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Mendeleev Commun., 1991, **1(2)**, 49–50
Mendeleev Communications

A Regiospecific Synthesis of 1-Phosphonatodiazene-2-oxides

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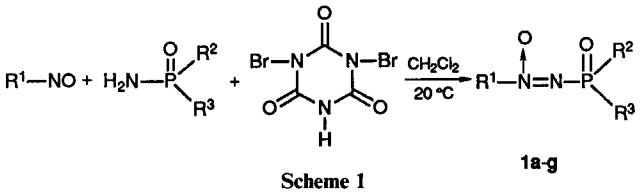
New azoxy compounds, containing an azoxy group directly bonded to a phosphorus atom, have been prepared by the reaction of nitroso derivatives with amidophosphonates in the presence of dibromoisocyanurate.

Many compounds containing the azoxy group have valuable pharmacological (antiinflammatory,[1] immunosuppressive,[2] antibacterial,[3] cytotoxic[4] and other) activities. Only azoxy compounds with C,[5] N,[6] O,[7] S,[8] F,[9] Cl[10] and Br[11] atoms at the azoxy group have been described previously. Information on phosphorus-containing azoxy compounds is lacking as far as we know.

Herein we report the regiospecific synthesis of the 1-phosphonatodiazen-2-oxides **1**, compounds with directly bonded azoxy and phosphonate fragments. The suggested synthesis of **1** is based on the reaction of nitroso derivatives with amidophosphonates in the presence of dibromoisocyanurate (DBI) which has been widely used recently for the regiospecific formation of diazene- and triazene-oxide groups.[11–15]

A mixture of the nitroso derivative (10 mmol), amidophosphate (10 mmol) and DBI (20 mmol) in methylene chloride (10 ml) was stirred for 12 h at 20 °C. The excess of DBI and cyanuric acid was filtered and washed off with CH_2Cl_2 (2 × 5 ml). Evaporation of the solvent and subsequent TLC of the residue (Silica gel, eluent ether) yielded pure azoxy compounds **1a–g** (Scheme 1).

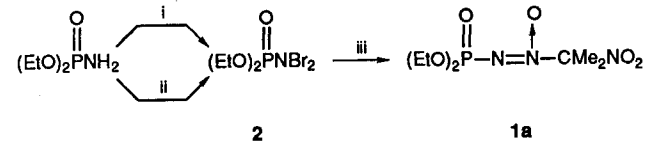
The reaction has a very wide range. Alkyl and aryl esters of amidophosphorus acid as well as bisamidophosphates can be used as starting materials. Alkyl-, aryl- and heteroaryl-nitroso derivatives, including compounds with other functional groups, can be involved in the process. Yields of **1a–g** or 47–92% were obtained (Table 1).



Scheme 1

The reaction is regiospecific. Products **1a–g** are individual regioisomers with a phosphonate group at the non-oxidized N-atom. The structures of **1a–g** were confirmed by elemental analysis, IR and ^1H, ^{13}C, ^{14}N, ^{31}P NMR spectroscopy, including ^{13}C–^{14}N decoupling experiments (Table 1).†

The probable reaction scheme involves the formation of the *N,N*-dibromoaminophosphonates[16] with subsequent trapping of the latter by nitroso compounds, similar to that of *N,N*-dihalouretane and *N,N*-dihalosulphamides.[17] This assumption was confirmed by the isolation of *O,O*-diethyl (*N,N*-dibromoamido)phosphonate **2** from the reaction of *O,O*-diethylaminophosphonate and DBI in the absence of the nitroso compound and by the formation of **1a** from **2** prepared by the method in ref. 16 and 2-nitro-2-nitrosopropane under the reaction conditions (Scheme 2).



