed a dramatic decrease of Z selectivity when n decreased (5b). The loss of deuterium observed when starting with a labeled compound was however much too small to support the intramolecular proton abstraction mechanism.
The Wittig-Horner reaction can be used to give either the Z (by direct condensation) or the E alkene (by acylation of the ylid and reduction to the threo alcohol) (7a). Efficient purification is achieved by crystallisation. The elimination is carried out with NaH, DMF at 50°C. E selectivity is increased in ethers-TMEDA and at a low (-100°C) temperature (7b). With trifluoro-ethyl phosphonates, unsaturated esters were prepared with high Z selectivity (7c). The use of base systems with minimally complexing counter-ions is recommended (K HMDS, 18-crown-6)(facilitate elimination).
Particularly mild conditions (LiCl + DBU or DIPEA) could be used to carry out the HWE reactions with base sensitive compounds (7d).

Silicon ylids (for a recent review see (8))
Recent progress in the Peterson reaction include an easy access to α-lithio silanes (even tertiary) from dithioacetals by reduction (Li, dimethylamino naphtalene) silylation--reduction (9). The E/Z ratio of olefins is not affected by the counter ion or added salts ; the formation of the β-silylalkoxides is probably irreversible. The Z/E ratio increases, however, as the bulk of the R groups on the silicon increases (Me_3Si 1/1.3 ; Ph_3Si 1/0.5) (10).
The threo hydroxysilane is stereoselectively formed through reduction of the corresponding silyl ketone (11). The E olefin can then be obtained by syn elimination with KH, THF whereas the Z olefin is formed with BF_3, ether. The syn elimination has been used to invert the configuration of olefins (12). 1.3-dienes could be prepared stereoselectively with bis-1.3-trimethyl silyl propenyl lithium (13).

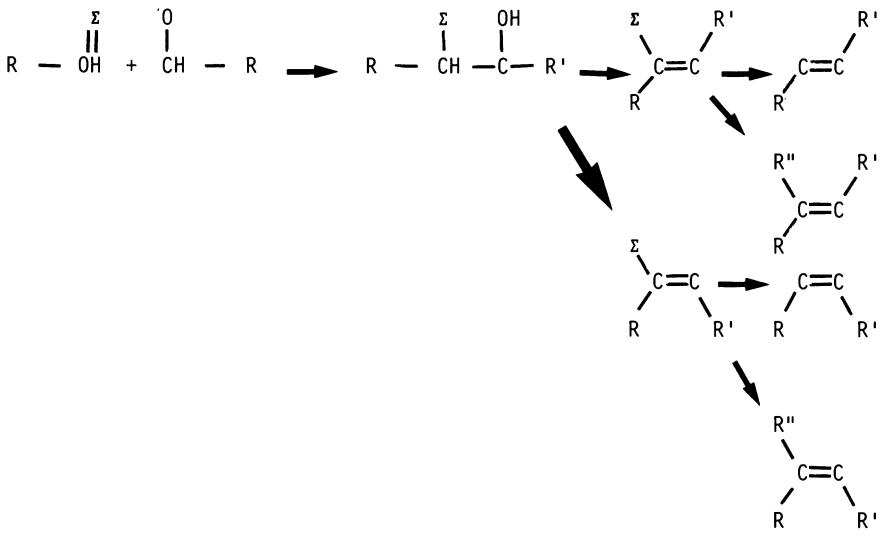
Boron ylids
A boron analog of the Wittig reaction was recently described and found highly trans stereoselective (14).

SULFONES

α-Sulfonyl carbanions can be alkylated ; base promoted elimination then brings about the formation of a new double bond. The elimination is carried out efficiently only when one or more extra unsaturations : C=C and/or C=O are conjugated with the new double bond. More generally sulfone ylids can be condensed with aldehydes or ketones.



