Tetrahedron Letters No. 2, pp 195 - 198, 1977. Pergamon Press. Printed in Great Britain.

# SYNTHESIS OF CHIRAL OLEFINS BY THE WITTIG REACTION.

Piero Salvadori*, Sergio Bertozzi, and Raffaello Lazzaroni

Centro di Studio del C.N.R. per le Macromolecole Stereoordinate ed Otticamente Attive
Istituto di Chimica Organica, Facoltà di Scienze M.F.N., Università di Pisa, Italy.

(Received in UK 12 October 1976; accepted for publication 29 November 1976)

The work made up to now on the stereochemistry of the Wittig reaction mainly deals with factors influencing the geometrical isomerism of the produced internal olefins [1] or with the retention of absolute configuration at the phosphorus atom when chiral phosphines are employed [2]. There are no exhaustive reports on the stereospecificity of this reaction with respect to the optical isomerism in preparing chiral olefins with an asymmetric carbon atom α or β to the double bond.

The series of internal cis and trans olefins reported in Table 1, characterized by the presence of one or two asymmetric carbon atoms with high prevalence of S chirality, was prepared following the Hauser procedure for the Wittig reaction [3]. With the sole exception of (S)-4-methylhex-2-ene [4], III, these olefins have not been described till now.

According to the olefin structure, the chiral aldehydes [5,6] and the chiral bromides [7] were both necessarily used in the preparation of (3S,6S)-3,6-dimethyloct-4-ene, I, and (3S,8S)-3,8-dimethyldec-5-ene, IV. (S)-2,6-dimethyloct-4-ene, II, and III were both obtained either from (S)-2-methylbutanal and the suitable bromide or from (S)-1-bromo-2-methylbutane and the suitable aldehyde. Finally (S)-2,7-dimethylnon-4-ene, V, was prepared by using the chiral aldehyde (S)-3-methylpentanale [6] and 1-bromo-3-methylbutane.

The yield strongly depends on the structure of the reagents[3], and the cis/trans ratio is as high as expected in the case of unstabilized ylids [1](Table 1). The separation of the geometrical isomers to a purity greater than 99.5% was successfully achieved by a Perkin Elmer Model 251 spinning band column or by preparative gas-chromatography using $AgNO_3$ in ethylenglycol as a stationary phase.

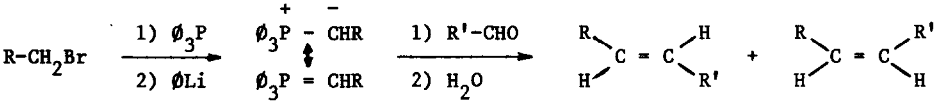
The structure of the olefins prepared and some physical properties of their geometrical isomers are reported in Tables 1 and 2.

The optical purity of the samples was determided by converting the olefin into the corresponding ozonide ($CHCl_3$, -30°) and successive reduction to the alcohol by $LiAlH_4$ (Scheme, route A).

In all cases no racemization was observed by comparing the optical purity of the alcohol with that of the bromide or of the aldehyde employed in the synthesis of the olefin, so that the same optical purity of the alcohol can be assigned to the latter (Table 2).

Table 1

Structure and some physical properties of chiral olefins obtained by the Wittig reaction



| Olefin | R | R' | Yield[a] (%) | cis/trans[b] | Geom. isomer | b.p. (°C) | $d_4^{25}$ | $n_D^{25}$ |
|---|---|---|---|---|---|---|---|---|
| I | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | 28 | 67/33 | cis<br>trans | 149-151<br>154-155 | 0.7316<br>0.7302 | 1.4166<br>1.4166 |
| II | $CH_3-\underset{CH_3}{CH}-CH_2-$ | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | 60 | 70/30 | cis | 154-155 | 0.7359 | 1.4184 |
| | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | $CH_3-\underset{CH_3}{CH}-CH_2-$ | 25 | 72/28 | trans | 156-157 | 0.7351 | 1.4164 |
| III | $CH_3-$ | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | 58 | 79/21 | cis [c] | 87-88 | 0.6951 | 1.4001 |
| | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-$ | $CH_3-$ | 24 | 85/15 | trans[c] | 87-88 | 0.6932 | 1.3997 |
| IV | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH_2-$ | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH_2-$ | 78 | 68/32 | cis<br>trans | 93-94 [d]<br>93-94 [d] | 0.7676<br>0.7622 | 1.4365<br>1.4311 |
| V | $CH_3-\underset{CH_3}{CH}-CH_2-$ | $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH_2-$ | 75 | 70/30 | cis<br>trans | 83-84 [e]<br>83-84 [e] | 0.7529<br>0.7464 | 1.4278<br>1.4244 |

