SYNTHESIS OF ALKENES BY WITTIG REACTION USING LITHIUM 1,3-DIAMINOPROPANE AS A BASE

Ludvík STREINZ, David ŠAMAN, Karel KONEČNÝ and Miroslav ROMAŇUK

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

Received August 29, 1989
Accepted November 17, 1989

It has been found that the lithium 1,3-diaminopropane (*X*) can be used for generation of non-stabilized ylides from alkyltriphenylphosphonium salts. These ylides with aldehydes afford olefins in moderate yield with high *Z*-stereoselectivity. The reaction conditions were studied.

The synthesis of many compounds bearing double bonds was often based on the Wittig reaction because of the fact that this reaction could be used for preparation of desired geometrical isomers by changing reaction conditions only[1,2]. Much effort was devoted to the study of different factors having an influence on *E*/*Z* ratio i.e. the type of base used[4], the character of alkyl groups attached to the phosphorus atom of ylide[5] or aldehyde[3-5], the influence of solvent[3,4,6,7] and presence of soluble inorganic salts[4,8]. It was found that the highest *Z*-stereoselectivity was easily achieved by using of polar aprotic solvents[3,6,7] or techniques where the soluble inorganic salts were not present[5,8-10] (lithium salt free conditions), or by using of instant ylides[11,12].

As a rule, the super bases derived from 1,3-diaminopropane which were used for isomerisation of triple bond (zipper reaction[13]) are easily accesible and even more these amines are known to have strong solvatation effect which would influence favourably the stereoselectivity of the Wittig reaction. These facts encouraged us to investigate the capability of these bases to generate unstabilized ylides from alkyltriphenylphosphonium salts and to influence the stereoselectivity of their reaction with aldehydes. The results are given in the Table I.

All these reactions were performed at sufficiently low temperatures (below −70°C) in order to decrease the amount of *E* isomer in the reaction mixture[4,8] irrespective of the other conditions influencing the stereoselectivity. When carried out at 0°C, the reaction mixture contained higher amount of the *E* isomer (see Table I, entry 5–7). Besides of the lithium 1,3-diaminopropane base, butyllithium was used for every combination of the aldehyde-ylide pair (see Table I). Butyllithium is reffered to give the mixture with often prevailing *E* isomer and these mixtures were used for identification of both *E* and *Z* isomers in question (by comparing of both ^{1}H NMR

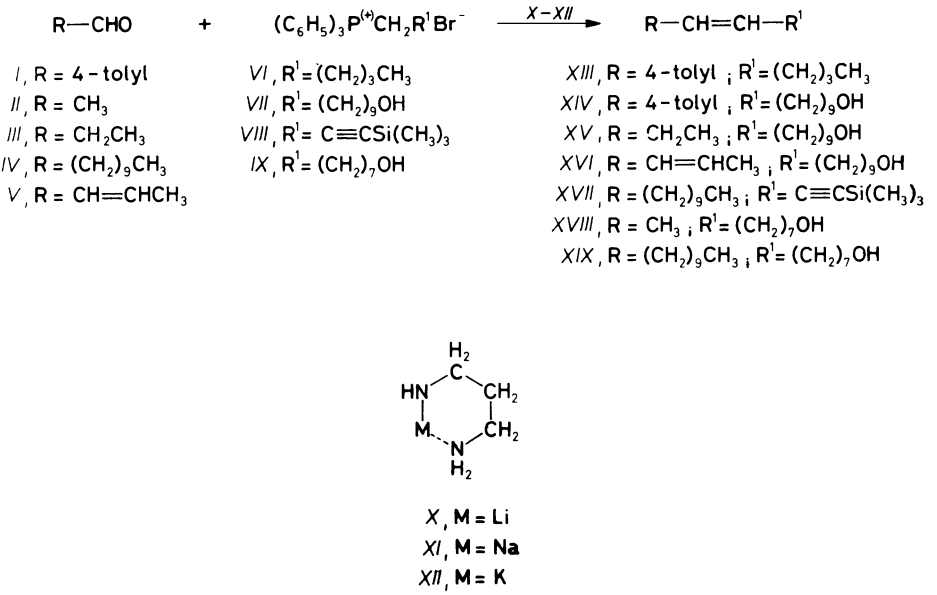
and GLC data). Hexamethylphosphorous triamide which was added to the solvent gave the product with higher amount of *E* isomer unlike that of the same reaction