Scheme 2 *Reagents and conditions*: i, DBI, CH_2Cl_2; ii, (*a*) K_2CO_3, (*b*) Br_2 (ref. 16); iii, ONC Me_2NO_2, CH_2Cl_2, 20 °C

† *Data* for **1b**: ^{14}N NMR δ (in CD_3COCD_3 relative to $MeNO_2$) − 34.5 [—N(O)=]; ^{13}C NMR δ (relative to solvent, δ 30.00) 148.8 (d, iso-C, $^3J_{C-P}$ 15 Hz), 134.9 (*p*–C), 130.4 (*m*–C), 123.6 (*o*–C), 65.0 (d, CH_2, $^2J_{C-P}$ 6 Hz), 16.7 (d, CH_3, $^3J_{C-P}$ 6 Hz). The contraction of the signal of the oxidized N-atom [—^{14}N(O)=] in **1b** by iso-^{13}C–^{14}C N decoupling shows the presence of the iso-^{13}C—$^{14}N(O)$ bond and, consequently, the structure of 1-(*O,O*-diethylphosphonato)-2-phenyl-diazene-2-oxide for **1b**.

Table 1 Yields and selected properties of 1-phosphonatodiazene-2-oxides **1**

Compound	R^1	R^2	R^3	M.p. /°C	Yield /%	IR spectra ν/cm^{-1}	^{1}H NMR spectra[a] δ	Elem. Anal./% (found/calc.) C	H	N	P
1a	$-CMe_2NO_2$	OEt	OEt	Oil	72	980 (P—N) 1020 (P—O—C) 1250 (P=O) O ↑ 1510 (N=N) 1570 (NO_2)	1.31 (t, 6H, CH_3, *J* 7.0) 2.20 (s, 6H, CH_3) 4.24 (m, 4H, CH_2, *J* 7.0)	31.45/31.22	6.0/5.94	14.45/15.61	11.9/11.52
1b	Ph	OEt	OEt	Oil	92	1030 (P—O—C) 1260 (P=O) O ↑ 1500 (N=N)	1.35 (t, 6H, CH_3, *J* 7.0) 4.32 (m, 4H, CH_2) 7.64 (t, 2H, *m*-H, C_6H_5) 7.78 (t, 1H, *p*-H, C_6H_5) 8.27 (d, 2H, *o*-H, C_6H_5)	46.0/46.51	5.85/5.81	10.7/10.85	11.95/12.04
1c	2-$NO_2C_6H_4$	OEt	OEt	58–60[b]	58	1240 (P=O) O ↑ 1490 (N=N) 1530 (NO_2)	1.34 (t, 6H, CH_3, *J* 7.0) 4.28 (m, 4H, CH_2) 7.97 (m, 2H, C_6H_4) 8.14 (m, 2H, C_6H_4)	39.4/39.60	5.00/4.62	13.05/13.86	10.0/10.23
1d	—CC(Me)NON	OEt	OEt	Oil	66	1030 (P—O—C) 1270 (P=O) O ↑ 1500 (N=N) 1590 (cycle)	1.37 (t, 6H, CH_3, *J* 7.0) 2.68 (s, 3H, CH_3) 4.34 (m, 4H, CH_2)	32.25/31.82	5.0/4.92	27.45/21.21	10.95/11.74
1e	$-CMe_2NO_2$	OEt	—N(CH_2)$_2$OCH_2CH_2	94–96[b]	60	1030 (P—O—C) 1250 (P=O) O ↑ 1510 (N=N) 1575 (NO_2) 2870, 2920, 2990 (CH)	1.33 (t, 3H, CH_3, *J* 7.0) 2.21 (s, 3H, CH_3) 2.23 (s, 3H, CH_3) 3.17 (m, 4H, CH_2H) 3.55 (m, 4H, CH_2O) 4.17 (m, 2H, CH_2O)	34.9/34.84	6.1/6.13	17.35/18.06	9.71/10.00
1f	Ph	OEt	OPh	Oil	71	1030 (P—O—C) 1280 (P=O) O ↑ 1490 (N=N)	1.37 (t, 3H, CH_3, *J* 7.0) 4.47 (m, 2H, CH_2) 7.24 (t, 1H, C_6H_5) 7.39 (m, 4H, C_6H_5) 7.63 (t, 2H, C_6H_5) 7.78 (t, 1H, C_6H_5) 8.27 (d, 2H, C_6H_5)	54.6/54.90	4.95/4.90	8.85/9.15	9.85/10.13
1g	2-$NO_2C_6H_4$	OPh	—N(CH_2)$_2$OCH_2CH_2	Oil	47	1250 (P=O) O ↑ 1490 (N=N) 1530 (NO_2) 2860, 2910, 2980 (CH)	3.08–3.62 (m, 8H, CH_2CH_2) 7.28 (m, 5H, C_6H_5) 7.97 (m, 2H, C_6H_4) 8.14 (m, 2H, C_6H_4)	48.95/48.97	4.6/4.33	13.65/14.28	7.9/7.91

