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New phosphonium salts based on 3-(diphenylphosphino)propanoic and ω-haloalkanoic acids

Semyon R. Romanov,*[a] Yana V. Dolgova,[a] Maxim V. Morozov,[a] Kamil A. Ivshin,[b] Dmitriy A. Semenov,[c] Yulia V. Bakhtiyarova,[a] Irina V. Galkina,[a] Olga N. Kataeva[b] and Vladimir I. Galkin[a]

[a] *A. M. Butlerov Institute of Chemistry, Kazan Federal University, 420008 Kazan, Russian Federation. E-mail: semyonromanov@yandex.ru*

[b] *A. E. Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of the Russian Academy of Sciences, 420088 Kazan, Russian Federation*

[c] *Elabuga Institute, Kazan Federal University, 423600 Elabuga, Russian Federation*

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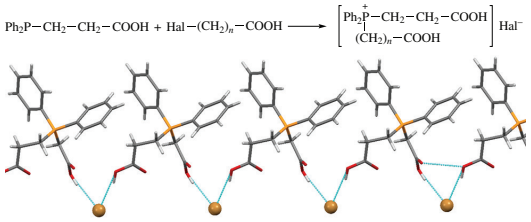
Quarternization of 3-(diphenylphosphino)propanoic acid with ω-haloalkanoic acids affords novel phosphonium salts containing two carboxy groups. The phosphonium salts were treated with 1 M alkali solution to obtain corresponding carboxylate phosphabetaines. The structure of the compounds was established by IR and NMR spectroscopy, elemental analysis and X-ray single crystal diffraction.



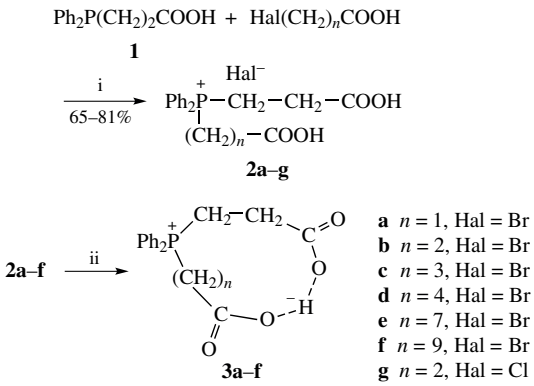
Keywords: 3-(diphenylphosphino)propanoic acid, phosphonium salts, carboxylic acids, phosphabetaines, crystal structure.

The chemistry of phosphonium salts and carboxylate phosphabetaines attracts attention owing to their wide application. Phosphonium salts are used as ionic liquids,[1–3] separation agents of rare-earth metals[4] and catalysts;[5,6] they demonstrate high antimicrobial activity[7–9] and possess anticancer activity.[10–12] Carboxylate phosphabetaines, analogues of amino acids, are suitable ligands for metal complexes,[13,14] can be used as bifunctional catalysts[15] and difluoromethylation agents.[16] Zwitterionic structures in recent years have been actively employed in hemodialysis membranes.[17–19]

In the last few years, our group has explored the synthesis, structure and reactivity of phosphonium salts and carboxylate phosphabetaines. Along with nucleophilic addition of tertiary phosphines at unsaturated carboxylic acids,[20,21] the nucleophilic substitution of triphenylphosphine to ω-haloalkanoic acids was found to be good synthetic strategy.[22] Within the framework of this study, we were interested in moving to another tertiary phosphine, namely, 3-(diphenylphosphino)propanoic acid **1**. Along with the tertiary phosphorus atom, this compound contains the carboxy group, so its reactions with ω-haloalkanoic acids should afford phosphonium salts bearing two carboxy groups. Elongation of polymethylene spacer in ω-haloalkanoic acids should also provide long-chained derivatives generally known for improved antimicrobial activity.

In fact, quaternization of phosphine **1** with ω-bromoalkanoic acids in MeCN at 80 °C for 10 h afforded stable at room temperature phosphonium salts **2a–f** in yields from 74 to 81% (Scheme 1, Table 1).

Compounds **2a–c** are crystalline substances while homologues **2d–f** are oils at room temperature (see Table 1). The structure of the synthesized compounds was unambiguously proved by IR, ^{1}H, ^{13}C, ^{31}P NMR spectroscopy and elemental analysis. In their ^{31}P NMR spectra, single phosphorus signals were observed corresponding to the obtained phosphonium salts. According to



Scheme 1 *Reagents and conditions*: i, MeCN, 80 °C, 10 h; ii, NaOH, MeCN, room temperature.