TABLE I
Preparation of olefins *XIII*—*XIX*

Entry	Aldehyde	Ylide	°C[a]	Base	Solvent	Product[b]	Ratio		Yield[c] %
							% *E*	% *Z*	
1	*I*	*VI*	−78	*X*	THF	*XIII*	3·5	96·5	43
2	*I*	*VI*	−78	*XI*	THF	*XIII*	6·1	93·9	36
3	*I*	*VI*	−78	*XII*	THF	*XIII*	8·9	91·1	41
4	*I*	*VI*	−78	BuLi	THF	*XIII*	60·5	39·5	46
5	*I*	*VI*	0	*X*	THF	*XIII*	25·8	74·2	52
6	*I*	*VI*	0	*XI*	THF	*XIII*	0	0	0
7	*I*	*VI*	0	*XII*	THF	*XIII*	0	0	0
8[d]	*I*	*VI*	−78	*X*	THF/HMPT	*XIII*	12·5	87·5	13
9	*I*	*VI*	−78	*XI*	THF/HMPT	*XIII*	33·3	66·7	35
10	*I*	*VI*	−78	*XII*	THF/HMPT	*XIII*	0	0	0
11	*I*	*VI*	−78	*X*	ether	*XIII*	16·4	83·6	42
12	*I*	*VI*	−78	*XI*	ether	*XIII*	9·6	90·4	15
13	*I*	*VI*	−78	*XII*	ether	*XIII*	10·5	89·5	25
14[e]	*I*	*VI*	−78	*X*	THF	*XIII*	14·9	85·1	47
15[f]	*I*	*VI*	−78	*X*	THF	*XIII*	10·2	89·8	35
16	*I*	*VII*	−78	*X*	THF	*XIV*	6·0	94·0	66
17	*I*	*VII*	−78	*XI*	THF	*XIV*	0	0	0
18	*I*	*VII*	−78	*XII*	THF	*XIV*	0	0	0
19	*I*	*VII*	−78	BuLi	THF	*XIV*	32·7	67·3	60
20	*III*	*VII*	−78	*X*	THF	*XV*	1·3	98·7	31
21	*III*	*VII*	−78	BuLi	THF	*XV*	12·4	87·6	39
22[g]	*V*	*VII*	−78	*X*	THF	*XVI*	17·6	82·4	32
23[g]	*V*	*VII*	−78	BuLi	THF	*XVI*	21·0	79·0	32
24	*IV*	*VIII*	−78	*X*	THF	*XVII*	87·4	12·6	56
25	*IV*	*VIII*	−78	BuLi	THF	*XVII*	81·4	18·6	61
26[h]	*II*	*IX*	−78	*X*	THF	*XVIII*	7·0	93·0	31
27[i]	*II*	*IX*	−78	*X*	THF	*XVIII*	5·0	95·0	43
28	*II*	*IX*	−78	BuLi	THF	*XVIII*	33·3	67·7	55
29[j]	*IV*	*IX*	−78	*X*	THF	*XIX*	8	92	33
30[j]	*IV*	*IX*	−78	BuLi	THF	*XIX*	20	80	57

[a] The aldehyde was added to the ylide at this temperature; [b] see Experimental; [c] isolated yield; [d] THF–HMPT mixture (3 : 1); [e] sonication 5 min at −78°C; [f] 0·9M solution of lithium 1,3-diaminopropane in 1,3-diaminopropane was used; [g] (10*Z*,12*E*)-isomer; [h] the inorganic salts were removed by centrifugation; [i] crystalline Wittig salt was used; [j] the ratio of isomers was determined by means of ^{1}H NMR spectroscopy.

where the butyllithium as a base was used and the high stereoselectivity was expected[7]. When the diethyl ether instead of tetrahydrofuran was used as a solvent the stereoselectivity was also low (11–13). Sonication of the reaction mixture led to the decrease of stereoselectivity and the same was observed when the diluted solution of lithium 1,3-diaminopropane was used (14, 15). The presence of insoluble inorganic salts when removed by means of centrifugation did not seem to have any effect on stereoselectivity (26). Using of alkyltriphenylphosphonium salts in crystaline state is more suitable (1–15, 27).