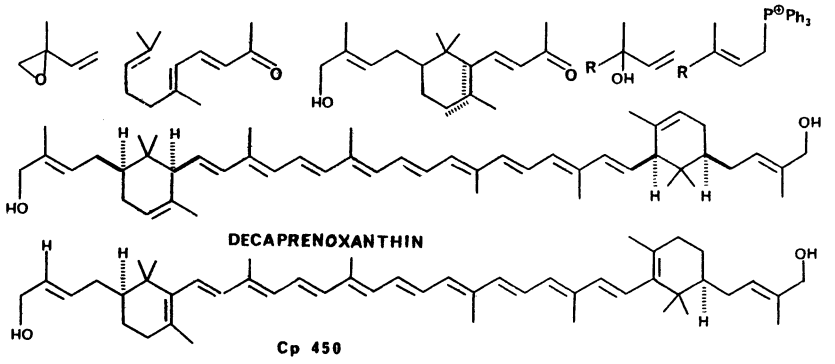
Reduction of the hydroxysulfones (or derivatives thereof) leads in high yield to the regioselective formation of a new double bond (15). This is mainly E, however the reaction can be said to be stereoselective only when substituents are present in the α position (s) (16a). It has been used in recent syntheses of diumycinol (16b) and of pseudomonic acid C (16c). Acetylenes can be produced either by sodium amalgam reduction of ketosulfonesenolesters (16d,16e) or through base promoted elimination on acetoxysulfones (16f). Disproportionation of the triple bond into two double bonds was used in a synthesis of retinoic acid.
More generally, disubstituted olefins could be prepared stereoselectively through : a) selective formation of threo hydroxysulfones by reduction of the ketosulfones and anti-elimination to the Z alkenyl sulfones. b) convergent elimination on the mixture of acetoxysulfones to the E alkenyl sulfone c) stereospecific hydrogenolysis of the sulfonyl group with retention of configuration (17). This could be effected either with sodium dithionite (18) preferably under p.t.c. conditions or with reducing grignards in the presence of palladium or nickel catalysts (19). Trisubstituted olefins could be prepared by stereospecific coupling of grignards with alkenyl sulfones catalysed by iron salts (20).
1-1-Disulfones proved particularly interesting for stereoselective syntheses owing to the bulk of the two sulfone groups and/or their high melting points which make purification easy. Partial hydrogenolysis leads to E allylic or homoallylic sulfones. This permitted the olefin synthesis mentioned above to be extended to the preparation of conjugated or skipped dienes (22a).



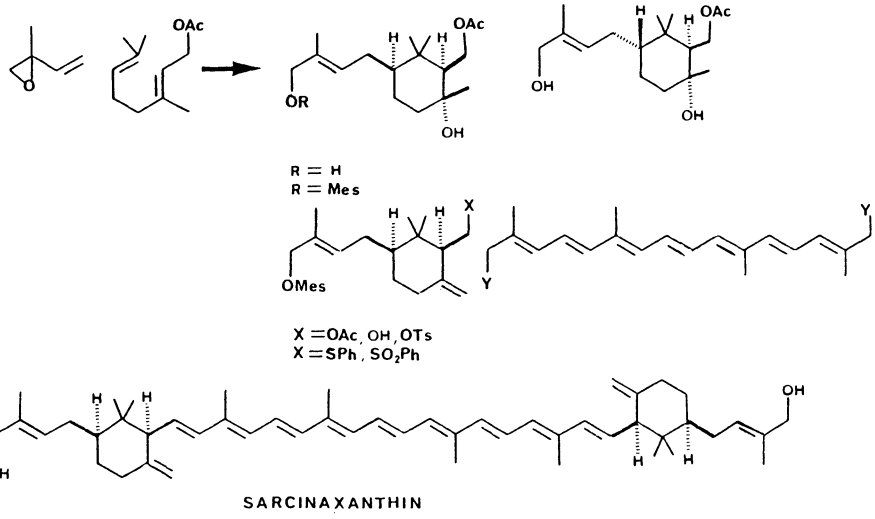
Crystalline, readily purified, sulfone-containing intermediates were used in a synthesis of hindered stereoisomers of retinal (22b).
Two groups have recently used the pyrolysis of sulfolenes to produce dienes stereoselectively (23,24).

