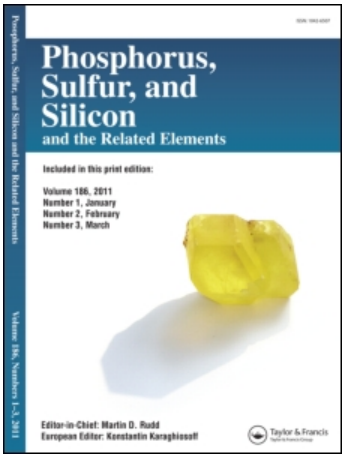

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS AND MASS SPECTRA OF ADAMANTYLPHOSPHORYL DERIVATIVES

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To cite this Article Duddeck, Helmut , Hani, M. , Elgamal, A. and Hanna, Atef G.(1986) 'SYNTHESIS AND MASS SPECTRA OF ADAMANTYLPHOSPHORYL DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 28: 3, 307 — 314
To link to this Article: DOI: 10.1080/03086648608072822
URL: http://dx.doi.org/10.1080/03086648608072822

Phosphorus and Sulfur, 1986, Vol. 28, pp. 307–314
0308-664X/86/2803–0307/$15.00/0

SYNTHESIS AND MASS SPECTRA OF ADAMANTYLPHOSPHORYL DERIVATIVES

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(*Received November 25, 1985; in final form December 12, 1985*)

The syntheses of 25 phosphorylated adamantane derivatives are described and their mass spectra are discussed.

INTRODUCTION

In the past we have used adamantane compounds as models for NMR spectroscopic investigations because they represent rigid cage molecules which are nearly free of strain and consist of fused six-membered ring subunits which, in contrast to cyclohexanes, adopt nearly ideal chair conformations. Very recently, we reported on the ^{13}C, ^{17}O and ^{31}P NMR spectra of various bridgehead-phosphorylated adamantanes.[1,2] Although this class of compounds may possess pharmacological activity, very little has been published on adamantanes directly bonded to a phosphorus atom. Therefore, we present here our experience with the synthesis of the title compounds. In the course of this study we found that the fragmentations of these molecules in the mass spectrometer are characteristic. Thus, a brief discussion of their mass spectra is justified which renders information of possible future utility when analogous constitutions are questionable.

RESULTS AND DISCUSSION

Synthesis of 1-Adamantylphosphoryl Derivatives **1**, **4** *and* **5**

Inspite of the existence of numerous reports on adamantane chemistry[3] little has been published on phosphorylated adamantane derivatives.[4,5] We found that the best method for the phosphorylation of an adamantane molecule at the bridgehead position was that described by Stetter *et al.*[5] who treated 1-bromoadamantane with

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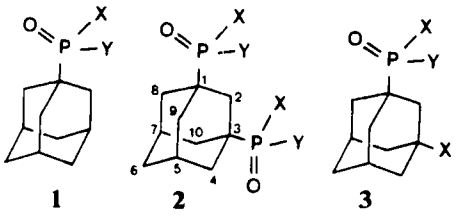
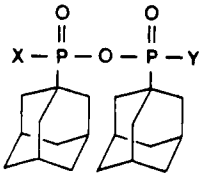


1 **2** **3**

	a	b	c	d	e	f	g	h
X	Cl	Br	OMe	OEt	OPr^n	OBu^n	OPh	OCH_2
Y	Cl	Br	OMe	OEt	OPr^n	OBu^n	OPh	OCH_2

	i	j	k	k	m	n	o	p
X	NHBu^n	$NHCH_2$	OMe	OEt	OPr^n	OPh	OEt	OPh
Y	NHBu^n	$NHCH_2$	Cl	Cl	Cl	Cl	Br	Br

	q	r	s
X	NHEt	NHBu^n	N◯
Y	Cl	Cl	Cl



	4	5
X	NHBu^n	N◯
Y	NHBu^n	Cl

SCHEME 1 Structures of adamantylphosphoryl derivatives.