SCHEME 1

Our results summarized in Table I allowed us to suggest the influence of other factors on the course of the Wittig reaction. In lower alifatic and aromatic aldehydes (Scheme 1, R = methyl, ethyl, 4-tolyl) the reaction with high yield of *Z*-isomer was observed. When the aldehyde *IV* was used as a substrate, the GLC method of isomer separation failed (see ref.[11]), therefore the gross ratio of *E* and *Z* isomers was determined by interpretation of ^{1}H NMR spectra (29, 30). When (*E*)-2-butenal was used as a substrate there was practically no difference in composition of isomers considering the base used (22, 23), even when the decrease of stereoselectivity in similar cases was also reported[5].

The effect of alkyl group of alkyltriphenylphosphonium bromide i.e. the length and presence of ω-functional groups seems to be negligible (1, 16). Using the phosphonium salt *VIII* we obtained a product where the *E* isomer prevailed (24, 25).

This fact is not surprising because ylides (generated from *VIII*) are known to react *trans*-stereospecifically[14].

There is a very interesting effect depending on the cation used (*X*–*XII*). The highest stereoselectivity was obtained when lithium 1,3-diaminopropane as a base was used in contrary to the generally accepted theory. There is well known fact that the soluble lithium halogenides which are generated during the reaction decrease[4] "*erythro* (*cis*) selectivity of adduct forming step" affecting the final ratio of isomers in the product. One can hence accept an explanation that in our case the originated lithium salts solvated with 1,3-diaminopropane thus preventing the complex to interfere in the transition state.

We can conclude that 1,2-disubstituted olefins can be obtained with better then 95% *Z*-stereoselectivity when the reaction is performed in tetrahydrofuran at −78°C and when lithium 1,3-diaminopropane is used as a base. The reaction can be used i.a. for the synthesis of aliphatic unsaturated pheromones.

EXPERIMENTAL

^{1}H NMR spectra were measured on a spectrometer Varian XL-200 (200·01 MHz, FT mode) in deuterochloroform using tetramethylsilane as internal standard. Chemical shifts (in ppm) and coupling constants (in Hz) were determined by first-order analysis. The ^{1}H NMR data of *E*-isomers were obtained by the analysis of the mixture of isomers. IR spectra were taken on UR-20 spectrometer (Zeiss, Jena) in tetrachloromethane and the wave-numbers are given in cm^{-1}. Mass spectra were taken on a ZAB EQ (VG Great Britain, EI 70 eV) apparatus. For determination of *E* and *Z* isomers the HP 5890 GLC device was used (0·3 mm i.d. × 25 m fused silica column coated with HP-5 phase, nitrogen 0·3 ml/min). For dissolving of alkyltriphenylphosphonium salts the ultrasonic cleaner (TESLA UCOO5A1, 38 kHz, 35 W) was used. Separation of products was performed using column chromatography (Gebr. Herrmann silicagel, 60–160 μm, F.R.G.) and the fractions were checked using Silufol foils (Kavalier, Czechoslovakia) with subsequent $KMnO_4$ detection. All reactions and handlings were performed under dry argon. 1,3-Diaminopropane was dried by refluxing with benzene and then by distilling over calcium hydride. Lithium, sodium and potassium 1,3-diaminopropanes were prepared according to refs[13,16]. Butyllithium (1·6M solution in hexane) was a commercial product. Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl.

