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## LETTERS TO THE EDITOR

# The First Example of Ni(II)-Catalyzed Asymmetric Addition of β-Oxophosphonate to Nitroalkene

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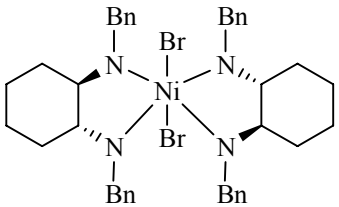
Polyfunctional chiral phosphonates are of interest as intermediates in the synthesis of bioactive molecules [1–5]. A possible approach to preparation of these compounds is asymmetric addition of β-oxophosphonates to nitroalkenes [6]. Earlier, we have shown that complexes of nickel [7], cobalt, and manganese [8] with chiral diamines are efficient catalysts for enantioselective addition of 1,3-dicarbonyl compounds to nitroalkenes. This reaction has been used as a key step in synthesis of chiral amino acids showing neurotropic activity [9], and of alicyclic polyfunctional derivatives [10].

Since the complex **I** is an efficient catalyst for asymmetric addition of 1,3-dicarbonyl compounds to nitroalkenes [9, 11], we expected its high activity in the similar reactions of β-oxophosphonates showing noticeable CH-acidity (Scheme 1).

In this work, the possibility of using complex **I** for catalysis of asymmetric addition of 2-oxophosphonates to nitroalkenes was studied.

Phosphonate **VI** was synthesized from bromoketone **II** via the Arbuzov reaction according to the Scheme 2.

**Scheme 1.**



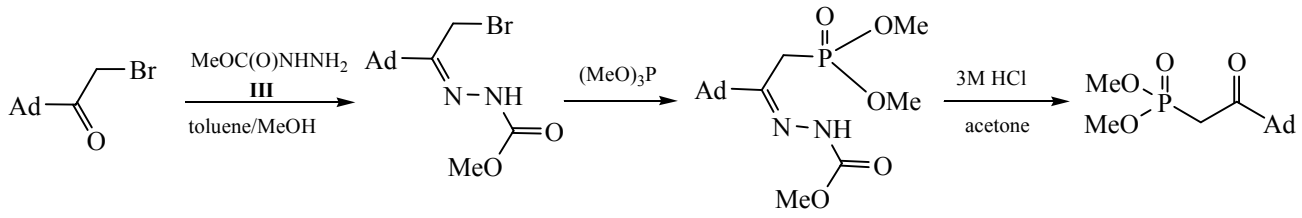
**I**

Protection of the carbonyl group in bromoketone **II** was necessary in order to eliminate the possibility of the side Perkov reaction [12] at the phosphonate synthesis stage. Subsequently, the protecting group was removed via acid hydrolysis of **V** in an aqueous-organic medium.

Reaction of 2-oxophosphonate **VI** with ω-nitrostyrene **VII** in the presence of chiral complex **I** led to formation of diastereomeric products **VIIIa** and **VIIIb** in a ratio of 1.2 : 1 (NMR) (Scheme 3).

According to the literature data on the stereoselective addition of 1,3-dicarbonyl compounds to ω-nitrostyrene [11] in the presence of complex **I**, we

**Scheme 2.**



**II** **IV** **V** **VI**

**Scheme 3.**


assumed that the asymmetric atom at position 2 in **VIII** could be assigned to *S*-configuration.

After chromatographic purification, phosphonate **VIIIa** was isolated with *de* 75.7%. Assignment of the signals of diastereomers **VIIIa** and **VIIIb** was made by comparing the NMR spectra of the isolated diastereomer **VIIIa** and of diastereomers mixture.

Relative configuration of compounds **VIIIa** and **VIIIb** was determined basing on the available data on the spin-spin coupling constant $^3J_{HH}$ of the methine groups of related phosphonates, their structures being independently established using X-ray diffraction [6]: 11.2 Hz for (*R*,*R*)- and 6.4 Hz for (*S*,*R*)-isomer. Hence, the isomer **VIIIb** could be attributed to (1*R*,2*S*)-configuration.

Compounds **I**–**III** were prepared according to the procedures [11, 13, 14], respectively.