PCl_3 in the presence of $AlBr_3$ to form a complex $(1\text{-Ad})PCl_3^+AlBr_4^-$. Hydrolysis during work-up afforded 1-adamantylphosphonic dichloride (**1a**).[5] In an analogous way we synthesized **1b** using PBr_3. These two compounds served as starting materials for various esters. Stetter *et al.*[5] had reported that **1a** does not react with alcohol. We found, however, that reflux of **1a** in abs. MeOH for 10 days yielded 55% **1c**. If it is treated with NaOMe in methanol under reflux, **1c** is formed readily; at $-50°$ it gives a mixture of **1c** and the chloridate **1k**. The dibromide **1b** reacts similarly but less quickly with NaOEt to give a mixture of **1d** and **1o**. In general, we observed that the products resulting from the alcoholysis of **1a** depend strongly on the nature of the alcohol and alkoxide reagents and on their molar ratio. For details of the synthesis of **1e**, **1f**, **1g**, **1h**, **1l**, **1m**, **1n** and **1p** prepared by this procedure we refer to the experimental section.

The diamide **1i** was obtained from the reaction of the dibromide **1b** with n-butylamine. Surprisingly, the dichloride **1a** did not afford the same product but gave a mixture of the chloridate **1r** and the anhydride **4** under identical conditions. With ethylamine **1a** did not exchange both chlorine atoms either; here we isolated **1q** only; with pyrrolidine we obtained **1s** and with piperidine **5**. Compound **1s** is

remarkably stable and did not react with NaOMe/MeOH under reflux for seven days. On the other hand, the cyclic diamide **1j** could be isolated easily from the reaction of **1a** and ethylene-diamine.

The formation of the anhydrides **4** and **5** is probably due to the presence of traces of water[6] which may be introduced from the laboratory atmosphere.

Synthesis of 1,3-Disubstituted Adamantylphosphoryl Derivatives 2 and 3

Phosphorylation of 1,3-dibromoadamantane[7] with PCl_3 in the presence of 3 moles $AlBr_3$ gave **2a**. However, it afforded a mixture of **3a** and its 3-bromo analogue if only 1 mole of $AlBr_3$ is used, i.e. in the latter case the phosphorylation is accompanied partially by a halogen exchange. Compound **3a** represents by far the major constituent and could not be separated from its adjunct by various chromatographic trials. Treatment of 1,3-dibromoadamantane with PBr_3 under the same conditions formed **2b**. The bromination of **1b** with Br_2 in the presence of an $AlBr_3$/*t*-butylbromide mixture in a glass autoclave afforded **3b**. Confirmation for the structures of **2a**, **2b** and **3b** could be deduced from the ^{13}C chemical shifts[1] and by calculating the ^1H chemical shifts[3] assuming additivity of the substituent effects derived from the respective monosubstituted adamantanes[3] (Table I).

TABLE I

^1H Chemical shifts of **2a**, **2b** and **3b**,[a] calculated values[3] in parentheses (cf. text)

	H-2	H-8/9	H-4/10	H-5/7	H-6
2a	2.35		2.14	2.47	1.81
	(2.42)		(2.12)	(2.47)	(1.82)
2b	2.36		2.12	2.39	1.79
	(2.52)		(2.17)	(2.39)	(1.82)
3b	2.55	2.06	2.30	2.16	1.70
	(2.69)	(2.11)	(2.34)	(2.34)	(1.77)

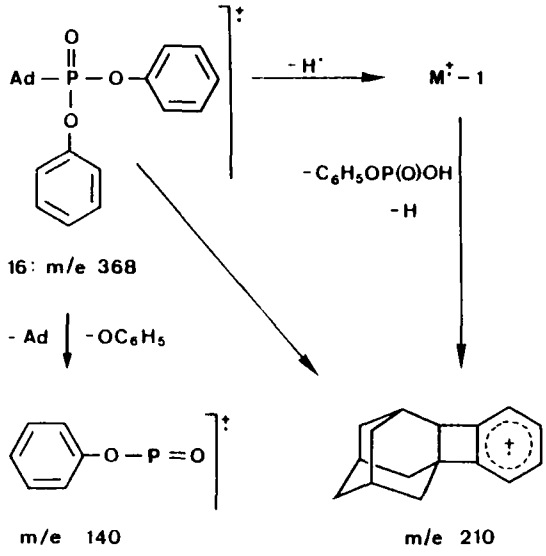
[a] Spectra recorded at 400 MHz.

