closely related to sialic acid. On the other hand, such an interaction is not possible for the side chains of the other two sugar units since the rigidity is created by the glycosidic linkage fixed at C-8. Other possible explanations cannot be simply ruled out. For example, the different pK_a values of these carboxyl groups[8] may result in such regioselectivity. However, our speculation waits for the isolation and purification of both monolactone trimers for further NMR studies;[6] computer modeling is currently in progress.

In conclusion, two different methods are presented to obtain the two possible monolactones of an α-2,8-linked trisialic acid with regioselectivity. The neuraminidase hydrolysis demonstrates a novel way to distinguish both regioisomers from each other. The methods developed here can be further extended and applied to prepare other lactonized oligomers for the investigation of their unknown biological functions.

Experimental Section

Reagents: *N*-Acetylneuraminic acid trimer ($[\rightarrow 8\text{Neu5Ac}\alpha 2\rightarrow]_3$) was obtained from NGK Biochemical Ltd. (Handa, Japan) with the help of Prof. Yasuo Inoue. Neuraminidase from *Anthrobacter ureafaciens* was purchased from Sigma (St. Louis, USA). All other reagents for reactions and high-performance capillary electrophoresis (HPCE) were of the highest grade commercially available.

Lactonization of the α-2,8-linked tri-*N*-acetylneuraminic acid: Free trimers of [$\alpha 2\rightarrow 8$] *N*-acetylneuraminic acid (25 µg) were incubated in glacial acetic acid (1 mL) at room temperature. The reaction mixtures were frozen with liquid nitrogen and then dried immediately by SpeedVac (Savant, USA) to remove acetic acid. Dried samples were dissolved in doubly distilled water, and an aliquot (5 µL) of the mixture was analyzed by HPCE.

Preparation of the dilactone **4**: free trimers of [$\alpha 2\rightarrow 8$] *N*-acetylneuraminic acid (25 µg) were left in glacial acetic acid (1 mL) at room temperature for 8 h, frozen with liquid nitrogen, and then dried immediately by SpeedVac (Savant, USA) to remove acetic acid.

Hydrolysis of **4**: A sample of **4** (50 µg) was dissolved in 0.1 N $(NH_4)_2CO_3$ (500 µL) at 37 °C. After 20, 40, and 80 min an aliquot was removed, frozen with liquid nitrogen, and then dried by SpeedVac (Savant, USA). Dried samples were dissolved in doubly distilled water, and an aliquot (5 µL) of the mixture was analyzed by HPCE.

Chromatographic analysis: Capillary electrophoreses (CE) were performed on a Beckman capillary electrophoresis system (P/ACE 2100) with a fused silica capillary (118 cm × 75 µm (inner diameter)) at 20 kV and 25 °C. Phosphate buffer (50 mM, pH 8.0) was used as the running buffer. The UV absorption at 200 nm was monitored. Samples were injected into the capillary under a high pressure of nitrogen (1.3 bar) for 3 s. The capillary was regenerated by washing with doubly distilled water for 3 min and then 0.1 N NaOH for 5 min.

Neuraminidase hydrolysis: Partially lactonized samples (10 µg) in 100 mM ammonium acetate buffer (pH 5) were digested with neuraminidase (1 mU) from *Anthrobacter ureafaciens* in 20-µL CE vials at room temperature. The progress of hydrolysis was monitored by HPCE at regular time intervals.

Fast atom bombardment (FAB) mass spectrometry: Negative-mode FAB mass spectra of the samples were obtained on an Autospec OA-TOF mass spectrometer (Micromass, UK) fitted with a cesium ion gun operated at 26 kV. Samples were dissolved in Milli Q water for loading on to the probe tip coated with monothioglycerol as matrix.