ALLYL REARRANGEMENTS

A hydroxymethyl group in the chain of a carotenoid has been introduced via allylic anionotropy (25). Claisen rearrangements have proved very useful for the stereoselective synthesis of olefinic compounds (1b,26a). Allyldithiocarbonates (DTC) thus allow substitution at both ends of an allylic group. High E stereoselectivity is observed (26b).
When allylalcohols are converted into their tributylstannyl methylethers, tin-lithium exchange brings about a rearrangement to Z (> 95%) homoallyl alcohols (27). Obviously the early transition state with axial butyl is strongly preferred. The selectivity was much less pronounced in the formation of disubstituted olefins.
Vinyloxiranes react regio- and stereoselectively (E) with cuprates. Z alkenyl cuprates lead to Z-E dienes (28). Alternatively organolithium compounds with TMEDA give the Z (96%) allylic alcohol (29). Diethyl aluminium benzene thiolate converts isoprene epoxide into the 1.4-addition product with high Z stereoselectivity. A cyclic transition state is suggested (30a). Similarly trans 1.2 di- or 1.1.2 tri-substituted oxiranes are smoothly isomerized into E allylic alcohols by diethylaluminium 2.2,6,6-tetramethyl piperidide (DEATMP) (30b).
Isoprene oxide was used to hydroxy-prenylate pseudoionone in a biomimetic synthesis of C50 carotenoids. Under $ZnCl_2$ catalysis, cyclized products were obtained directly. The double bond in the side chain had pure E stereochemistry. The cyclic α-cis, α-trans and β-isomers could be separated, no γ-isomer was detected. Conversion into the corresponding vinyl-ionols and ionylidene triphenyl phosphonium salts, followed by condensation with dimethyl octatrienal led to E, cis decaprenoxanthin when starting with the α-cis hydroxy prenylionone and Cp450 from the β-isomer.



On the other hand, geranyl acetate could be hydroxyprenylated-cyclized directly. Selective protection of the primary E-allylic-hydroxyl group allowed dehydration to the γ-position and conversion of the acetoxy group into the sulfone which is a key intermediate for sarcinaxanthin (31).



SARCINAXANTHIN

ACETYLENIC PRECURSORS

Acetylenes

Acetylenes are an obviously attractive starting material for olefin synthesis. Disubstituted olefins E or Z are formed by semi-hydrogenation. Evidence has been presented to show that "poisons" (Pb, quinoline) in the very widely used Lindlar catalyst do not block active sites but act to rearrange the surface of the catalyst. (Palladium foil is extremely selective) (37). Lithium aluminium hydride in THF (usually as a slurry) is well known to reduce acetylenic alcohols to E allylic alcohols. It has been found however that clear solutions of LAH in ether led to the Z isomer with > 99% selectivity (38). Hydrometalation of terminal acetylenes can also be used for the synthesis of disubstituted olefins in different ways.

Vinyl derivatives

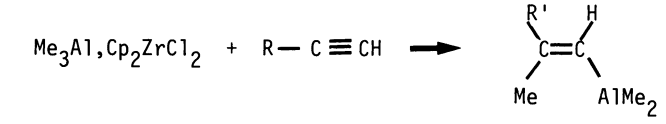
Considerable effort has been invested in the stereoselective formation and stereospecific coupling of vinyl halides. Boron and aluminium hydrides have been used (32). A very elegant solution to the problem is provided by the coupling of E or Z 1.2-dichloroethylene with one or two Grignard reagents (saturated, vinylic or acetylenic) under Ni or Pd catalysis (33).

Alkyl thio groups are stereospecifically displaced from an sp^2 carbon by grignards under nickel catalysis (34). The stereoselective synthesis of thiovinylethers is however not so easy. The problem could be solved by deoxygenation of the corresponding E-sulfoxides, obtained by α-metalation-alkylation of (E+Z) vinylsulfoxides (35). Another solution made use of the greater reactivity of the alkylthio group cis to the olefinic hydrogen atom in keten thioacetals (36).

