ISSN 1070-4280, Russian Journal of Organic Chemistry, 2015, Vol. 51, No. 7, pp. 943–946. © Pleiades Publishing, Ltd., 2015. Original Russian Text © E.A. Ishmaeva, A.Z. Alimova, Ya.A. Vereshchagina, D.V. Chachkov, O.I. Artyushin, E.V. Sharova, 2015, published in Zhurnal Organicheskoi Khimii, 2015, Vol. 51, No. 7, pp. 963–966.

Synthesis, Polarity, and Structure of 2-Chloro-*N*-[2-(methylsulfanyl)phenyl]- and 2-(Diphenylthiophosphoryl)-*N*-[2-(methylsulfanyl)phenyl]acetamides

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Received March 11, 2015

Abstract—Conformations of 2-chloro-*N*-[2-(methylsulfanyl)phenyl]- and 2-(diphenylthiophosphoryl)-*N*-[2-(methylsulfanyl)phenyl]acetamides have been studied by the dipole moment method and quantum chemical calculations. 2-(Diphenylthiophosphoryl)-*N*-[2-(methylsulfanyl)phenyl]acetamide has been found to exist as an equilibrium mixture of two conformers with *synclinal* and *anticlinal* orientations of the C_{sp3} — C_{sp2} and P=S bonds. 2-Chloro-*N*-[2-(methylsulfanyl)phenyl]acetamide is represented by one preferred conformer.

DOI: 10.1134/S107042801507009X

(Carbamoylmethyl)phosphine oxides are universal bidentate ligands with a broad range of practical applications, e.g., in the radioactive waste processing [1]. Less common thiophosphoryl analogs of (carbamoylmethyl)phosphine oxides [2], as well as P(X)-modified (carbamoylmethyl)phosphine oxides and sulfides having a third coordination site (e.g., P=S group) [3], are more appropriate ligand for the complexation and purification of thiophiles (Ag, Pd, Pt, etc.). We have synthesized a new complexing agent of this sort, a thiophosphoryl analog of (arylcarbamoylmethyl)phosphine oxides having a methylsulfanyl group in the benzene ring, and studied its structure in solution.

Conformational analysis of 2-aminophenyl-, 2-aminobenzyl-, and 2-nitrobenzyl(diphenyl)phosphine oxides by the dipole moment, vibrational spectroscopy, and quantum chemical methods [4] has



shown that phosphine oxide derivatives with a primary amino group exist as only one conformer with intramolecular hydrogen bond.

In the present work we performed conformational analysis of *N*-[2-(methylsulfanyl)phenyl]acetamides **1** and **2** by the dipole moment method and DFT quantum chemical calculations with the B3PW91, wB97XD and M06 functionals and 6-311++G(df,p) basis set. The experimental dipole moments of compounds **1** and **2** were determined by the second Debye method (Table 1). The coefficients of equations used in the calculations and orientational polarizations are also given. The structures of most favorable conformers of **1** and **2** are shown in figure. The theoretical dipole moments of the energetically preferred conformers of **1** and **2** and

 Table 1. Coefficients of equations used in the calculations, orientational polarizations, and experimental dipole moments of compounds 1 and 2

| Comp. no. | α | γ | $P_{\rm or.},{\rm cm}^3$ | μ, D |
|-----------|-------|-------|--------------------------|------|
| 1 | 4.669 | 0.187 | 181.968 | 2.97 |
| 2 | 3.696 | 0.425 | 224.762 | 3.37 |



Structures of the most stable conformers of compounds 1 and 2 according to DFT quantum chemical calculations (some hydrogen atoms are not shown).

their relative energies were calculated by the above listed quantum chemical methods, and the dipole moments of these conformers were calculated by the vector addition method (Table 2).