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[6] Based on the results of 2D NMR experiments, the partial assignment of compound **2** is given in the following. The detailed and complete NMR characterizations are currently in progress and will be published in due course. ^{1}H NMR (500 MHz, HOD): $\delta = 1.694$ (1 H, t, $J_{3a\text{-}3e} = J_{3e\text{-}4} = 12$ Hz, H-3a[II]), 1.740 (1 H, t, $J_{3a\text{-}3e} = J_{3e\text{-}4} = 12$ Hz, H-3a[III]), 1.830 (1 H, t, $J_{3a\text{-}3e} = J_{3e\text{-}4} = 13$ Hz, H-3a[I]), 2.065 (6 H, s, 2 acetyl), 2.088 (3 H, s, acetyl), 2.229 (1 H, dd, $J_{3e\text{-}3a} = 12$, $J_{3e\text{-}4} = 4.5$ Hz, H-3e[I]), 2.254 (1 H, dd, $J_{3e\text{-}3a} = 12$, $J_{3e\text{-}4} = 4.5$ Hz, H-3e[III]), 2.814 (1 H, dd, $J_{3e\text{-}3a} = 12$, $J_{3e\text{-}4} = 4.5$ Hz, H-3e[II]), 3.625 (1 H, m, H-4[II]), 3.651 (1 H, m, H-4[III]), 3.802 (1 H, m, H-5[III]), 3.895 (1 H, m, H-5[I]), 3.973 (1 H, m, H-5[II]), 4.022 (1 H, m, H-4[I]). [I] is defined as the sugar unit located at the reducing terminal of **2**, and [III] is at the nonreducing end. For this assignment, see also T. Ercégovic, G. Magnusson, *J. Org. Chem.* **1996**, *61*, 179–184; ref. [4].

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Convergent Route to Organometallic Dendrimers Composed of Platinum–Acetylide Units[**]

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Nobuaki Ohshiro, and Shigetoshi Takahashi[*]

There is increasing interest in the development of new strategies to synthesize well-defined nanosize macromolecules with specific functions. Dendrimers have a regularly branched architecture and have large, spherical dimensions to meet the requirements for new materials.[1] One method for the functionalization of dendrimers is the incorporation of

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transition metals that exhibit some characteristic properties. Most organometallic dendrimers reported previously, however, contain metal atoms either only at the core[2] or at the surface,[3] and organometallic dendrimers with transition metals in every generation have so far been less studied.[4] Since such organometallic dendrimers are built up by successive organometallic reactions, the strategy is severely limited because of the low stability of organometallic complexes relative to organic compounds.

We reported previously the synthesis of platinum–acetylide dendrimers, which utilized triethynylmesitylene as a bridging ligand to build up a heneicosanuclear complex, which is a second generation dendrimer.[5] Metal–acetylide dendrimers may have potential applicability as new materials, since some metal acetylides are known to show unique properties.[6] However, it would be difficult to extend the method that we employed previously to synthesize higher generation dendrimers, because of the large effort required to isolate the resulting dendrimers from the reaction mixture when no protecting groups were used. Herein we wish to report an efficient route for the synthesis of an organometallic dendrimer composed of platinum–acetylide units in the main chain by a convergent method. The methodology involves the use of two kinds of trialkylsilyl protecting groups, trimethylsilyl and tri(isopropyl)silyl, of the terminal acetylene unit for the synthesis of platinum–acetylide dendrimers.[7]

