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Tetrakis(trimethylsilyl) isocyanatomethylenebisphosphonate

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Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(N–C) = 0.003 Å
Disorder in main residue
R factor = 0.035
wR factor = 0.102
Data-to-parameter ratio = 21.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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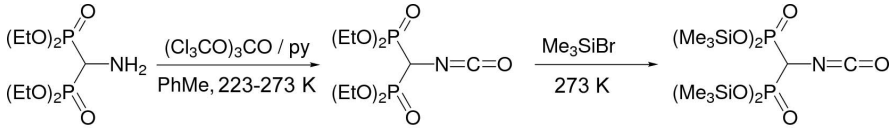
Syntheses of tetraethyl isocyanatomethylenediphosphonate and the title compound, $C_{14}H_{37}NO_7P_2Si_4$, are reported. The structure of the latter shows disorder of the isocyanate group, but bond lengths and angles within this group are normal.

Comment

Bisphosphonates are a valuable class of compounds due to their ability to participate in calcium metabolism in bones, thus opening up possibilities for effective treatment of various bone diseases (Body, 1998; Sparidans *et al.*, 1998). Recently, bisphosphonates have been used in the treatment of bone metastasis diseases (Mundy & Yoneda, 1998; Smith, 2003). A relatively new use for bisphosphonic acids has been in the development of targeted anticancer drugs (El-Mabhouh *et al.*, 2004), leading us to view compounds bearing the desired bisphosphonate moiety and a reactive pre-linker as our synthetic targets. We report here an efficient synthetic approach, leading to the title compound, (3), as a precursor to new drugs.



(1) (2) (3)

Reaction of tetraethyl aminomethylenediphosphonate, (1), with triphosgene affords tetraethyl isocyanatomethylenediphosphonate, (2), which may be treated with trimethylsilyl bromide to produce the title compound, tetrakis(trimethylsilyl) isocyanatomethylenebisphosphonate, (3). The structure of (3) is shown in Fig. 1. Although the isocyanate group is disordered (Fig. 2), the distances and angles involving the disordered components are in satisfactory mutual agreement. The isocyanate N=C bond distance values are slightly less than the shortest previously observed (1.131 Å) for an isocyanate group bound to carbon (Chini *et al.*, 1988), but the difference is statistically insignificant (and the aforementioned disorder makes the present values less reliable).

Experimental

For the preparation of tetraethyl isocyanatomethylenediphosphonate, (2), a solution of tetraethyl aminomethylenediphosphonate, (1) (3.0 g, 9.9 mmol), and pyridine (1.57 g, 1.60 ml, 19.8 mmol) in toluene (50 ml) was slowly (15 min) added dropwise to a stirred cooled (223 K) solution of triphosgene [$(Cl_3CO)_2C{=}O$: 1.2 g, 3.7 mmol] in toluene (100 ml). After the addition was complete, the reaction mixture was allowed to warm to 273 K and stirred at this temperature

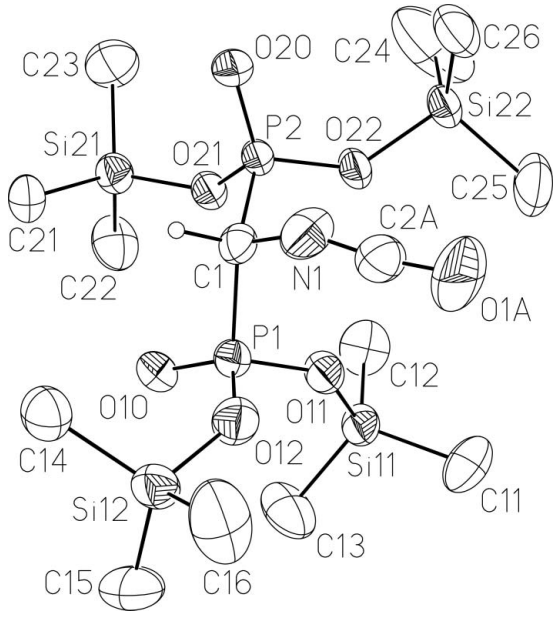


Figure 1
View of (3), with displacement ellipsoids drawn at the 50% probability level. The methine H atom is drawn as a sphere of arbitrary radius, while methyl H atoms are not shown. Atoms O1*A* and C2*A* were refined at 0.65 occupancy (O1*B* and C2*B* of 0.35 occupancy are not shown).

