Russian Journal of General Chemistry, Vol. 71, No. 6, 2001, pp. 977–978. Translated from Zhurnal Obshchei Khimii, Vol. 71, No. 6, 2001, pp. 1039–1040.

LETTERS TO THE EDITOR

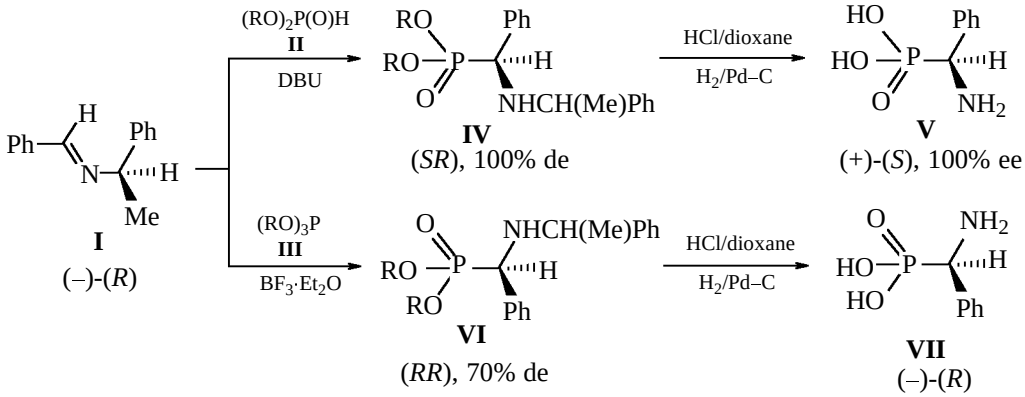
Double Asymmetric Induction in the Addition Reaction of Chiral Phosphites to C=N Compounds

O. I. Kolodyazhnyi and S. Yu. Sheiko

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, Kiev, Ukraine

Received August 3, 2000

We found that using two asymmetric inductors, instead of one, in the addition reaction of C=N compounds **I** and chiral phosphites **II, III** considerably favors a much more stereoselective reaction.



R = (1*S*,2*S*,5*R*)-2-menthyl, DBU = diazabicycloundecene.

Thus, addition of chiral hydrogen di[(1*R*,2*S*,5*R*)-2-menthyl] phospite (**II**) to chiral (*R*)-α-methylbenzylbenzaldimine (**I**) in the presence of a catalytic amount of diazabicycloundecene (DBU) results in a single diastereomer of *N*-substituted aminophosphonic diester **V**. The $^{31}P–\{^{1}H\}$ NMR analysis of crude crystalline reaction products revealed no second diastereomer. For comparison, similar reactions of chiral phospite **II** with achiral benzylbenzaldimine and of achiral diethyl hydrogen phosphite with chiral (*S*)-α-methylbenzylbenzaldimine result in a 30-45% diastereomeric excess of aminophosphonic diesters [1, 2].

Reaction of tri[(1*R*,2*S*,5*R*)-2-menthyl] phospite (**III**) with **I**, too, occurs with a much higher stereocontrol (up to 70%). Earlier we showed that the asymmetric induction of the reaction of chiral phosphite **III** with achiral benzylbenzaldimines is no more than 30–50% [3].

The configuration of the compounds was determined chemically. Initially, the menthyl groups were removed from the phosphorus atom by hydrolysis of the diesters with hydrochloric acid. Then the α-methylbenzyl group was eliminated under the action of gaseous hydrogen in the presence of palladium on carbon. As a result, monochiral stereoisomers **V** and **VII** were obtained, and their configuration was elucidated from a comparison of their optical rotation angles with those of earlier described *R*- and *S*-α-aminobenzylphosphonic acids [4].

We found that reaction of hydrogen di[(1*R*,2*S*,5*R*)-2-menthyl] phosphite (**II**) with (*R*)-α-methylbenzylbenzaldimine results in formation of (*S*)-α-aminobenzylphosphonic acid, while trimethyl phosphite with (*R*)-α-methylbenzylbenzaldimine gives (*R*)-α-aminobenzylphosphonic acid.