**1-(1-Adamantyl)-2-bromoethanone methoxycarbonylhydrazone (IV).** A solution of 15.2 g (59.0 mmol) of bromoketone **II** and 4.10 g (45.5 mmol) of methylhydrazinecarboxylate **III** in 53 mL of toluene and 37 mL of methanol was stirred at room temperature for 5 h, and then incubated for at 0°C during 12 h. The resulting precipitate was filtered off, washed with 100 mL of diethyl ether, and dried. Yield 8.25 g (55%), mp 115–117°C. IR spectrum (KBr), ν, $cm^{-1}$: 2916, 2855, 1740, 1713, 1551, 1011. $^1$H NMR spectrum, δ, ppm: 1.65–1.75 m (6H, Ad), 1.80–1.85 m (6H, Ad), 2.00–2.07 m (3H, Ad), 3.82 s (2H, $CH_2$), 3.84 s (3H, $CH_3$), 8.03 s (1H, NH). $^{13}$C NMR spectrum, $\delta_C$, ppm: 17.38 ($CH_2$), 28.13 (CH, Ad), 36.59 ($CH_2$, Ad), 39.57 ($CH_2$, Ad), 40.83 (C, Ad), 53.14 ($CH_3$), 154.39 (C=O), 155.26 (C=N). Found, %: C 51.01; H 6.51; N 8.44. $C_{14}H_{21}BrN_2O_2$. Calculated, %: C 51.07; H 6.43; N 8.51.

***O*,*O*-Dimethyl[2-(1-adamantyl)-1-oxoethyl]phosphonate (VI).** 8.25 g (25.0 mmol) of hydrazone **IV** was added upon stirring under argon within 40 min to a boiling solution of 3.20 g (26.1 mmol) of trimethylphosphite in 25 mL of toluene. The mixture was stirred during 3 h, cooled, and washed with water. The organic layer was evaporated in vacuum. The aqueous layer was extracted with chloroform (3 × 50 mL). The combined organic layers were dried over calcium chloride. The solvent was evaporated in vacuum. The resulting phosphonate **V** (7.16 g, 80%) was further used without purification.

A mixture of 7.16 g (20 mmol) of **V** in 12 mL of acetone and 12 mL of 3 mol/L hydrochloric acid was stirred at room temperature for 3.5 h. Then acetone was evaporated in vacuum, and the residue was extracted with chloroform (3 × 50 mL). The extract was dried over calcium chloride and evaporated in vacuum. The reaction product was purified by chromatography (Kieselgel 60, eluent – chloroform). Yield 3.50 g (61%). IR spectrum (KBr), ν, $cm^{-1}$: 3456, 2909, 2854, 1697, 1450, 1250, 1033, 864, 810. $^1$H NMR spectrum, δ, ppm, (*J*, Hz): 1.57–1.68 m (6H, Ad), 1.70–1.75 m (6H, Ad), 1.97 br.s (3H, Ad), 3.06 d (2H, $CH_2$, $^2J_{HP}$ 21.6), 3.70 d (6H, $CH_3O$, $^3J_{HP}$ 11.0). $^{13}$C NMR spectrum, $\delta_C$, ppm: 27.77 s (CH, Ad), 34.39 d ($CH_2P$, $^1J_{CP}$ 136.0), 36,36 s ($CH_2$, Ad), 37,76 s ($CH_2$, Ad), 47.50 d (C, Ad, $^3J_{CP}$ 3.8), 52.96 d ($CH_3O$, $^2J_{CP}$ 4.8), 206.99 d (C=O, $^2J_{CP}$ 6.7). $^{31}$P NMR spectrum: $\delta_P$ 25.14 ppm. Mass-spectrum, *m*/*z* ($I_{rel}$): 286 (5) $[M]^+$, 258 (5), 151 (25), 135 (100) $[Ad]^+$, 125 (10), 109 (14), 93 (22), 79 (42), 67 (18), 55 (10). $M_{calc}$ 286.30. Found, %: C 58.64; H 8.16. $C_{14}H_{23}O_4P$. Calculated, %: C 58.73; H 8.10.