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According to the calculations, the most favorable conformer of **1** is **1A** ($\Delta E = 0.0 \text{ kJ/mol}$) where the S–CH₃ bond is orthogonal to the benzene ring plane (the dihedral angle CCSCH₃ is 93°) and the planar NHC(O)CH₂Cl fragment lies almost in that plane (CCNC 4°). This conformer features a nonclassical C–H···O contact between the 6-H hydrogen atom and carbonyl oxygen atom; the H····O distance is 2.20 (B3PW91) or 2.22 Å (wB97XD, M06,). The relative energies of other possible conformers of **1** are higher than 25 kJ/mol. The experimental dipole moment of **1** is slightly larger than the theoretical one (Tables 1, 2), whereas the dipole moment calculated by the vector addition method is very consistent with the experimental value.

Two stable conformers, **2A** and **2B** were found for amide **2** by quantum chemical calculations. As in **1A**, the S–CH₃ bond in **2A** and **2B** is also orthogonal to the benzene ring plane (the corresponding dihedral angles CCSC are 99 and 90°, respectively), and the NHC(O) CH₂ fragment is planar. The NHC(O)CH₂ fragment in **2A** deviates from the benzene ring plane to form a dihedral angle CCNC of 19°, the phenyl substituents are oriented *gauche* and *cis* with respect to the P=S bond (CCPS 37 and 13°), and the $C_{sp^3}-C_{sp^2}$ bond is *gauche* with respect to the latter ($C_{sp^3}C_{sp^2}PS$ 71°). The NHC(O)CH₂ fragment in conformer **2B** lies almost in the benzene ring plane (CCNC_{sp2} 3°); the phenyl substituents on the phosphorus are oriented *gauche* and *cis* with respect to the P=S bond (CCPS 33 and 21°), while the $C_{sp^3}-C_{sp^2}$ bond is oriented *trans* ($C_{sp^3}C_{sp^2}PS$ 151°).

Conformer **2A** turned out to be the most stable according to the B3PW91/6-311++G(df,p) calculations, and the energy of **2B** was slightly higher. Analysis of the μ_{calc} values suggests conformational equilibrium of **2A** and **2B** in solution at a ratio of 80:20. However, wB97XD/6-311++G(df,p) calculations showed conformer **2B** to be preferred. Therefore, the results were verified by the M06/6-311++G(df,p) calculations which confirmed the wB97XD data. In any case, the energy difference between conformers **2A** and **2B** is fairly small, so that conformational equilibrium between **2A** and **2B** in solution is quite possible.

Unlike conformer **2A**, two C–H···O contacts between *ortho*-hydrogen atoms of two benzene rings and carbonyl oxygen atom were observed in conformer **2B**; the H···O distances are 2.20 and 2.22 Å (B3PW91) or 2.20 and 2.26 Å (wB97XD, M06).

Thus, 2-(diphenylthiophosphoryl)-*N*-[2-(methylsulfanyl)phenyl]acetamide (1) is conformationally het-

Table 2. Relative energies (ΔE , kJ/mol) of the most stable conformers of compounds 1 and 2 and their theoretical dipole moments (μ_{theor} , D) and dipole moments calculated by the vector addition method (μ_{calc} , D)

| Conformer | B3PW91/6-311++G(<i>df</i> , <i>p</i>) | | wB97XD/6-311++G(<i>df</i> , <i>p</i>) | | M06/6-311++G(<i>df</i> , <i>p</i>) | | |
|-----------|---|---------------|---|---------------|--------------------------------------|---------------|--------------|
| | ΔE | μ_{theor} | ΔE | μ_{theor} | ΔE | μ_{theor} | μ_{calc} |
| 1A | 0.0 | 1.85 | 0.0 | 1.44 | 0.0 | 1.49 | 2.98 |
| 2A | 0.0 | 3.24 | 10.7 | 3.48 | 6.6 | 3.44 | 2.61 |
| 2B | 2.9 | 4.07 | 0.0 | 4.25 | 0.0 | 3.77 | 5.36 |

erogeneous, and it exists as an equilibrium mixture of *synclinal* and *anticlinal* conformers. 2-Chloro-*N*-[2-(methylsulfanyl)phenyl]acetamide (1), like 2-amino-phenyl(diphenyl)phosphine oxide [4], exists as a single conformer.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Magna IR750 spectrometer. The ¹H, ³¹P, and ¹³C NMR spectra were measured on Bruker AV-300 and AV-400 spectrometers from solutions in CDCl₃. 2-(Methylsulfanyl)-aniline was commercial product (Aldrich). Compounds **1** and **2** were synthesized according to procedures analogous to those reported by us previously [3].