Carbometalation

Carbometalation of acetylenes has developed into a major synthetic tool for the synthesis of trisubstituted double bonds (39).

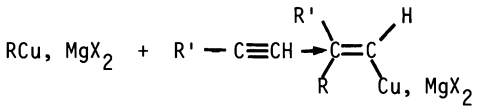
The addition of trialkylalanes to acetylenes is usually plagued with side reactions : metalation of ≡ CH, lack of regioselectivity and competing di- and polymerisation . In the presence of Cp_2ZrCl_2 however the addition of Me_3Al is highly regio- and stereoselective (39b). Various substitution reactions can be carried out with the vinylalane thus formed.



Unfortunately higher alanes, so far, give poorer results. $TiCl_4$ however gives a very selective reaction of Et_2AlCl with 3-butyn-1-ol ; chelation through the oxygen probably accounts for the results (40).

Carbozincation of alkynes (Cp_2ZrI_2 catalysed) (41) has been described recently. The addition of C-Zn, and not C-Zr, to the acetylene is shown by the reaction of Et_2Zn + Cp_2ZrIMe which gives ethylmetalation without any methylmetalation.

Carbocupration is effected by the reaction of organocopper compounds RCu, MgX_2 (or RCuX, MgX) ; RR' CuM, with terminal acetylenes (43) in a regio and stereoselective way : side reactions include vinyl-vinyl and vinyl-alkyl coupling.



Coordinating groups in the alkyne can reverse the usual direction of addition. The proportion of linear-branched product also depends on the main group metal used (Mg or Li) and on the solvent 44.

The Z-alkenyl copper derivatives are thus very readily available. They will undergo a number of reactions when the metal is displaced by a proton, a halogen or other heteroatom. Substitution with alkyl halides works very well with reactive allylic halides but with saturated ones, it is often necessary to add HMPA and $P(OEt)_3$. Reaction with CO, acid chlorides, aldehydes, epoxides, enones and enals (44)) are efficient. Stereoselectivity is very high and the scope is large indeed.
Hydroalumination of propargyl alcohol, transmetalation with tributyltin triflate and acetylation provided a building block for a recurrent synthesis of skipped poly -Z olefins. The process is started with a Z-alkenylmetal formed by carbocupration of acetylene and transmetalation (42).
Addition of Li diorganocuprates to acetylenic acetals and metals provided an easy access to a variety of carbonyl derivatives.

MISCELLANEOUS

Decarboxylative elimination of β-hydroxy carboxylic acids by dimethylformamide acetals, reminiscent of the biological process, proceeds in the anti mode (46). Condensation of carboxylate dianions with carbonyl derivatives leads, after closing the (threo) β-lactone ring and pyrolysis, to sterically congested olefin in a stereoselective way (47).
β-Acetoxy γ-unsaturated acids undergo a Pd-catalysed fragmentation reaction. The new double bond is 80-90% E starting with either diastereoisomer (48). Retinoic acid was synthesized as an illustration of the new method (49).
Insertion of ready made double bonds. The idea is to carve out a piece of a readily available molecule containing the desired double bond and to insert it at the right position in the new molecule : this has been done with the double bonds of oleic acid (for muscalure via the Kolbe reaction or umpolung with sulfones) (50) or of geraniol/nerol derivatives after ozonolysis of the double bond (51).