The triethynylbenzene derivatives, which were used as the bridging ligand, were protected as shown in Scheme 1. Treatment of 1,3-dibromo-5-iodobenzene (**1**) with one equivalent of tri(isopropyl)silylacetylene at room temperature in the presence of a $[PdCl_2(PPh_3)_2]$/CuI catalyst in diethylamine led to the selective formation of the mono(silylethynyl) derivative **2**, which was converted quantitatively into a tri(silylethynyl) derivative **3** by the reaction with excess trimethylsilylacetylene in triethylamine under reflux.[8] Since a tri(isopropyl)sily group is less reactive towards a base than a trimethylsilyl group,[7] selective desilylation of the trimethylsilyl group was performed with K_2CO_3 in acetone to give compound **4**, which had two terminal acetylenic groups in the molecule. *p*-Methoxyphenylethynylplatinum groups, which would eventually become the chain-end groups of our dendrimers, were introduced by the reaction of **4** with two equivalents of the platinum complex **5** in the presence of a CuCl catalyst at room temperature to give the dinuclear acetylide complex **6**.[9] Removal of the tri(isopropyl)silyl group in **6** by the treatment with Bu_4NF gave the first generation dendron **7**. The molecular structure of **7** was determined by X-ray analysis (Figure 1).[10]. The Pt–C bond distances are in the range of 1.992(9)–2.01(1) Å, which are slightly longer than those of the triethynylmesitylene-bridged triplatinum complex **8** because of the strong *trans* influence of an ethynyl group relative to a chloride ligand.[5] The coordination planes around the Pt atoms in **7** are approximately perpendicular to the aromatic plane of the central bridge and parallel to the aromatic plane of *p*-methoxyphenylethynyl groups, while in **8** the former arrangement has dihedral angles of about 60°.[5]

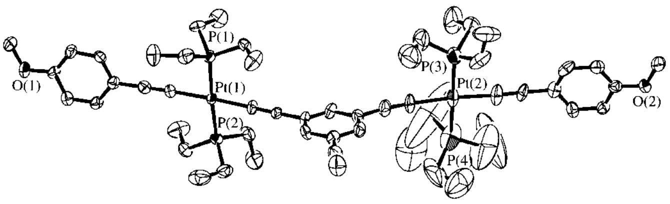
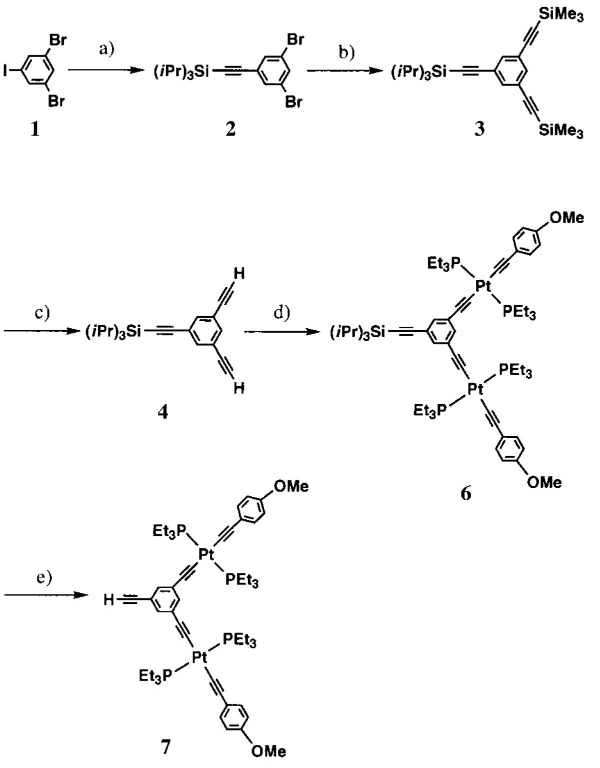


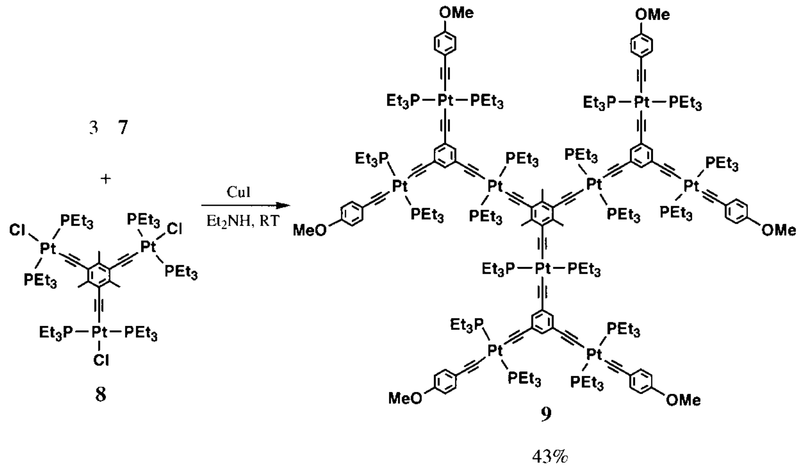
Figure 1. Molecular structure of the first generation dendron **7**. Hydrogen atoms are omitted for clarity.