General Procedure for Preparation of Olefins

The alkyltriphenylphosphonium bromides were prepared according to ref.[12] and known amount of this compound was dried using 13 Pa vacuum at 100°C for 1 h just before use. This amount was then covered with tetrahydrofuran (3 ml), sonicated at room temperature until the all amount becomes an emulsion. To a stirred emulsion of alkyltriphenylphosphonium bromide (1 mmol) at −78°C and under argon, 2·7M solution of lithium, sodium or potasium 1,3-diaminopropane in 1,3-diaminopropane (2·17 mmol) was added dropwise during 15 min. During this time the orange color of yielding ylide appeared. The stirring was continued for 30 min at −78°C and then the reaction was warmed up to room temperature. After stirring at this temperature for 1 h the reaction mixture was cooled to the −78°C again and the solution of aldehyde (1 mmol) in tetrahydrofurane (3 ml) was added dropwise. After this the reaction mixture was warmed

up to 0°C (about 20—30 min) slowly decomposed with water (250 μl) and finally worked up by extraction with the mixture of light petroleum–ether (3 : 1), then brine and dried over magnesium sulfate. The compounds were chromatographed on silicagel (10 fold excess) using light petroleum–ether (3 : 1) as a mobil phase, and solvent evaporated. The products were dried using 13 Pa vacuum at 60°C for 30 min. Yields are given in Table I.

(*Z*)-1-(4-Methyl)phenyl-1-hexen (*XIII*)

For $C_{13}H_{18}$ (174·3) calculated: 89·59% C, 10·42% H; found: 89·32% C, 10·45% H. IR spectrum: 801, 816, 840, 3 010, 3 020, 3 085. Mass spectrum, *m/z*: 174 (M^+), 131 (100%), 118, 105, 91. ^{1}H NMR spectrum of (*Z*)-isomer: 0·89 t, 3 H (3 × H-6, $J(6, 5) = 7·1$); 1·23—1·52 m, 4 H (2 × H-5, 2 × H-4); 2·32 dq, 2 H (2 × H-3, $J(3, 1) = 2·0$; $J(3, 2) = J(3, 4) = 7·2$); 2·34 bs, 3 H (CH_3-arom.); 5·61 dt, 1 H (H-2, $J(2, 1) = 11·6$; $J(2, 3) = 7·2$); 6·35 dt, 1 H (H-1, $J(1, 2) = 11·6$; $J(1, 3) = 2·0$); 7·00 m, 4 H (4 × H-arom.). ^{1}H NMR spectrum of (*E*)-isomer: 0·92 t, 3 H (3 × H-6, $J(6, 5) = 7·1$); 1·30—1·53 m, 4 H (2 × H-4, 2 × H-5); 2·19 dq, 2 H (2 × H-3, $J(3, 1) = 1·0$; $J(3, 2) = J(3, 4) = 6·9$); 2·31 bs, 3 H (CH_3-arom.); 6·15 dt, 1 H (H-2, $J(2, 1) = 15·9$; $J(2, 3) = 6·6$); 6·34 bd, 1 H (H-1, $J(1, 2) = 15·9$); 7·05—7·26 m, 4 H (4 × H-arom.).

(*Z*)-11-(4-Methyl)phenyl-10-undecen-1-ol (*XIV*)

For $C_{18}H_{28}O$ (260·4) calculated: 83·02% C, 10·84H H; found: 82·94% C, 10·60% H. IR spectrum: 969, 1 056, 1 650, 3 050, 3 090, 3 640. Mass spectrum, *m/z*: 260 (M^+), 149, 131, 105, 82, 69, 55 (100%), 41. ^{1}H NMR spectrum of (*Z*)-isomer: 1·18—1·55 m, 14 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × H-7, 2 × H-8); 2·24 dq, 2 H (2 × H-9, $J(9, 10) = J(9, 8) = 7·2$; $J(9, 11) = 1·9$); 2·26 bs, 3 H (CH_3-arom.); 3·55 t, 2 H (2 × H-1, $J(1, 2) = 6·6$); 5·53 dt, 1 H (H-10, $J(10, 9) = 7·2$; $J(10, 11) = 11·8$); 6·28 dt, 1 H (H-11, $J(11, 9) = 1·9$; $J(11, 10) = 11·8$); 6·98—7·21 m, 4 H (4 × H-arom.). ^{1}H NMR spectrum of (*E*)-isomer: 1·18—1·55 m, 14 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × H-7, 2 × H-8); 2·11 bq, 2 H (2 × H-9, $J(9, 8) = J(9, 10) = 6·8$); 2·24 bs, 3 H (CH_3-arom.); 3·55 t, 2 H (2 × H-1, $J(1, 2) = 6·5$); 6·07 dt, 1 H (H-10, $J(10, 9) = 6·5$; $J(10, 11) = 15·8$); 6·27 bd, 1 H (H-11, $J(11, 10) = 15·8$); 6·98—7·21 m, 4 H (4 × H-arom.).