Table 1 Selected characteristics of prepared phosphonium compounds **2a–g**.[a]

Compound	Haloalkanoic acid applied	ν(COOH)/ cm^{-1}	^{31}P NMR, δ (D_2O)	mp/°C	Yield (%)
2a	$BrCH_2COOH$	1720	25.27	210–212	80
2b	$Br(CH_2)_2COOH$	1720	27.42	180–182	81
2c	$Br(CH_2)_3COOH$	1720	27.2	119–120	77
2d	$Br(CH_2)_4COOH$	1715	27.2	oil	79
2e	$Br(CH_2)_7COOH$	1715	26.8	oil	74
2f	$Br(CH_2)_9COOH$	1715	26.9	oil	78
2g	$Cl(CH_2)_2COOH$	1736	27.2	186–189	65

[a] For synthetic details and full NMR data, see Online Supplementary Materials.

IR spectroscopy, all products had absorption bands in the region of 1715–1735 cm^{-1} corresponding to two carboxyl groups of phosphonium salts **2a–f**. The structure of representative **2a** was

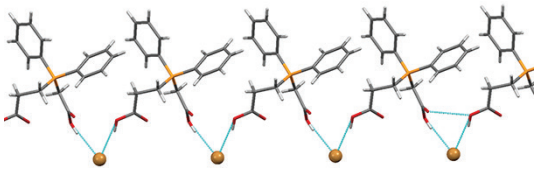


Figure 1 A fragment of crystal packing of (2-carboxyethyl)(carboxymethyl)diphenylphosphonium bromide **2a** showing hydrogen bonds of carboxy groups with bromine anions.

investigated by single crystal X-ray diffraction.† Phosphonium cations form one-dimensional hydrogen-bonded chains in which carboxy groups interact with bromine anions (Figure 1).

The similar reactions of phosphino acid **1** with ω-chloroalkanoic acids proceeded essentially slower. Only in the case of 3-chloropropanoic acid after 20 h of processeing the corresponding phosphonium salt **2g** was obtained in 65% yield (see Scheme 1 and Table 1). In cases of higher ω-chloroalkanoic acids the reaction rate was even lower, and the corresponding phosphine oxide was formed as the by-product. According to ^{31}P NMR spectroscopy data, after heating the mixture of phosphino acid **1** and 4-chlorobutyric acid for 45 h the conversion of **1** approached 50% with the formation of phosphonium salt (40%) and phosphine oxide (9%). In the case of 5-chlorovaleric acid, 50 h processing provided only 20% conversion while the ratio between the phosphonium salt and phosphine oxide was 1 : 1. After prolonged standing at room temperature for several months, the percentage of reactant **1** in these reactions decreased slightly. The ^{31}P NMR monitoring of these processes is outlined in Online Supplementary Materials (Figures S15 and S16).

Treatment of phosphonium salts **2a–f** with 1 M alkali solution gave the corresponding carboxylate phosphabetaines **3a–f** (see Scheme 1). The most informative method for carboxylate phosphabetaines identification is IR spectroscopy. Medium intensity bands in the region of 1335–1340 cm^{-1} correspond to symmetric stretching vibrations in the carboxylate groups, and bands in the region of 1553–1567 cm^{-1} are attributed to antisymmetric stretching vibrations in these groups. In this case, the absorption band of the free carboxy group in the region of 1715–1740 cm^{-1} disappears.

In conclusion, the nucleophilic substitution between 3-(diphenylphosphino)propanoic acid and ω-bromoalkanoic acids affords the corresponding phosphonium compounds in high yields. The similar process involving chloroalkanoic acids is slower and leads to the side formation of phosphine oxides. The alkali treatment of the phosphonium salts gives the corresponding carboxylate phosphabetaines.

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† *Crystal data for* **2a**. $C_{17}H_{18}BrO_4P$, M = 397.19 g mol^{-1}, triclinic, space group $P\bar{1}$ (no. 2), Z = 2, a = 8.0672(5), b = 9.4323(6) and c = 12.7937(8) Å, α = 88.123(3)°, β = 82.330(3)°, γ = 65.723(3)°, V = 879.21(10) Å^3, ρ_{calc} = 1.500 g cm^{-3}, μ = 2.445 mm^{-1}, 42122 reflections collected ($-10 \leqslant h \leqslant 10$, $-12 \leqslant k \leqslant 12$, $-17 \leqslant l \leqslant 17$), θ range of 1.607° to 28.872°, 4578 independent (R_{int} = 0.0249) and 4437 observed reflections [$I \geqslant 2\sigma(I)$], 216 refined parameters, R_1 = 0.0182, wR_2 = 0.0472, GOOF 1.049, max(min). Residual electron density 0.362 (–0.482) eÅ^{-3}. For more details, see Online Supplementary Materials.

CCDC 2035123 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.03.032.