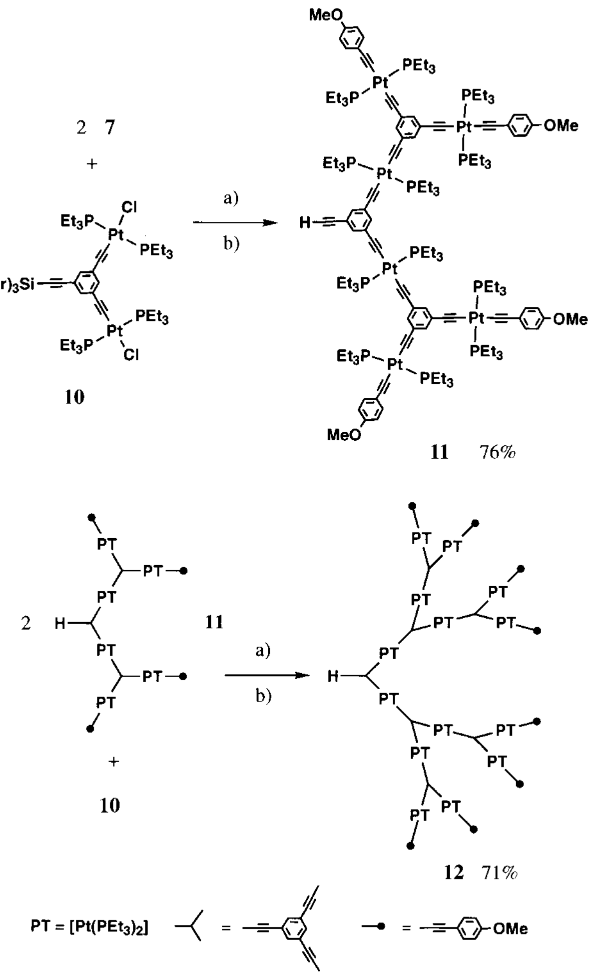
Scheme 1. Synthesis of the first-generation dendron **7**. a) $HC{\equiv}CSi\textit{i}Pr_3$, $[Pd(PPh_3)_2Cl_2]$ (cat.), CuI (cat.), Et_2NH, RT, quantitative yield; b) $HC{\equiv}CSiMe_3$, $[Pd(PPh_3)_2Cl_2]$ (cat.), CuI (cat.), Et_3N, benzene, reflux, 90%; c) K_2CO_3 (aq), acetone, reflux, 95%; d) $Cl(Et_3P)_2Pt{\equiv}CC_6H_4OMe$ **5** (2 equiv), CuI (cat.), Et_2NH, RT, 96%; e) Bu_4NF, THF, −78 °C → RT, 95%.

The first-generation dendrimer **9**, which contained nine platinum atoms, was prepared by the reaction of **7** with the core complex **8** in a 3:1 molar ratio (Scheme 2). The ^1H NMR spectrum of **9** showed two singlets at $\delta = 2.57$ and 3.78 in a 1:2 integral ratio; the former signal is assignable to the methyl protons of the central mesitylene group and the latter to the methoxy protons of the end group. The $^{31}P\{^1H\}$ NMR spectrum of **9** exhibited two singlets at $\delta = 10.88$ ($J_{Pt,P} = 2381$ Hz) and 11.10 ($J_{Pt,P} = 2392$ Hz) in a 2:1 integral ratio, which correspond to the phosphane groups bound to the six outer and to three inner platinum atoms, respectively. These data are consistent with the expected structure of **9**, which is also supported by IR and elemental analyses.