Mass Spectra

The mass spectra of halogen-containing 1-adamantylphosphoryl compounds mostly exhibit molecular ions of extremely low intensity reflecting their instability upon electron impact. However, the relative abundance of the molecular ions is increased in dimethyl (**1c**), diethyl (**1d**) and diphenyl (**1g**) 1-adamantyl phosphonates to 26, 22 and 40%, respectively, but decreased again when longer *n*-alkyl side chains are involved (**1e** and **1f**).

The most characteristic fragmentation processes involve expulsion or degradation of the phosphoryl group to give the adamantyl ion with m/e 135 as the base peak in nearly all cases. This ion is then cleaved and the elision of C_2H_4 ($C_8H_{11}^+$: m/e 107), C_3H_6 ($C_7H_9^+$: m/e 93), C_4H_8 ($C_6H_7^+$: m/e 79) or C_5H_8 ($C_5H_7^+$: m/e 67) species continues until fragments of mostly undecided structures are formed.[8-13]

In addition, the molecular ions may lose fragments of the substituent itself, e.g. from the alkyl residues of esters and amides by α-scission or a McLafferty rearrangement. Many of the resulting ions are listed in the Experimental section.



SCHEME 2

A fragmentation of the diphenylester **1g** is noteworthy: The ion at m/e 210 is believed to result from the molecular ion by the loss of one hydrogen and a Ph—O—P(O)OH moiety along with a formation of a linkage between the adamantane and the remaining phenyl ring (Scheme 2). The $M^+ - 1$ peak is also observed with 5% relative intensity. Such a type of fragmentation was also found in the mass spectra of triphenyl, trio-*o*-, -*m*- and -*p*-tolylphosphonate derivatives and our structure proposal follows these reports.[14,15] Another ion appears at m/e 140 is due to the loss of the adamantane moiety and one phenoxy group from M^+.

EXPERIMENTAL

Melting points are uncorrected. Silica gel was used for column chromatography and elution was performed by petrol ether—acetone mixtures.

IR spectra were measured on a Perkin-Elmer 1310, Bruker IFS 45 or Beckman Akkulab 10 as a thin film or using KBr pellets.

NMR spectra were recorded on following spectrometers: ^1H, Varian T-60 (60 MHz), Bruker WM-250 (250 MHz) and AM-400 (400 MHz). ^{13}C, ^{17}O and ^{31}P NMR spectra have been reported previously.[1,2]

Mass spectra were measured on Varian MAT CH-5 and CH-7 instruments. Mass spectral data are in m/e units, relative intensities in parentheses; asterisks indicate that the ion could be observed only by using the field ionization technique.

Syntheses. Compound **1a** was prepared according to a known procedure.[5] The yields refer to isolated material after chromatographic purification and are not optimized.

1-Adamantylphosphonic dichloride (**1a**)[5]. IR (KBr, cm^{-1}): 1270, 770, 540, 502; ^1H NMR ($CDCl_3$, δ): 2.17 (m, 3 H), 2.08 (dm, 6 H, $^2J_{PH} = 7.8$ Hz), 1.78 (m, 3 H); MS: 252 (0.3): M^+, 135 (100): $C_{10}H_{15}^+(Ad^+)$, 107 (6), 93 (16), 79 (17), 67 (6).

1-Adamantylphosphonic dibromide (**1b**). A mixture of 1-bromoadamantane (10.7 g, 50 mmol), PBr_3 (100 ml) and $AlBr_3$ (20 g, 75 mmol) were heated under reflux with stirring for 3 hrs. Then it was cooled in an ice-bath, the precipitate was filtered off, washed with benzene, suspended in CCl_4 and gradually hydrolyzed with cooling. The organic layer was washed with water, dried over $CaCl_2$ and evaporated.

After column chromatography **1b** was obtained as colourless crystals (4 g, 24%), m.p. 115–116°C. IR (KBr, cm^{-1}): 1250, 480; ^1H NMR ($CDCl_3$, δ): 2.3–2.0 (m, 9 H), 1.8 (m, 6 H); MS (relative intensity): m/e 340 (0.1)*: M^+, 135 (100): Ad^+, 107 (5), 93 (16), 79 (17), 67 (5).

