Monatsh Chem (2011) 142:753–754
DOI 10.1007/s00706-011-0529-z

ORIGINAL PAPER

Reactions of mercaptobenzimidazole with allenylphosphonates

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Received: 30 March 2011 / Accepted: 16 May 2011 / Published online: 16 June 2011

Abstract Reactions of 2-mercaptobenzimidazole with 3-methylbuta-1,2-dienylphosphonates involve the mercapto group of the heterocyclic compound and the 1,2-double bond of allenylphosphonate.

Keywords Heterocycles · Allenes · Phosphorus compounds · Nucleophilic additions · 3-Methylbuta-1,2-dienylphosphonates

Introduction

Benzimidazole and its derivatives represent an important class of core structures in pharmaceutical compounds [1–3]. Introduction of different functional groups into these compounds leads to modification of their biological activity. Functional derivatives of benzimidazole with a phosphoryl group are of special interest. Thus, the usage of phosphonates as antibacterial, antiviral, antiretroviral, and chemotherapeutic agents is well documented [4–8]. Earlier we found that the reaction of imidazole with 3-methylbuta-1,2-dienylphosphonates or vinylphosphonates proceeds with formation of products of the addition of the ring N atom to the β-carbon atoms of the unsaturated substrate [9]. Besides we have shown that the reaction of 2-aminobenzothiazole with 3-methylbuta-1,2-dienylphosphonate also involves the endocyclic N atom of the heterocyclic compound and the 1,2-double phosphonate bond, not the exocyclic amino group [10].

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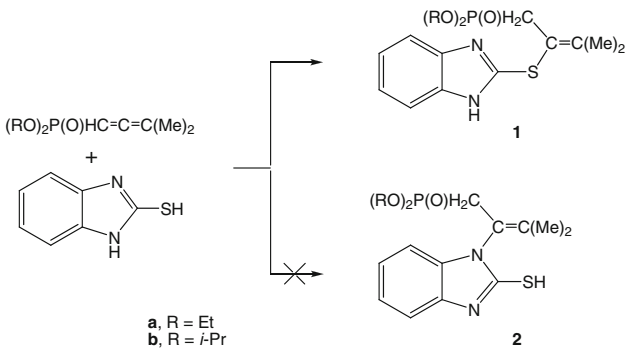
Results and discussion

We investigated the reactions of 2-mercaptobenzimidazole with 3-methylbuta-1,2-dienylphosphonates. Two pathways are possible for this reaction: the central C atom of the allene system could be attacked by the ring N atom (adduct **2**) or the S atom of the exocyclic mercapto group (adduct **1**) (Scheme 1).

Heating of an equimolar mixture of the starting materials gave a crystalline product in each case. The IR spectra of the adducts lack a cumulated double bond absorption band (1,960 cm^{-1}). The ^{31}P NMR spectra of the adducts in solution show a single intense signal. The ^{1}H NMR spectra of the adducts contain doublets for the protons of two methyl groups attached to an sp^2-hybridized C atom; a signal at approximately 3.0 ppm ($^{2}J_{PH} = 21$ Hz) for protons of a methylene group α to the phosphoryl fragment; and no signal



Scheme 1

for an SH proton (at 2.6 ppm for 2-mercaptobenzimidazole). Thus, the addition of 2-mercaptobenzimidazole to 3-methylbuta-1,2-dienylphosphonates takes place via the attack of the nucleophilic mercapto group of the heterocyclic compound on the 1,2-double bond of the phosphonate (adduct **1**).

Experimental

The IR spectra were recorded on a UR-20 spectrometer. The ^{1}H and ^{31}P NMR spectra were registered on a Varian-Unity-300 spectrometer (300 and 121.42 MHz) in $CDCl_3$. The ^{13}C NMR spectra were recorded on a Bruker-Evans-500 instrument (126 MHz) in acetone-d_6. The ^{1}H and ^{13}C NMR chemical shifts were measured relative to the signals of the residual protons of the deuterated solvents. The ^{31}P NMR chemical shifts were measured relative to 85% H_3PO_4 as the external standard. Elemental analyses (C, H) were performed using a Perkin-Elmer CHNS/O 2400 apparatus; the results were in favorable agreement with the calculated values.