2-Chloro-N-[2-(methylsulfanyl)phenyl]acetamide (1). A mixture of 1.39 g (0.01 mol) of 2-(methylsulfanyl)aniline and 1.01 g (0.01 mol) of triethylamine in 10 mL of chloroform was cooled to -20°C, and 1.13 g (0.01 mol) of chloroacetyl chloride was added dropwise under stirring. The mixture was stirred for 2 h at -20°C, 20 mL of 5% aqueous HCl was added, the organic layer was separated, and the aqueous layer was extracted with 5 mL of chloroform. The extracts were combined with the organic phase, dried over Na₂SO₄, and evaporated under reduced pressure, and the residue was subjected to silica gel chromatography using hexane-methylene chloride (5:3) as eluent. Yield 1.57 g (73%), mp 54-55°C. IR spectrum (KBr), v, cm⁻¹: 3239 (NH), 3205, 1670 (C=O), 1538, 1443, 1407, 1271, 751. ¹H NMR spectrum, \delta, ppm: 9.52 br.s (1H, NH), 8.31 d.d (1H, 6-H, ${}^{3}J = 8.0, {}^{4}J = 1.0 \text{ Hz}$, 7.51 d.d (1H, 3-H, ${}^{3}J = 7.8, {}^{4}J = 1.0 \text{ Hz}$), 7.32 d.t (1H, 5-H, ${}^{3}J = 7.3, {}^{4}J = 1.0 \text{ Hz}$), 7.12 d.t (1H, 4-H, ${}^{3}J = 7.5$, ${}^{4}J = 1.0$ Hz), 4.24 s (2H, CH₂Cl), 2.40 s (3H, CH₃S). ¹³C NMR spectrum, δ_{C} , ppm: 163.86 s (C=O), 137.27 s (C¹), 133.04 s (C⁶), 128.85 s (C³), 126.10 s (C²), 125.05 s (C⁵), 120.18 s (C⁴), 43.20 s (CH₂Cl), 18.69 s (CH₃S). Found, %: C 50.21; H 4.67; N 6.47; S 14.97. C9H10CINOS. Calculated, %: C 50.12; H 4.67; N 6.49; S 14.86.

2-(Diphenylphosphorothioyl)-N-[2-(methylsulfanyl)phenyl]acetamide (2). Sodium hydride, 0.12 g (5 mmol; 60% suspension in oil), was added at 0°C to a solution of 1.09 g (5 mmol) of diphenylphosphine sulfide in 20 mL of THF, and the mixture was stirred for 30 min until hydrogen no longer evolved. A solution of 1.08 g (5 mmol) of chloroacetamide 1 in 10 mL of THF was added at 0°C to the resulting transparent solution. The cooling bath was removed, and the mixture was stirred for 24 h at 20°C. The solvent was distilled off, 30 mL of methylene chloride and 10 mL