Dimethyl 1-adamantylphosphonate (**1c**). (a) A solution of **1a** (300 mg, 1.2 mmol) was heated under reflux in abs. MeOH (10 ml) for 10 days. The product obtained after evaporation from excess MeOH was purified on a silica gel column to give 160 mg **1c** (55%), m.p. 59–60°C. IR (KBr, cm^{-1}): 1242, 1026; ^1H NMR ($CDCl_3$, δ): 3.75 (d, 6 H, $^2J_{PH}$ = 11.6 Hz), 2.1–1.8 (m, 9 H), 1.8 (broad s, 6 H); MS: 244 (26): M^+, 135 (100): Ad^+, 107 (6), 93 (16), 79 (17), 67 (5).

(b) A solution of **1a** (100 mg, 0.4 mmol) in abs. MeOH (5 ml) was added dropwise to freshly prepared NaOMe (0.9 mmol) in MeOH at room temperature. After 3 hrs. water (10 ml) was added and the reaction mixture exhaustively extracted with CH_2Cl_2. The organic layer was washed with water, dried and evaporated. Chromatographic purification gave 40 mg of **1c** (41%).

(c) The dibromide **1b** (300 mg, 0.09 mmol) was heated under reflux with MeOH (10 ml) for 72 hrs. and worked up as described under (a) to give **1c** (190 mg) in 88% yield.

Methyl 1-adamantylphosphonochloridate (**1k**) *and* **1c**. Freshly prepared NaOMe (92 mg Na, 4 mmol, in 5 ml abs. MeOH) was cooled to −50°C with dry-ice. With effective stirring a solution of **1a** (500 mg, 2 mmol) in 10 ml abs. MeOH was gradually added. The temperature was raised slowly to room temperature and the mixture was left overnight. After working up in the usual manner the chromatographic separation yielded two fractions. The first was the chloridate **1k** (340 mg, 69%), m.p. 72–73°C. IR (KBr, cm^{-1}): 1260, 1020, 786, 692, 556; ^1H NMR ($CDCl_3$, δ): 3.82 (d, 3 H, $^2J_{PH}$ = 12 Hz), 2.1–1.9 (m, 9 H), 1.7 (m, 6 H); MS: 248 (2): M^+, 135 (100): Ad^+, 107 (5), 93 (12), 79 (14), 67 (5).

The second fraction was **1c** (30 mg, 6%).

Ethyl 1-adamantylphosphonochloridate (**1l**). A solution of **1a** (500 mg, 2 mmol) in 10 ml abs. EtOH was added to vigorously stirred, freshly prepared NaOEt (46 mg Na, 2 mmol, in 3 ml abs. EtOH) which was cooled to −50°C. Treatment as described for **1k** gave **1l** as colourless crystals (212 mg, 41%), m.p. 36–37°C. IR (KBr, cm^{-1}): 1264, 1020, 762, 688, 554; ^1H NMR ($CDCl_3$, δ): 4.33 (m, 4H), 2.2–1.8 (m, 9 H), 1.8–1.7 (m, 9 H), 1.47 (t, 6 H); MS: 262 (1): M^+, 135 (100): Ad^+, 107 (4), 93 (12), 79 (14), 67 (5).

Ethyl 1-adamantylphosphonobromidate (**1o**) *and diethyl 1-adamantylphosphonate* (**1d**). The dibromide **1b** (680 mg, 2 mmol) was treated with NaOEt (4 mmol) in abs. EtOH as described for **1k** and **1l**. The first fraction from column chromatography was **1o** (300 mg, 49%), m.p. 42–44°C. IR (KBr, cm^{-1}): 1248, 1010, 506; ^1H NMR ($CDCl_3$, δ): 4.20 (m, 2 H), 1.98 (m, 9 H), 1.8–1.7 (m, 6 H), 1.35 (t, 3 H); MS: 308/306 (0.8, 0.8)*: M^+, 262 (1): $(Ad)P(OH)(Br)^+$, 227 (0.1)*: $(Ad)P(O)(OEt)^+$, 135 (100): Ad^+, 107 (14), 93 (10), 79 (12), 67 (4).