1070-3632/01/7106-0977 $25.00 © 2001 MAIK "Nauka/Interperiodica"

The reaction described in this communication is probably the first example of double asymmetric induction involving organophosphorus compounds. Of particular importance are the high yield of the reaction and the high optical purity of its products, which allows to preparation, on a multigram scale, of enaniomerically pure α-aminophosphonic acids without use of fractional crystallization or chromatography.

Di[(1*R*,2*S*,5*R*)-2-menthyl] (*RS*)-[(α-phenylethylamino)phenylmethyl]phosphonate (IV). Yield 80% (100% before crystallization), mp 128°C (acetone), $[\alpha]_D^{20}$ –68.0 (*c* 1, toluene). ^{31}P NMR spectrum ($CDCl_3$): δ_P 21.94 ppm. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.5 m (menthyl group), 0.75–1.05 m (18H, menthyl CH_3 groups), 1.28 d (3H, CH_3CH, J_{HH} 6.5), 1.0–2.0 m (16H, CH_2 + CH), 3.82 q (1H, $CHCH_3$, J_{HH} 6.4), 4.2 d (1H, CHP, J_{HP} 16.7), 4.3 m (1H, NH), 7.25 m (10H, C_6H_5). Mass spectrum (70 eV): *m/z* 568 (M^+). Found, %: P 5.34. $C_{35}H_{54}NO_3P$. Calculated, %: P 5.45.

Di[(1*R*,2*S*,5*R*)-2-menthyl] (*RR*)-[(α-phenylethylamino)phenylmethyl]phosphonate (VI). Yield 65%, mp 132.5°C (hexane), $[\alpha]_D^{20}$ –88.0 (*c* 1, toluene). ^{31}P NMR spectrum ($CDCl_3$): δ_P 22.05 ppm. Mass spectrum (70 eV): *m/z* 568 (M^+). Found, %: P 5.38. $C_{35}H_{54}NO_3P$. Calculated, %: P 5.45.

(*S*)-α-Aminobenzylphosphonic acid (III). Hydrochloride. Yield 90%, mp 226°C, $[\alpha]_D^{20}$ = +20 (*c* 0.32, 0.1 N aqueous NaOH). The product is similar to earlier described (–)-(*S*)-[(amino)phenylmethyl]phosphonic acid, $[\alpha]_D^{20}$ = –19 (*c* 1, 0.1 N aqueous NaOH) [4]. ^{1}H NMR spectrum (D_2O), δ, ppm: 7.28 s (5H, C_6H_5), 4.25 d (1H, PCH, J_{HP} 17 Hz).

(*R*)-α-Aminobenzylphosphonic acid (VII). Hydrochloride. Yield 90%, mp 226°C, $[\alpha]_D^{20}$ = +20 (*c* 0.32, 0.1 N aqueous NaOH). The product is similar to earlier described (+)-(*R*)-[(amino)phenymethyl]phosphonic acid, $[\alpha]_D^{20}$ = +19 (*c* 1, 0.1 N aqueous NaOH) [4]. ^{1}H NMR spectrum (D_2O), δ, ppm: 7.28 s (5H, C_6H_5), 4.25 d (1H, PCH, J_{HP} 17 Hz).

The NMR spectra were obtained on Varian (300 MHz) and JEOL (90 MHz) instruments in deuterated solvents, external reference 85% phosphoric acid (^{31}P NMR).

ACKNNOWLEDGMENTS

The work was financially supported by the Ukrainian Foundation for Basic Research (project no. 3.04/0188) and by the SPECS Ukrainian-Holland Joint-Stock Company.

REFERENCES

1. Kolodiazhnyi, O.I., *Tetrahedron: Asymmetry,* 1998, vol. 9, no. 8, pp. 1279–1332.
2. Kolodiazhnyi, O.I., Grishkun, E.V., Sheiko, S., Demchuk, O., Thoennessen, H., Jones, P., and Schmutzler, R., *Tetrahedron: Asymmetry,* 1998, vol. 9, no. 10, pp. 1645–1648.
3. Kolodiazhnyi, O.I., Sheiko, O., and Grishkun, E.V., *J. Heteroatom. Chem.,* 2000, vol. 11, no. 2, pp. 138–143.
4. Kafarski, P., Lejczak, B., and Szewczyk, J., *Can. J. Chem.,* 1983, vol. 61, p. 2425.