of water were added to the residue, the organic phase was separated and dried over Na₂SO₄, the solvent was removed under reduced pressure, and the residue was recrystallized from methanol. Yield 1.50 g (76%), mp 141–142°C. IR spectrum (KBr), v, cm⁻¹: 3241, 3052, 2963, 1647 (C=O), 1521, 1526, 1438, 1435, 1308, 1099, 748, 692. ¹H NMR spectrum, δ, ppm: 9.40 br.s (1H, NH), 7.98 d.d (1H, 6-H, ${}^{3}J = 8.0, {}^{4}J =$ 1.3 Hz), 7.87–7.94 m (4H, *m*-H), 7.44–7.56 m (6H, o-H, p-H), 7.42 d.d (1H, 3-H, ${}^{3}J = 7.7$, ${}^{4}J = 1.3$ Hz), 7.18 d.t (1H, 5-H, ${}^{3}J = 7.8$, ${}^{4}J = 1.3$ Hz), 7.05 d.t (1H, 4-H, ${}^{3}J = 7.6$, ${}^{4}J = 1.4$ Hz), 3.73 d (2H, PCH₂, ${}^{2}J_{PH} =$ 14.0 Hz), 2.35 s (3H, CH₃S). ¹³C NMR spectrum, δ_{C} , ppm: 162.63 d (C=O, ${}^{2}J_{PC} = 4.7$ Hz), 137.57 s (C¹), 132.15 s (C⁶), 131.97 d (C^{*p*}, ${}^{4}J_{PC} = 3.3$ Hz), 131.40 d $(C^{i}, {}^{1}J_{PC} = 83.6 \text{ Hz}), 131.08 \text{ d} (C^{m}, {}^{3}J_{PC} = 11.0 \text{ Hz}),$ $128.75 \text{ d} (\text{C}^{o}, {}^{2}J_{\text{PC}} = 14.0 \text{ Hz}), 127.91 \text{ s} (\text{C}^{3}), 127.54 \text{ s}$ (C^2) , 124.91 s (C^5) , 121.63 s (C^4) , 44.02 d $(PCH_2, {}^{1}J_{PC} = 45.1 \text{ Hz})$, 18.93 s (CH_3S) . ³¹P NMR spectrum: δ_P 37.40 ppm, s. Found, %: C 63.71; H 5.07; N 3.59; P 7.73; S 16.23. C₂₁H₂₀NOPS₂. Calculated, %: C 63.45; H 5.07; N 3.52; P 7.79; S 16.13.

The dielectric permittivities of dilute solutions of 1 and 2 in benzene were determined at 25°C on a BI-870 instrument (Brookhaven Instruments) with an accuracy of ± 0.01 . The refractive indices of these solutions were measured with an accuracy of ± 0.0001 using an RA-500 refractometer (Kyoto Electronics). The dipole moments were calculated by the vector addition method on the basis of geometric parameters determined by quantum chemical calculations; the following bond and group moments were used: m(P=>S) 3.29 D (calculated from μ_{exp} of PhP=S [5]), $m(C_{sp3} \rightarrow P)$ 0.83 D [5], $m(Ph \rightarrow P)$ 1.09 D [6], m(C=>O) 1.94 D [6], $m(C_{sp3} \rightarrow Cl)$ 1.58 D (calculated from μ_{exp} of MeCl [7]), $m(N \rightarrow H)$ 1.31 D (calculated from μ_{exp} of NH₃ [7]), $m(C_{arom} \rightarrow N)$ 2.12 D (calculated from μ_{exp} of PhNH₂ [7]), $m[N \rightarrow C_{sp2}(O)]$ 0.94 D (calculated from μ_{exp} of MeC(O)NH₂ [7]), $m(CH_3 \rightarrow S)$ 1.14 D (calculated from μ_{exp} of Me₂S [7]), $m(C_{arom} \rightarrow S)$ 0.30 D (calculated from μ_{exp} of PhSH [7]), $m(H \rightarrow C_{sp3})$ 0.28 D [8], $m(H \rightarrow C_{sp2})$ 0.7 D [8].

Quantum chemical calculations were performed at the Kazan Branch, Joint Supercomputer Center, Russian Academy of Sciences (*http://wt.knc.ru*) using GAUSSIAN 09 software package [9] with full geometry optimization. In all cases, stationary points were identified as energy minima by calculating second derivatives.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 13-03-00067a).

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