The second fraction was **1d** (47 mg, 9%) as a colourless oil. IR (cm^{-1}): 1242, 1026, 744, 688; ^1H NMR ($CDCl_3$, δ): 4.04 (m, 4 H), 2.0–1.6 (m, 12 H), 1.28 (t, 6 H); MS: 272 (22): M^+, 244 (5): $(Ad)P(O)(OH)(OEt)^+$, 135 (100): Ad^+, 107 (4), 93 (11), 79 (14), 67 (4).

n-Propyl 1-adamantylphosphonochloridate (**1m**) *and di-n-propyl 1-adamantylphosphonate* (**1e**). A solution of **1a** (500 mg, 2 mmol) in dry ether (25 ml) was added to freshly prepared NaO-*n*-Pr (4 mmol) in dry ether (50 ml) cooled to −50°C. Usual work-up and chromatographic separation afforded two fractions. The first was **1m** as a colourless oil (85 mg, 15%). IR (cm^{-1}): 1244, 1000, 554; ^1H NMR ($CDCl_3$, δ): 4.13 (m, 2 H), 2.2–1.8 (m, 9 H), 1.8–1.5 (m, 8 H), 0.97 (t, 3 H); MS: 276/278 (0.3/0.1)*: M^+, 235/237 (3/1): $(Ad)P(OH)_2(Cl)^+$, 135 (100): Ad^+, 107 (4), 93 (11), 79 (13), 67 (4).

The second fraction was **1e** as a colourless oil (410 mg, 68%). IR (cm^{-1}): 1250, 1010; ^1H NMR ($CDCl_3$, δ): 4.00 (q, 4 H), 2.1–1.8 (m, 9 H), 1.8–1.7 (m, 6 H), 1.62 (m, 4 H), 0.94 (t, 6 H); MS: 300 (1): M^+, 259 (30): $M^+—C_3H_5$, 217 (22): $(Ad)P(OH)_3^+$, 135 (100): Ad^+, 107 (4), 93 (10), 83 (5), 79 (13), 67 (5).

Di-n-butyl 1-adamantylphosphonate (**1f**). The diester **1f** was prepared by gradual addition of a solution of **1a** (500 mg, 2 mmol) in dry ether (25 ml) to NaO-*n*-Bu/*n*-BuOH (4 mmol) in dry ether (50 ml) as described for **1m**. Chromatographic purification gave **1f** as a colourless oil (410 mg, 63%): IR (cm^{-1}): 1244, 1020; ^1H NMR ($CDCl_3$, δ): 3.97 (m, 4 H), 2.1–1.2 (m, 23 H), 0.9 (m, 6 H); MS: 328 (4): M^+, 273 (46): $M^+—C_4H_7$, 217 (44): $(Ad)P(OH)_3^+$, 135 (100): Ad^+, 107 (5), 93 (12), 86 (30), 84 (50), 79 (14), 67 (6).

Cyclic ethylene 1-adamantylphosphonate (**1h**). To a stirred mixture of 0.11 ml ethylene glycol (2 mmol) and 92 mg Na (4 mmol) in 50 ml dry ether a solution of **1a** (500 mg, 2 mmol) in dry ether (25 ml) was added. This reaction mixture was refluxed for 10 hrs. and left overnight. After usual work-up **1h** was obtained as colourless crystals (75 mg, 16%), m.p. 158–161°C. IR (KBr, cm^{-1}): 1262, 1030; ^1H NMR

($CDCl_3$, δ): 4.6–4.0 (m, 4 H), 2.1–1.8 (m, 9 H), 1.8–1.7 (m, 6 H); MS: 242 (15): M^+, 135 (100): Ad^+, 107 (6), 93 (14), 79 (18), 67 (7).

Phenyl 1-adamantylphosphonochloridate (**1n**) *and diphenyl 1-adamantylphosphonate* (**1g**). The dichloride **1a** (2 mmol) was treated with NaOPh (4 mmol) as described for **1e/1m**. The product was separated into two fractions by column chromatography. The first fraction was **1n** (290 mg, 47%) as a colourless oil. IR (cm^{-1}): 3070, 1600, 1498, 1460, 1272, 1200, 938, 542; ^1H NMR ($CDCl_3$, δ): 7.3–7.0 (m, 5 H), 2.2–1.9 (m, 9 H), 1.8–1.6 (m, 6 H); MS: 310/312 (6/2): M^+, 135 (100): Ad^+, 107 (3), 93 (10), 79 (11), 67 (5).