[a] computed with respect to the phosphonium salt

[b] determined by vapour phase chromatography on the reaction product

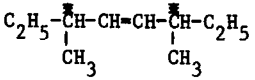
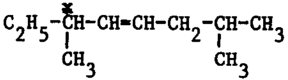
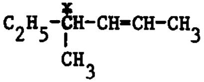
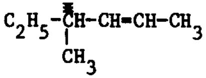
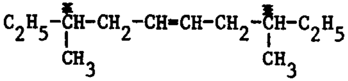
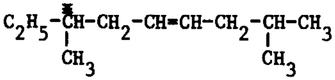
[c] for the physical costants reported in literature see reference 4

[d] measured at 16 mm Hg

[e] measured at 20 mm Hg

Table 2

Relationship between optical rotatory power and optical purity (o.p.) of the olefins and racemization in their hydrogenation.

| Chiral olefin | | | | Chiral compound used in the synthesis | | Alcohol (scheme, route A) | | Paraffin (scheme, route B) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structure | Isomer | $[\alpha]_D^{25}$ | Type | o.p. (%) | $[\alpha]_D^{25}$ | o.p. (%) | $[\alpha]_D^{25}$ | o.p. (%) | Racemization (%) |
| I |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH=CH-\underset{CH_3}{\overset{*}{C}H}-C_2H_5$ | cis | +50.67 | aldehyde | 96.0 | -5.59 | 96.1 [a] | +14.96 | 71 [b] | 25 |
| | | trans | +64.83 | bromide | 97.0 | -5.60 | 95.9 [a] | | | |
| II |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH=CH-CH_2-\underset{CH_3}{CH}-CH_3$ | cis | +17.41 | aldehyde | 96.0 | - | - | + 9.0 | 89 [c] | 7 |
| | | trans | +29.19 | | | | | | | |
| III |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH=CH-CH_3$ | cis | +28.57 | aldehyde | 96.0 | -5.56 | 95.6 [a] | + 8.73 | 88 [d] | 8 |
| | | trans | +37.64 | | | | | | | |
| III |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH=CH-CH_3$ | cis | +28.97 | bromide | 97.5 | -5.66 | 97.3 [a] | - | - | - |
| | | trans | +38.09 | | | | | | | |
| IV |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH_2-CH=CH-CH_2-\underset{CH_3}{\overset{*}{C}H}-C_2H_5$ | cis | + 7.61 | aldehyde | 96.4 | +8.40 | 96.0 [b] | +16.1 | 92 [b] | 4 |
| | | trans | + 3.98 | bromide | 96.4 | | | | | |
| V |  $C_2H_5-\underset{CH_3}{\overset{*}{C}H}-CH_2-CH=CH-CH_2-\underset{CH_3}{CH}-CH_3$ | cis | + 4.04 | aldehyde | 96.4 | +8.39 | 96.0 [b] | - | - | - |
| | | trans | + 2.56 | | | | | | | |

[a] L.Lardicci and P.Pino, Gazz.Chim.Ital., 91, 441 (1961).

[b] P.Pino, L.Lardicci, and A.Stefani, Ann.Chim., 52, 456 (1962).

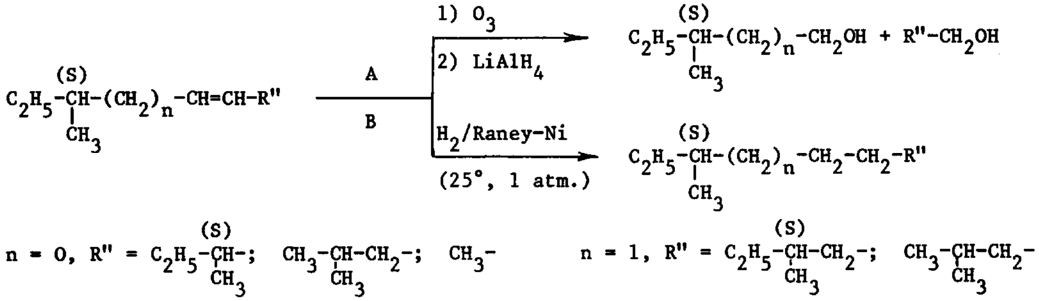
[c] F.Ciardelli and P.Pino, Gazz.Chim.Ital., 95, 1201 (1965).

[d] P.A.Levene and R.E.Marker, J.Biol.Chem. 103, 302 (1933).

From the results obtained one has to conclude that the Wittig reaction occurs without racemization even if a tertiary asymmetric carbon atom is in the α position to the double bond, both starting with the bromide or the aldehyde as optically active materials.

This fact makes the Wittig reaction a very useful stereospecific method for the synthesis of chiral olefins in high optical yield.

Scheme



Following the route B (Scheme), that in principle could be an alternative method for the optical purity determination, a racemization of 4 to 25% was detected by comparing the optical purity of the paraffins with that of the chiral starting compounds.

Such a racemization cannot be connected with the Wittig reaction as shown by the reductive ozonization of the olefin and hence it occurs during the hydrogenation of the double bond.

In this connection it is worth noting that, contrary to what observed in the case of the α-olefins [8,9], the catalytic hydrogenation of chiral olefins with an internal double bond produces racemization in some extent.

## References

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