(*Z*)-10-Tridecen-1-ol (*XV*)

For $C_{13}H_{26}O$ (198·4) calculated: 78·72% C, 13·21% H; found: 77·32% C, 13·64% H. IR spectrum: 1 057, 1 070, 1 650, 3 010, 3 080, 3 640. Mass spectrum, *m/z*: 198 (M^+), 180, 165, 138, 124, 109, 96, 82 (100%), 68, 55. ^{1}H NMR spectrum of (*Z*)-isomer: 0·88 t, 3 H (3 × H-13, $J(13, 12) = 6·9$); 1·15—1·40 m, 14 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × H-7, 2 × H-8); 1·95 m, 4 H (2 × H-9 and 2 × H-12); 3·57 t, 2 H (2 × H-1, $J(1, 2) = 6·6$); 5·34 m, 2 H (H-10, H-11). ^{1}H NMR spectrum of (*E*)-isomer: 0·88 t, 3 H (3 × H-13, $J(13, 12) = 6·9$); 1·15 to 1·40 m, 14 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × H-7, 2 × H-8); 1·95 m, 4 H (2 × H-9, 2 × H-12); 3·57 t, 2 H (2 × H-1, $J(1, 2) = 6·6$); 5·27 m, 2 H (H-10, H-11).

(10*Z*,12*E*)-10,12-Tetradecadien-1-ol (*XVI*)

For $C_{14}H_{26}O$ (210·4) calculated: 79·94% C, 12·46% H; found: 79·76% C, 12·40% H. IR spectrum: 727, 950, 987, 1 656, 3 020, 3 640. Mass spectrum, *m/z*: 210 (M^+), 192, 163, 149, 135, 121, 110, 95, 68 (100%), 55. ^{1}H NMR spectrum: 1·24—1·32 m, 14 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × H-7, 2 × H-8, 1·56 m, 2 H (2 × H-2); 1·77 dd, 3 H (3 × H-14' $J(14, 12) = 1·6$; $J(14, 13) = 6·6$); 2·15 bq, 2 H (2 × H-9, $J(9, 8) = J(9, 10) = 7·3$); 3·64 t

2 H (2 × H-1, J(1, 2) = 6·5); 5·28 bdt, 1 H (H-10, J(10, 9) = 7·4; J(10, 11) = 11·0); 5·66 bdq, 1 H (H-13, J(13, 12) = 15·0, J(13, 14) = 6·6); 5·93 bt, 1 H (H-11, J(11, 10) = J(11, 12) = 11·0); 6·32 m, 1 H (H-12, J(12, 10) = 1·2; J(12, 11) = 11·0; J(12, 13) = 15·0; J(12, 14) = 1·6).

(*E*)-1-Trimethylsilyl-3-tetradecen-1-yn (*XVII*)

For $C_{17}H_{32}Si$ (264·5) calculated: 77·19% C, 12·19% H; found: 76·69H C, 11·91% H. IR spectrum: 855, 956, 2 138, 2 150, 2 180, 3 025, 3 312. Mass spectrum, *m/z*: 264 (M^+), 249, 190, 177, 163, 149, 135, 121, 107, 93, 79 (100%), 67. ^{1}H NMR spectrum: 0·18 s, 9 H ($(CH_3)_3Si$); 0·88 t, 3 H (3 × H-14, J(14, 13) = 6·5); 1·22—12·8 m, 16 H (2 × H-6, 2 × H-7, 2 × H-8, 2 × H-9, 2 × H-10, 2 × H-11, 2 × H-12, 2 × H-13); 2·10 bq, 2 H (2 × H-5, J(5, 3) = 1·6; J(5, 4) = = J(5, 6) = 6·9); 5·49 dt, 1 H (H-3, J(3, 5) = 1·6; J(3, 4) = 16·0); 6·22 dt, 1 H (H-4, J(4, 3) = = 16·0; J(4, 5) = 6·9).