The second fraction afforded **1g** as colourless crystals (210 mg, 29%), m.p. 124–125°C. IR (KBr, cm^{-1}): 3062, 1600, 1500, 1460, 1260, 1198, 924; ^1H NMR ($CDCl_3$, δ): 7.3–7.0 (m, 10 H), 2.3–2.0 (m, 9 H), 1.8–1.7 (m, 6 H), MS: 368 (40): M^+, 367 (5): M^+-1, 210 (8): $C_{16}H_{18}^+$ (cf. text), 140 (2): $PhOPO^+$, 135 (100): Ad^+, 107 (5), 93 (16), 79 (22), 77 (11): $C_6H_5^+$, 67 (7).

Phenyl 1-adamantylphosphonobromidate (**1p**) *and* **1g**. The procedure used for the synthesis of **1e/1m** was applied for the reaction of **1b** (2 mmol) with NaOPh (4 mmol). After column chromatography two fractions were isolated. The first was **1p** (313 mg, 44%) as a colourless oil. IR (cm^{-1}): 3080, 1598, 1494, 1460, 1262, 1198, 926 and 504; ^1H NMR ($CDCl_3$, δ): 7.3–7.0 (m, 10 H), 2.3–2.0 (m, 9 H) 1.8–1.7 (m, 6 H); MS: 354/356 (3/3): M^+, 135 (100): Ad^+, 107 (4), 93 (11), 79 (13), 67 (5).

The second fraction was **1g** (176 mg, 24%).

P-1-Adamantyl-N-ethylphosphonamidic chloride (**1q**). Dried gaseous ethylamine was passed through a solution of **1a** (500 mg, 2 mmol) in CCl_4 at room temperature until a precipitate appears. The mixture was refluxed for 2 hrs., left overnight and worked up as usual to afford **1q** as colourless crystals (150 mg, 29%), m.p. 187–188°C. IR (KBr, cm^{-1}): 3220, 1224, 1120, 520; ^1H NMR ($CDCl_3$, δ): 3.4–3.0 (m, 2 H), 2.2–1.8 (m, 9 H), 1.8–1.7 (m, 6 H), 1.21 (t, 3 H); MS: 261/263 (1/0.3): M^+, 246 (0.4): $(Ad)P(O)(Cl)(NHCH_2)^+$, 135 (100): Ad^+, 107 (4), 93 (11), 79 (12), 67 (4).

P-1-Adamantyl-N-n-butylphosphonamidic chloride (**1r**) *and P-1-adamantyl-N-n-butylphosphonamidic acid, anhydride* (**4**). To a stirred solution of freshly distilled *n*-butylamine (0.8 ml, 8 mmol) in benzene (2 ml) a solution of **1a** (500 mg, 2 mmol) in CCl_4 (25 ml) was added. The mixture was refluxed for 6 hrs. and then allowed to stand overnight at room temperature. After usual work-up the residue was fractionated by column chromatography. The first fraction gave **1r** as colourless crystals (76 mg, 10%), m.p. 163–165°C. IR (KBr, cm^{-1}): 3208, 1226, 1090, 522; ^1H NMR ($CDCl_3$, δ): 3.2–2.8 (m, 2 H), 2.2–1.8 (m, 9 H), 1.8–1.6 (m, 6 H), 1.6–1.2 (m, 4 H), 0.96 (m, 3 H); MS: 289/291 (4/1): M^+, 246/248 (10/3): $(Ad)P(O)(Cl)(NHCH_2)^+$, 135 (100): Ad^+, 107 (4), 93 (10), 79 (12), 67 (5).

The second fraction was **4** as colourless crystals (30 mg, 3 %), m.p. 272–273°C. IR (KBr, cm^{-1}): 3200, 1230, 942, 930; ^1H NMR ($CDCl_3$, δ): 3.3–2.8, (m, 4 H), 2.2–1.1 (broad m, 19 H), 0.92 (m, 6 H); MS: 524 (23): M^+, 481 (4): $(Ad)P(O)(NHC_4H_9)—O—P(O)Ad(NHCH_2)^+$, 469 (3): $(Ad)P(O)(NC_4H_9)—O—P(O)(Ad)(NH)^+$, 453 (55): $(Ad)P(O)(NHC_4H_9)—O—P(OH)(Ad)^+$, 389 (4): $(Ad)P(O)(NHC_4H_9)—O—P(O)(NHC_4H_9)^+$, 318 (73): $(Ad)P(O)(NHC_4H_9)—O—P(OH)^+$, 272 (5): $(Ad)P(OH)_2(NHC_4H_9)^+$, 135 (100): Ad^+, 107 (6), 93 (16), 79 (16), 72 (11), 67 (6).