References

1 K. Tsunashima, A. Kawabata, M. Matsumiya, S. Kodama, R. Enomoto, M. Sugiya and Y. Kunugi, *Electrochem. Commun.*, 2011, **13**, 178.
2 B. Yu, D. G. Bansal, J. Qu, X. Sun, H. Luo, S. Dai, P. J. Blau, B. G. Bunting, G. Mordukhovich and D. J. Smolenski, *Wear*, 2012, **289**, 58.
3 N. E. Leadbeater, *Chem. Commun.*, 2014, **50**, 1515.
4 M. Rzelewska-Piekut and M. Regel-Rosocka, *Sep. Purif. Technol.*, 2019, **212**, 791.
5 T. Werner, *Adv. Synth. Catal.*, 2009, **351**, 1469.
6 N. D. Harper, N. D. Nizio, A. D. Hendsbee, J. D. Masuda, K. N. Robertson, L. J. Murphy, M. B. Johonson, C. C. Pye and J. A. C. Clyburne, *Ind. Eng. Chem. Res.*, 2011, **50**, 2822.
7 N. R. Khasiyatullina, V. F. Mironov, S. K. Gumerova, A. D. Voloshina and A. S. Sapunova, *Mendeleev Commun.*, 2019, **29**, 435.
8 N. R. Khasiyatullina, A. M. Vazykhova, V. F. Mironov, D. B. Krivolapov, Yu. K. Voronina, A. D. Voloshina, N. V. Kulik and A. S. Strobykina, *Mendeleev Commun.*, 2017, **27**, 134.
9 S. Romanov, A. Aksunova, Y. Bakhtiyarova, M. Shulaeva, O. Pozdeev, S. Egorova, I. Galkina and V. Galkin, *J. Organomet. Chem.*, 2020, **910**, 121130.
10 A. Yu. Spivak, D. A. Nedopekina, E. R. Shakurova, R. R. Khalitova, R. R. Gubaidullin, V. N. Odinokov, U. M. Dzhemilev, Yu. P. Bel'skii, N. V. Bel'skaya, S. A. Stankevich, E. V. Korotkaya and V. A. Khazanov, *Russ. Chem. Bull., Int. Ed.*, 2013, **62**, 188 (*Izv. Akad. Nauk, Ser. Khim.*, 2013, 189).
11 D. A. Nedopekina, R. R. Gubaidullin, V. N. Odinokov, P. V. Maximchik, B. Zhivotovsky, Y. P. Bel'skii, V. A. Khazanov, A. V. Manuylova, V. Gogvadze and A. Yu. Spivak, *MedChemComm*, 2017, **8**, 1934.
12 O. V. Tsepaeva, A. V. Nemtarev, T. I. Salikhova, T. I. Abdullin, L. R. Grigor'eva, S. A. Khozyainova and V. F. Mironov, *Anti-Cancer Agents Med. Chem.*, 2020, **20**, 286.
13 I. Galkina, A. Tufatullin, D. Krivolapov, Y. Bakhtiyarova, D. Chubukaeva, V. Stakheev, V. Galkin, R. Cherkasov, B. Büchner and O. Kataeva, *CrystEngComm*, 2014, **16**, 9010.
14 I. Galkina, S. Romanov, A. Gerasimov, Y. Bakhtiyarova and V. Galkin, *J. Organomet. Chem.*, 2020, **910**, 121131.
15 D. Xu, H. Wei, Y. Zhen, Y.-Q. Gao, R. Li, X. Li, Y. He, Z. Zhang and W. Xie, *Org. Chem. Front.*, 2019, **6**, 1681.
16 P. Tian, H. Xiao, L. Wang, Y. Yu and Y. Huang, *Tetrahedron Lett.*, 2019, **60**, 1015.
17 M. Irfan and A. Idris, *Mater. Sci. Eng.*, 2015, **56**, 574.
18 A. Mollahosseini, A. Abdelrasoulab and A. Shoker, *Mater. Today Chem.*, 2020, **15**, 100227.
19 M. He, K. Gao, L. Zhou, Z. Jiao, M. Wu, J. Cao, X. You, Z. Cai, Y Su and Z. Jiang, *Acta Biomater.*, 2016, **40**, 142.
20 Yu. V. Bakhtiyarova, A. F. Aksunova, R. R. Minnullin, I. V. Galkina and V. I. Galkin, *Russ. Chem. Bull., Int. Ed.*, 2016, **65**, 1308 (*Izv. Akad. Nauk, Ser. Khim.*, 2016, 1308).
21 Yu. V. Bakhtiyarova, A. F. Aksunova, S. R. Romanov, D. I. Bakhtiyarov, K. A. Ivshin, O. N. Kataeva, S. N. Egorova, I. V. Galkina and V. I. Galkin, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 319.
22 S. R. Romanov, A. F. Aksunova, D. R. Islamov, A. B. Dobrynin, D. B. Krivolapov, O. N. Kataeva, Y. V. Bakhtiyarova, O. I. Gnezdilov, I. V. Galkina and V. I. Galkin, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2016, **191**, 1637.

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