REFERENCES

1) a) J. Reucroft and P.B. Sammes, Quart. Rev. Chem. Soc., 25, 135 (1971) b) D.J. Faulkner, Synthesis, 175 (1971) c) A.S. Arora and I.K. Ugi, Methoden Org. Chem. (Houben Weyl) 4th Ed., 5/1b, 728 (1972).
2) a) H.J. Bestmann, Pure and Applied Chem., 51, 515 (1979) b) I. Gosney and A.G. Rowley in Organophosphorous reagents in Organic Synthesis, J.I.G. Cadogan Ed., Acad. Press, London (1979), p.17. c) W.S. Wadsworth, Org. React., 25, 73 (1977).
3) E. Vedejs, G.P. Meier and K.A.J. Snoble, J. Am. Chem. Soc., 103, 2823 (1981) ; E. Vedejs and G.P. Meier, Angew. Chem., Int. Ed., 22, 56 (1983) b) A.B. Reitz, M.S. Mutter and B.E. Maryanoff, J. Am. Chem. Soc., 106, 1873 (1984).
4) a) A.I. Meyers, J.P. Lawson and D.R. Carver, J. Org. Chem., 46, 3119 (1981) b) M. Schlosser and B. Schaub, J. Am. Chem. Soc., 104, 5821 (1982).
5) a) W.G. Salmond, M.A. Barta and J.L. Havens, J. Org. Chem., 43, 790 (1978) b) B.E. Maryanoff, A.B. Reitz and B.A. Duhl-Einswiler, Tetrahedron Letters ; 24, 2477 (1983).
6) E.J. Corey and J. Kang, J. Am. Chem. Soc., 104, 4724 (1982).
7) a) A.D. Buss and S. Warren, J.C.S. Chem. Comm., 100 (1981) b) id. Tetrahedron Letters, 24, 3931 (1983) c) W.C. Still and C. Gennari, ibid., 4405 d) M.A. Blanchette, W. Choy, J.T. Davis, A.P. Essenfeld, S. Masamune, W.R. Roush and T. Sakai ib., 25, 2183 (1984).
8) D.J. Ager, Synthesis, 384 (1984).
9) T. Cohen, J.P. Sherbine, J.R. Matz, R.R. Hutchins, B.M. McHenry and P.R. Willey, J. Am. Chem. Soc., 106, 3245 (1984).
10) A.R. Bassindale, R.J. Ellis and P.G. Taylor, Tetrahedron Letters, 25, 2705 (1984).
11) P.F. Hudrlick and D. Peterson, J. Am. Chem. Soc., 97, 1464 (1975).