***O*,*O*-Dimethyl[1-(1-adamantylcarbonyl)-3-nitro-2-phenylpropyl]phosphonate (VIII).** 129 mg (0.16 mmol) of **I** was added to a solution of 2.30 g (8.00 mmol) of ketophosphonate **VI** and 1.30 g (8.80 mmol) of ω-nitrostyrene **VII** in 2 mL of toluene. The reaction mixture was incubated during 48 h at room temperature. Toluene was then evaporated in vacuum. The reaction product was purified by chromatography (Kieselgel 60, eluent – chloroform). Yield 1.75 g (49.0%), mp 88–90°C, $[\alpha]_D^{20}$ 10.48 (*c* 2.5, $CHCl_3$). IR spectrum (KBr), ν, $cm^{-1}$: 3050, 2916, 2855, 1690, 1547, 1253. $^1$H NMR spectrum, δ, ppm, (*J*, Hz):

(1*S*,2*S*)-(**VIIIa**), 1.49–1.66 m (12H, Ad), 1.93 br.s (3H, Ad), 3.63 d (3H, $CH_3O$, $^3J_{HP}$ 11.2), 3.67 d (3H, $CH_3O$, $^3J_{HP}$ 11.2), 4.15–4.25 m (2H, CHPh, CHP), 5.06 d (2H, $CH_2NO_2$, $^3J_{HH}$ 7.3), 7.10–7.35 m (5H, Ph); (1*R*,2*S*)-(**VIIIb**), 1.37 br.s (6H, Ad), 1.49–1.66 m (6H, Ad), 1.84 br.s (3H, Ad), 3.79 d (3H, $CH_3O$, $^3J_{HP}$ 11.2), 3.82 d (3H, $CH_3O$, $^3J_{HP}$ 11.2), 4.03 d. d (1H, CHP, $^2J_{HP}$ 18.3, $^3J_{HH}$ 11.0), 4.15–4.25 m (1H, CHPh), 4.85 m (1H, $CH_2NO_2$), 5.16 d. d (1H, $CH_2NO_2$, $^2J_{HH}$ 13.3, $^3J_{HH}$ 4.12), 7.10–7.35 m (5H, Ph). $^{13}C$ NMR spectrum, $\delta_C$, ppm: (1*S*,2*S*)-(**VIIIa**), 27.86 s (CH, Ad), 36.23 s ($CH_2$, Ad), 37.95 s ($CH_2$, Ad), 43.00 d (C, Ad, $^3J_{CP}$ 3.8), 47.96 s (CHPh), 49.60 d (CHP, $^1J_{CP}$ 126.5), 53.06 d ($CH_3O$, $^2J_{CP}$ 8.6), 53.98 d ($CH_3O$, $^2J_{CP}$ 8.6), 78.02 s ($CH_2NO_2$), 128.00 s ($C^2$, Ph), 128.36 s ($C^4$, Ph), 129.06 s ($C^3$, Ph), 137.50 d ($C^1$, Ph, $^3J_{CP}$ 11.5), 211.17 d (C=O, $^2J_{CP}$ 4.8); (1*R*,2*S*)-(**VIIIb**), 27.86 s (CH, Ad), 36.23 s ($CH_2$, Ad), 37.82 s ($CH_2$, Ad), 43.72 d (C, Ad, $^3J_{CP}$ 3.8), 47.41 s (CHPh), 49.44 d (CHP, $^1J_{CP}$ 124.6), 53.47 d ($CH_3O$, $^2J_{CP}$ 12.4), 54.00 d ($CH_3O$, $^2J_{CP}$ 12.4), 78.02 s ($CH_2NO_2$), 128.00 s ($C^2$, Ph), 128.44 s ($C^4$, Ph), 128.97 s ($C^3$, Ph), 137.27 d ($C^1$, Ph, $^3J_{CP}$ 16.3), 209.76 d (C=O, $^2J_{CP}$ 4.8). $^{31}P$ NMR spectrum, $\delta_P$, ppm: 22.78 [(1*S*,2*S*)-(**VIIIa**)], 23.39 [(1*R*,2*S*)-(**VIIIb**)]. Found, %: C 60.59; H 7.01; N 3.18. $C_{22}H_{30}NO_6P$. Calculated, %: C 60.68; H 6.94; N 3.22.

NMR spectra were recorded with a JEOL JNM ECX-400 (400 MHz) spectrometer in $CDCl_3$. IR spectra were recorded with a Schimadzu IR Affinity-1 spectrometer (KBr pellets). Mass spectra were obtained using a Finnigan Trace DCQ gas chromatography–mass spectrometer with a BPX-5 SGE capillary column (30 × 0.32) at 70 eV (EI). Elemental analysis was performed with a Euro Vector EA-3000 analyzer. Optical rotation angles were measured with a Rudolph Research Analytical Autopol V Plus automatic polarimeter.

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