General procedure for reaction of 2-mercaptobenzimidazole with 3-methylbuta-1,2-dienylphosphonates

2-Mercaptobenzimidazole (1.5 g, 0.01 mol) was added to 0.01 mol 3-methylbuta-1,2-dienylphosphonate. The reaction mixture was heated at 80–95 °C for 8 h. The resulting crystals were separated by decantation, washed repeatedly with ether, and dried in vacuo.

Diethyl 2-(1H-benzimidazol-2-ylthio)-3-methyl-2-butenylphosphonate (**1a**, $C_{16}H_{23}N_2O_3PS$)
Compound **1a** was obtained in 53% yield (1.88 g). M.p.: 125–126 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.34$ (t, $^{3}J_{HH} = 7.0$ Hz, 6H, CH_3), 1.54 (d, $^{5}J_{PH} = 8.3$ Hz, 3H, CH_3–C=), 1.97 (d, $^{5}J_{PH} = 5.2$ Hz, 3H, CH_3–C=), 3.13 (d, $^{2}J_{PH} = 20.9$ Hz, 2H, PCH_2), 4.16 (m, 4H, CH_2O–), 7.20 (d, 2H, $^{2}J_{HH} = 9.1$ Hz, Ar), 7.57 (d, 2H, $^{2}J_{HH} = 9.1$ Hz, Ar) ppm; ^{13}C NMR (126 MHz, $(CD_3)_2CO$): $\delta = 16.32$ (d, $^{3}J_{C,P} = 5.8$ Hz, 2 × CH_3CH_2O–), 23.03, 24.32 [$(CH_3)_2C$=], 36.15 (d, $^{1}J_{C,P} = 139.1$ Hz, –CH_2–P), 62.38 (d, $^{2}J_{C,P} = 7.1$ Hz, 2 × –CH_2O–), 110.31, 122.60, 133.42, 170.85 (benzimidazole), 115.24 (*C*=C–S), 123.38 (C=*C*–S) ppm; ^{31}P NMR (121.42 MHz, $CDCl_3$): $\delta = 28.6$ ppm; IR (KBr): = 3,240 (NH), 1,620 (C=C), 1,246 (P=O) cm^{-1}.

Diisopropyl 2-(1H-benzimidazol-2-ylthio)-3-methyl-2-butenylphosphonate (**1b**, $C_{18}H_{27}N_2O_3PS$)
Compound **1b** was obtained in 60% yield (2.29 g). M.p.: 115 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.28$ (d, $^{3}J_{HH} = 6.0$ Hz, 6H, CH_3), 1.35 (d, $^{3}J_{HH} = 6.0$ Hz, 6H, CH_3), 1.90 (d, $^{5}J_{PH} = 5.2$ Hz, 3H, CH_3–C=), 1.92 (d, $^{5}J_{PH} = 7.8$ Hz, 3H, CH_3–C=), 3.02 (d, $^{2}J_{PH} = 21.0$ Hz, 2H, PCH_2), 4.75 (dsept, $^{3}J_{HH} = 6.0$ Hz, $^{3}J_{PH} = 8.0$ Hz, 2H, P–OCH), 7.15–7.21 (m, 4H, Ar) ppm; ^{13}C NMR [126 MHz, $(CD_3)_2CO$]: $\delta = 23.01$, 24.30 [$(CH_3)_2C$=], 24.16, 24.28 (d, $^{3}J_{C,P} = 5.0$ Hz, 2 × $(CH_3)_2CHO$–), 36.16 (d, $^{1}J_{C,P} = 138.7$ Hz, P–CH_2–), 71.49 (d, $^{2}J_{C,P} = 7.5$ Hz, 2 × $(CH_3)_2CHO$–), 110.30, 122.60, 133.42, 170.85 (benzimidazole), 115.22 (*C*=C–S), 123.36 (C=*C*–S) ppm; ^{31}P NMR (121.42 MHz, $CDCl_3$): $\delta = 27.1$ ppm.

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