(*Z*)-8-Decen-1-ol (*XVIII*)

For $C_{10}H_{20}O$ (156·3) calculated: 76·85% C, 12·90% H; found: 76·24% C, 12·45% H. IR spectrum: 705, 1 040, 1 105, 1 651, 3 080, 3 640. Mass spectrum, *m/z*: 156 (M^+), 138, 115, 109, 95, 82, 68, 55 (100%), 41. ^{1}H NMR spectrum: 1·24—1·28 m, 10 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5); 1·53 bd, 3 H (3 × H-10, J(10, 9) = 5·2); 2·01 m, 2 H (2 × H-7); 3·57 t, 2 H (2 × H-1, J(1, 2) = 6·5); 5·33 m, 2 H (H-8, H-9).

(*Z*)-8-Nonadecen-1-ol (*XIX*)

For $C_{19}H_{38}O$ (282·5) calculated: 80·78% C, 13·56% H; found: 80·62% C, 13·56% H. IR spectrum: 725, 1 050, 1 652, 3 010, 3 070, 3 640. Mass spectrum, *m/z*: 282 (M^+), 264, 236, 222, 208, 194, 180, 169, 152, 138, 109, 96, 82 (100%), 69, 55, 43. ^{1}H NMR spectrum: 0·89 t, 3 H (3 × H-19, J(19, 18) = 6·6); 1·25—1·29 m, 26 H (2 × H-2, 2 × H-3, 2 × H-4, 2 × H-5, 2 × H-6, 2 × 4 H-11, 2 × H-12, 2 × H-13, 2 × H-14, 2 × H-15, 2 × H-16, 2 × H-17, 2 × H-18); 2·03 bq, 4 H (2 × H-7, J(7, 6) = J(7, 8) and 2 × H-10, J(10, 9) = J(10, 11) = 6·6); 3·65 t, 2 H (2 × H-1, J(1, 2) = 6·6); 5·35 m, 2 H (H-8, H-9).

The authors are indebted to Prof. Dr H. J. Bestmann, University of Erlangen, F.R.G., for valuable discussion of this topic and Dr J. Smolíková, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences for interpretation of IR *spectra.*

REFERENCES

1. Bestmann H. J., Wostrovsky O., Platz H., Brosche Th., Koschatzky K. H., Knauf W.: Tetrahedron Lett. *1979*, 497.
2. Schlosser M., Tuong H. B., Schaub B.: Tetrahedron Lett. *26*, 311 (1985).
3. Camps F., Coll J., Guerrero A., Riba M.: J. Chem. Ecol. *9*, 869 (1983).
4. Schlosser M., Schaub B., Olivera-Netto J., Jeganathan S.: Chimia *40*, 244 (1986).
5. Schaub B., Jeganathan S., Schlosser M.: Chimia *40*, 246 (1986).
6. Mukhopadhayay T., Seebach D.: Helv. Chim. Acta *65*, 385 (1982).
7. Sonnet P. E.: Org. Prep. Proceed. Int. *6*, 269 (1974).
8. Bestmann H. J., Stransky W., Wostrovsky O.: Chem. Ber. *109*, 1694 (1974).
9. Ujvary I., Voigt E., Csutak J., Kis-Tamas A., Novak L.: Acta Phytopatol. Entomol. Hung. *23*, 235 (1988).

10. Bestmann H. J., Wostrovsky O.: Tetrahedron Lett. *1974*, 207.
11. Moiseenkov A. M., Schaub B., Margot Ch., Schlosser M.: Tetrahedron Lett. *26*, 305 (1985).
12. Schaub B., Blaser G., Schlosser M.: Tetrahedron Lett. *26*, 307 (1985).
13. Abrams S. R.: J. Can. Chem. *62*, 1333 (1984).
14. Corey E. J., Ruden R. A.: Tetrahedron Lett. *1973*, 1495.
15. Macaulay S. R.: J. Org. Chem. *45*, 734 (1980).

Translated by the author (L.S.).