12) For a review on alkene inversion : P.E. Sonnet, Tetrahedron, 36, 577 (1980).
13) T.H. Chang and J.S. Li, J.C.S. Chem. Comm., 969 (1982).
14) A. Pelter, B. Singaram and J.W. Wilson, Tetrahedron Letters, 24, 635 (1983).
15) M. Julia and J.M. Paris, Tetrahedron Letters, 4833 (1973).
16) a) P.J. Kocienski, Chem. and Ind., 548 (1981) b) P. Kocienski and M. Todd, J.C.S. Chem. Comm. 1079 (1982) c) G. Keck, D. Kachensky and E.J. Enholm, J. Org. Chem., 49, 1464 (1984) d) P.A. Bartlett, F.R. Green, III and E.H. Rose, J. Am. Chem. Soc., 100, 4852 (1978) e) B. Lythgoe and I. Waterhouse, Tetrahedron Letters, 2625 (1978) f) T. Mandai, T. Yanagi, K. Araki, Y. Morisaki, M. Kawada and J. Otera, J. Am. Chem. Soc., 106 (12) 3670 (1984).
17) M. Julia, J.P. Stacino, J.N. Verpeaux and M. Launay, Tetrahedron Letters, 23, 2465 (1982).
18) J. Bremner, M. Julia, M. Launay and J.P. Stacino, ibid, 23, 3265 (1982).
19) J.L. Fabre and M. Julia, ibid, 24, 4311 (1983).
20) J.L. Fabre, M. Julia and J.N. Verpeaux, ibid, 23, 2469 (1982).
21) a) T. Cuvigny, C. Hervé du Penhoat and M. Julia, Bull. Soc. Chim. Fr., II, 44 (1982) b) id., Tetrahedron Letters, 24, 189 (1983).
22) a) T. Cuvigny, J.L. Fabre, C. Hervé du Penhoat and M. Julia, ibid, 24, 4319 (1983) b) J.P. Duchesne and M. Julia, unpublished.
23) R. Bloch and J. Abecassis, Tetrahedron Letters, 24, 1247 (1983) ; R. Bloch, D. Hassan and X. Mandard, ibid, 4691 ;
24) S. Yamada, H. Ohsawa, T. Suzuki and H. Takayama, Chem. Letters, 1003 (1983).
25) P.A. Butikofer and M.H. Eugster, Helv. Chim. Acta, 66, 1148 (1983).
26) a) G.B. Bennett, Synthesis, 589 (1977). b) T. Hayashi, M. Yanagida, Y. Matsuda and T. Oishi, Tetrahedron Letters, 24, 2665 (1983) ; T. Hayashi, I. Hori and T. Oishi, J. Am. Chem. Soc., 105, 2909 (1983).
27) W.C. Still and A. Mitra, J. Am. Chem. Soc., 100, 1927 (1978).
28) C. Cahiez, A. Alexakis and J.F. Normant, Synthesis, 528 (1978).
29) M. Tamura and G. Suzukamo, Tetrahedron Letters, 22, 577 (1981).
30) a) A. Yasuda, M. Takahashi and M. Takaya, ibid, 22, 2413 (1981). b)A. Yasuda, H. Yamamoto and H. Nozaki, Bull. Chem. Soc. Japan, 52, 1705 (1979).
31) J.-P. Ferezou and M. Julia, unpublished results.
32) E. Negishi, Organometallics in Organic Synthesis, vol. I, p.315; Wiley, New York, (1980).
33) V. Ratovelomanana and G. Linstrumelle, Tetrahedron Letters, 22, 315 (1981).
34) a) H. Okamura, H. Miura and H. Takei, Tetrahedron Letters, 43 (1979) ; b) E. Wenkert, T.W. Ferreira and E.L. Michelotti, J.C.S. Chem. Comm., 637 (1979).
35) H. Takei, H. Sugimura, M. Miura and H. Okamura, Chem. Letters, 1209 (1980).
36) E. Wenkert and T.W. Ferreira, J.C.S., Chem. Comm., 840 (1982).
37) A.B. McEwen, M.J. Guttieri, W.F. Maier, R.M. Laine and Y. Shvo, J. Org. Chem., 48, 4436 (1983).
38) M.L. Mancini and J.F. Honek, Tetrahedron Letters, 24, 4295 (1983).
39) a) E.I. Negishi, Pure Appl. Chem., 53, 2333 (1981) ; Acc. Chem. Res., 15, 340 (1982). b) G. Zweifel in Aspects of Mechanism and Organometallic Chemistry, J.H. Brewster, Ed. Plenum, New York, P.229 (1978).
40) F.W. Schultz, G. Ferguson and D.W. Thompson, J. Org. Chem. 49, 1736 (1984).
41) E.I. Negishi, D.E. Van Horn, T. Yoshida and C.L. Rand, Organometallics, 2, 563 (1983).
42) E.J. Corey and T.M. Eckrich, Tetrahedron Letters, 25, 2419 (1984).
43) J.F. Normant, Pure Appl. Chem., 50, 709 (1978).
44) a) J.F. Normant and A. Alexakis, Synthesis, 841 (1981) b) A. Marfat, P.R. McGuirck and P. Helquist, J. Org. Chem., 44, 3888 (1979).
45) A. Alexakis, A. Commerçon, C. Coulentianos and J.F. Normant, Tetrahedron, 40, 715 (1984).
46) G. Frater, Helv. Chim. Acta, 62, 1826 (1979).
47) W. Adam, G. Martinez, J. Thompson and F. Yany, J. Org. Chem., 46, 3359 (1981).
48) B.M. Trost and J.M. Fortunak, J. Am. Chem. Soc., 102, 2841 (1980).
49) B.M. Trost and J.M.D. Fortunak, Tetrahedron Letters, 22, 3459 (1981).
50) a) G.W. Gribble, J.K. Sanstead and J.W. Sullivan, J.C.S. Chem. Comm. 735 (1973) ; b) M. Julia and H. Mestdagh, unpublished.
51) G. Stork, M. Gregson and P.A Grieco, Tetrahedron Letters, 1391 (1969).