P-1-Adamantyl-N,N'-di-n-butylphosphonic diamide (**1i**). *n*-Butylamine was reacted with **1b** as described for **1r** and **4**. After chromatographic purification the product **1i** was obtained as a colourless oil with 53% yield. IR (cm^{-1}): 3272, 1176, 1130; ^1H NMR ($CDCl_3$, δ) 3.2–2.7 (m, 4 H), 2.5–1.5 (m, 15 H), 1.5–1.0 (m, 8 H), 0.96 (m, 6 H); MS: 326 (8): M^+, 283 (22): $(Ad)P(O)—(NHC_4H_9)(NHCH_2)^+$, 255 (12): $(Ad)P(OH)(NHC_4H_9)(NHCH_2)^+$, 135 (100): Ad^+, 120 (6): $P(OH)(NHC_4H_9)^+$, 107 (1), 93 (9), 79 (11), 72 (30): $C_4H_9NH^+$, 67 (4).

1-Adamantyl-1-pyrrolidinylphosphonic chloride (**1s**). The method described for **1r** and **4** was applied for the reaction of **1a** (2 mmol) and freshly distilled pyrrolidine (8 mmol) to give **1s** as colourless crystals with 63% yield, m.p. 115–116°C. IR (KBr, cm^{-1}): 1242, 1096, 524; ^1H NMR ($CDCl_3$, δ): 3.5–3.1 (m, 4 H), 2.2–1.8 (m, 9 H), 1.8–1.6 (m, 10 H); MS: 287/289 (1.3/0.4): M^+, 252 (0.25): M^+—Cl, 152 (2): M^+—Ad, 135 (100): Ad^+, 118 (2): $P(OH)(NC_4H_8)^+$, 107 (6), 93 (12), 79 (16), 70 (73): $NC_4H_8^+$, 67 (7).

2-(1-Adamantyl)-1,3,2-diazaphospholidine-2-oxide (**1j**). To a stirred solution of freshly distilled ethylenediamine (0.27 ml, 4 mmol) in 2 m benzene a solution of **1a** (500 mg, 2 mmol) in 25 ml CCl_4 was added, refluxed for 6 hrs. and allowed to stand overnight at room temperature. Water (40 ml) was added and the mixture extracted with CCl_4. The stirred aqueous layer was treated with Na_2CO_3 (0.5 g) for 1 hr. and extracted with CH_2Cl_2. After evaporation of the solvent from the combined organic layers and chromatographic purification **1j** (160 mg, 34%) was isolated as colourless crystals, m.p. 230–233°C. IR (KBr. cm^{-1}): 3244, 1170; ^1H NMR ($CDCl_3$, δ): 3.3–3.0 (m, 6 H), 2.0–1.7 (m, 15 H); MS: 240 (48): M^+, 183 (3): $(Ad)P(OH)^+$, 164 (10), 135 (100): Ad^+, 107 (11), 105 (10): M^+—Ad, 93 (17), 79 (19), 67 (8).

1-Adamantylphosphonochloridic acid, anhydride with 1-adamantylpiperidinophosphonic acid (**5**). This compound was prepared from **1a** (2 mmol) and freshly distilled piperidine (8 mmol) using the procedure described for **1r** and **4**. Chromatographic purification afforded **5** (30 mg, 4%) as colourless crystals, m.p. 210–213°C. IR (KBr, cm^{-1}): 3246, 1236, 1230, 942, 930; ^1H NMR ($CDCl_3$, δ): 3.3–3.0 (m, 6 H), 2.2–1.8 (m, 9 H), 1.8–1.5 (m, 12 H); MS: 499/501 (6/2): M^+, 464 (0.1): M^+—Cl, 416 (1): (Ad)P(O)(Cl)—O—P(Ad)(OH)$^+$, 364/366 (4/1.5): M^+—Ad, 282 (2): P(OH)(Cl)—O—P(Ad)(OH)$^+$, 266 (11): (Ad)P(O)$(NC_5H_{10})^+$, 265 (58): (Ad)P(O)$(NC_5H_9)^+$, 135 (100): Ad^+, 130 (16): P(O)$(NC_5H_9)^+$, 107 (5), 93 (13), 84 (100), 79 (15), 67 (6).