[a] Solvent used CD_3COCD_3. [b] Recrystallised from hexane.

The significance to the reaction of the halogenation stage was confirmed by a noticeable decrease in the yield of **1a** when the reaction was carried out in the presence of halogenation agents weaker than DBI [Br_2 0%, *N*-bromosuccinimide (NBS) 7%, Bu^{t}OCl 8%].

Received in USSR, 28th November 1990
Received in UK, 4th January 1991; Com. 0/05405D

References

1 J. Miessel, US Patent 3989680, CO7c107/04, 1976 (*Chem. Abstr.*, 1976, **85**, 20819g).
2 F. K. Hess, P. A. Stewart, G. Possanza and K. Freter, Ger. Offen., 2208368, CO7cA61k, 1973 (*Chem. Abstr.*, 1973, **79**, 146271s).
3 N. Imamura, H. Kuga, K. Otoguro, H. Tanaka and S.Omura, *J. Antibiot.*, 1989, **42**, 156.
4 R. Fruttero, R. Calvino, A. Distilo, A. Gasco, J. Galatulas and R. Bossa, *Pharmazie*, 1988, **43**, 499.
5 V. N. Yandovskii, B. V. Gidaspov and I. V. Tselinskii, *Uspekhi Khimii*, 1981, **50**, 296 (English translation in *Russ. Chem. Rev.*, 1981, **50**, 164).
6 R. L. Dutta and R. Sharma, *J. Sci. Ind. Res.*, 1981, **40**, 715.
7 V. N. Yandovskii, B. V. Gidaspov and I. V. Tselinskii, *Dokl. Akad. Nauk SSSR*, 1986, **289**, 381.
8 W. V. Farrar and J. M. Gulland, *J. Chem. Soc.*, 1944, 368.
9 H. M. Marsden and J. M. Shreeve, *J. Inorg. Chem.*, 1984, **23**, 3654.
10 W. J. LeNoble and W. S. Chang, *Synthesis*, 1973, 106.
11 A. M. Churakov, E. L. Goncharova, S. L. Ioffe, Yu. A. Strelenko and V. A. Tartakovskii, *Izv. Akad. Nauk, SSSR, Ser. Khim.*, 1990, 953.
12 S. G. Zlotin, E. A. Vinogradova, A. I. Podgurskii, Yu. A. Strelenko and O. A. Luk'yanov, *Izv. Akad. Nauk, SSSR, Ser. Khim.*, 1990, 1656.
13 S. G. Zlotin, O. V. Prokshits, N. F. Karpenko and O. A. Luk'yanov, *Izv. Akad. Nauk, SSSR, Ser. Khim.*, 1990, 1679.
14 S. G. Zlotin, N. V. Airapetova, E. A. Vinogradova, A. I. Podgurskii, Yu. A. Strelenko and O. A. Luk'yanov, *Izv. Akad. Nauk, SSSR, Ser. Khim.*, 1990, 2821.
15 O. A. Luk'yanov, G. A. Smirnov and A. M. Vasil'yev, *Izv. Akad. Nauk, SSSR, Ser. Khim.*, 1990, 2155.
16 A. Zwierzak and S. Zawadzki, *Synthesis*, 1971, 323.
17. R. C. Zawalski and P. Kovacic, *J. Org. Chem.*, 1979, **44**, 2130.