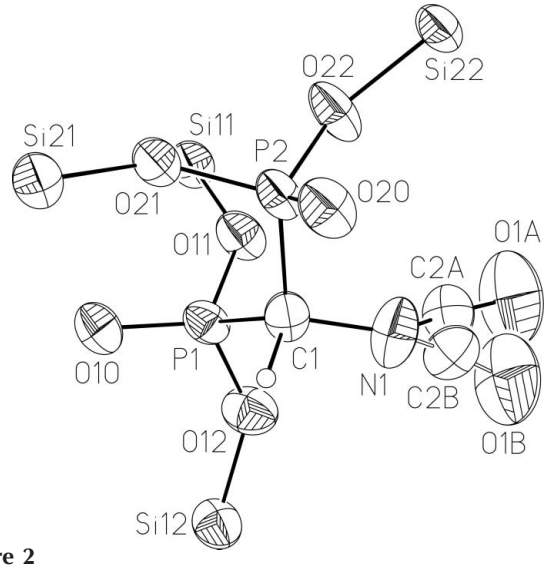


Figure 2
Illustration of the disorder of the isocyanate group. Methyl C atoms bound to silicon have been omitted.

for an additional 2 h. The precipitate of pyridinium chloride was filtered off under argon and washed with toluene (2 × 15 ml), after which the combined toluene solutions were evaporated under vacuum and the residue distilled (yield: 2.7 g, 8.1 mmol, 82%; b.p. 408–413 K/0.15 mm Hg). For the preparation of tetrakis(trimethylsilyl) isocyanatomethylenebisphosphonate, (3), neat (2) (1.67 g, 5.1 mmol) was reacted with an eightfold excess of Me_3SiBr (6.23 g, 5.35 ml, 4.07 mmol) at 273 K for 48 h. The excess Me_3SiBr was evaporated under vacuum and the residue distilled (yield: 2.4 g, 4.7 mmol, 93%; b.p. 393 K/0.05 mm Hg). The slightly yellow liquid solidifies on standing or cooling (m.p. 317–318 K). Single crystals suitable for diffraction measurements were obtained by slowly cooling molten (3).

Crystal data

$C_{14}H_{37}NO_7P_2Si_4$
M_r = 505.75
Monoclinic, $P2_1/n$
a = 10.2012 (6) Å
b = 26.7355 (15) Å
c = 11.0576 (6) Å
β = 107.6500 (9)°
V = 2873.8 (3) Å^3
Z = 4
D_x = 1.169 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 6971 reflections
θ = 2.4–26.4°
μ = 0.35 mm^{-1}
T = 193 (2) K
Prism, pale yellow
0.47 × 0.43 × 0.43 mm

Data collection

Bruker SMART 1000 CCD area-detector/PLATFORM diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.854, T_{max} = 0.865
21 491 measured reflections
5905 independent reflections
5076 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
θ_{max} = 26.4°
$h = -12 \rightarrow 12$
$k = -33 \rightarrow 33$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.102
S = 1.03
5905 reflections
272 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0569P)^2 + 0.9513P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

P1—O10	1.4596 (14)	Si12—O12	1.6713 (14)
P1—O11	1.5502 (12)	Si21—O21	1.6826 (13)
P1—O12	1.5617 (14)	Si22—O22	1.6730 (12)
P1—C1	1.8214 (17)	O1*A*—C2*A*	1.164 (9)
P2—O20	1.4653 (12)	O1*B*—C2*B*	1.162 (17)
P2—O21	1.5514 (13)	N1—C1	1.447 (2)
P2—O22	1.5539 (12)	N1—C2*A*	1.129 (9)
P2—C1	1.8253 (18)	N1—C2*B*	1.111 (17)
Si11—O11	1.6813 (13)		
O10—P1—O11	116.85 (8)	P1—O11—Si11	136.56 (9)
O10—P1—O12	115.46 (8)	P1—O12—Si12	135.64 (10)
O11—P1—O12	103.12 (8)	P2—O21—Si21	134.84 (8)
O10—P1—C1	113.06 (8)	P2—O22—Si22	136.75 (8)
O11—P1—C1	104.03 (7)	C1—N1—C2*A*	141.6 (4)
O12—P1—C1	102.63 (8)	C1—N1—C2*B*	151.4 (9)
O20—P2—O21	115.85 (7)	P1—C1—P2	117.44 (9)
O20—P2—O22	115.37 (7)	P1—C1—N1	111.79 (12)
O21—P2—O22	103.97 (7)	P2—C1—N1	107.95 (13)
O20—P2—C1	111.43 (8)	N1—C2*A*—O1*A*	170.3 (9)
O21—P2—C1	104.54 (7)	N1—C2*B*—O1*B*	174.8 (12)
O22—P2—C1	104.46 (8)		

Disorder within the isocyanate (—N═C═O) group was handled by splitting the C and O atoms into two sets of positions (C2*A*/O1*A* and C2*B*/O1*B*), which were given respective occupancy factors of 0.65 and 0.35. Occupancy factors were chosen that allowed the U_{eq} values for corresponding atoms (O1*A*/O1*B* and C2*A*/C2*B*) to refine to comparable values, and produced roughly equivalent N—C and C—O distances in the disordered fragments. H atoms were placed in idealized positions according to the sp^3 geometries about their parent C atoms, at C—H distances of 0.98 (methine) or 1.00 Å (methyl), and with $U_{iso}(H) = 1.2U_{eq}(C)$.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics:

SHELXTL (Bruker, 2003); software used to prepare material for publication: *SHELXTL*.

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