1,3-Adamantylidendiphosphonic dichloride (**2a**). A mixture of 1,3-dibromoadamantane (580 mg, 2 mmol),[7] PCl_3 (8 ml) and $AlBr_3$ (1.6 g, 6 mmol) was heated under reflux with vigorous stirring for 5 hrs. The solid which remained after filtration was washed with benzene, suspended in 30 ml CCl_4 and hydrolyzed with water under cooling. The organic layer was washed with water, dried and evaporated. Chromatographic purification afforded **2a** (220 mg, 30%) as colourless crystals, m.p. 171–173°C. IR (KBr, cm^{-1}): 1270, 560; ^1H NMR ($CDCl_3$, δ): see Table I; MS: 251/253 (62/39): M^+—$P(O)Cl_2$, 134 (14): $C_{10}H_{14}^+$, 133 (100): $C_{10}H_{13}^+$, 105 (15), 91 (25).

1,3-Adamantylidendiphosphonic dibromide (**2b**). A mixture of 1,3-dibromoadamantane (580 mg, 2 mmol)[7], PBr_3 (10 ml) and $AlBr_3$ (2.2 g, 8 mmol) were heated under reflux for 3 hrs. After purification by column chromatography **2b** (360 mg, 36%) was obtained as colourless crystals, m.p. 222–224°C. IR (KBr, cm^{-1}): 1252, 500; ^1H NMR ($CDCl_3$, δ): see Table I; MS: 339/341/343 (27/52/26): M^+—$P(O)Br_2$, 134 (13): $C_{10}H_{14}^+$, 133 (100): $C_{10}H_{13}^+$, 105 (14), 91 (24).

(3-Chloro-1-adamantyl)phosphonic dichloride (**3a**) *and (3-bromo-1-adamantyl)phosphonic dichloride.* The method used for the synthesis of **2a** was also applied for the syntheses of **3a** and its 3-bromo derivative, but only an equimolar amount of PCl_3 and $AlBr_3$ was used. Trials to separate the products by preparative chromatography failed. Their identification is based on the ^{13}C NMR spectrum of the mixture[1] and the mass spectrum: 251/253 (14/5): $C_{10}H_{14}P(O)Cl_2^+$, 213/215 (1/1): $C_{10}H_{14}Br^+$, 169/171 (100/51): $C_{10}H_{14}Cl^+$, 134 (6): $C_{10}H_{14}^+$, 133 (63): $C_{10}H_{13}^+$, 91 (30).

(3-Bromo-1-adamantyl)phosphonic dibromide (**3b**). 1-Adamantylphosphonic dibromide (**1b**) (500 mg, 1.5 mmol) was stirred in a glass autoclave with *t*-butylbromide (0.2 ml), $AlBr_3$ (4.4 g, 17 mmol) and 5 ml bromine at room temperature for 5 days. The viscous reaction mixture was poured onto crushed ice and extracted with methylene chloride. The organic phase was washed with 5% $NaHSO_3$ and Na_2CO_3 solutions and evaporated. After chromatographic purification **3b** (200 mg, 33%) was obtained as colourless crystals, m.p. 104–105°C. IR (KBr, cm^{-1}): 1258, 680, 488; ^1H NMR ($CDCl_3$, δ) see Table I; MS: 339/341/343 (24/47/23): M^+-$P(O)Br_2$, 213/215 (49/44): $C_{10}H_{14}Br^+$, 134 (15): $C_{10}H_{14}^+$, 133 (100): $C_{10}H_{13}^+$, 105 (16), 91 (33).

ACKNOWLEDGMENT

The authors are grateful to Dr. D. Müller, Bochum, for measuring the mass spectra. M.H.A.E. thanks the Alexander von Humboldt-foundation for a grant and A.G.H. the German Academic Exchange Service (DAAD) for a scholarship in the frame of the Channel Program between the Federal Republic of Germany and the Arab Republic of Egypt. This work was supported by the *Fonds der Chemischen Industrie*.

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