The first-generation dendron **7** was successfully grown to a second-generation dendron **11** by the reaction with **10** in a 2:1 molar ratio, followed by desilylation of the tri(isopropyl)silyl group (Scheme 3). The similar reaction of **10** with **11** resulted in the formation of the third generation dendron **12**. Reactions of **11** and **12** with **8** in a 3:1 molar ratio led to the formation of the second and third-generation dendrimers **13**

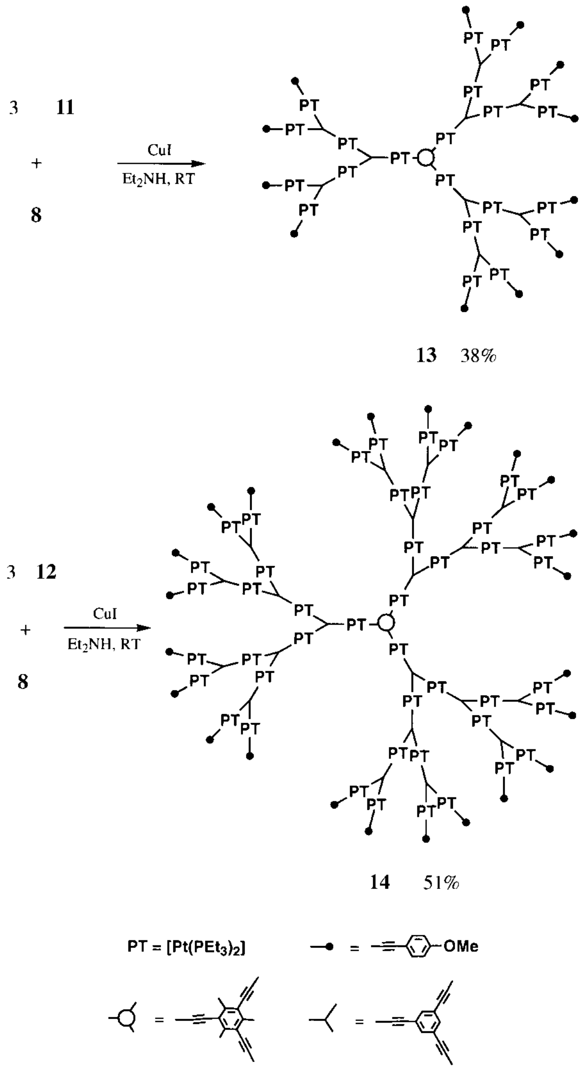


Scheme 2. Synthesis of the first generation dendrimer **9**.



Scheme 3. Synthesis of the second- and third-generation dendrimers **11** and **12**, respectively. a) CuI (cat.), Et_2NH, RT; b) Bu_4NF, THF, $-78\,^{\circ}C \rightarrow$ RT.

and **14**, respectively (Scheme 4). The ^1H NMR spectrum of **14** (Figure 2) is very simple in spite of it being an extremely large molecule ($M_r = 25\,840$), which indicates a highly symmetric structure. Two singlet signals are observed at $\delta = 2.57$ and 3.77 from the central mesitylene group and the methoxy end group, respectively, in a 1:8 integral ratio, which supports the proposed structure of **14**. The $^{31}P\{^1H\}$ NMR spectrum of **14** showed only two signals at $\delta = 10.84$ ($J_{Pt,P} = 2381$ Hz) and 11.04 (the coupling constant $J_{Pt,P}$ could not be determined since the satellite signals were too weak to be detected) in an about 14:1 integral ratio. The latter signal is assigned to the central six phosphanes, and the the former to the other eighty four phosphane atoms. To the best of our knowledge **14**, which contains 45 platinum atoms in a molecule, is one of the largest organotransition metal dendrimers and belongs to nanosize materials.



Scheme 4. Synthesis of the second- and third-generation dendrimers **13** and **14**.

In summary, a methodology for the efficient synthesis of very large platinum–acetylide dendrimers that contain up to 45 platinum atoms has been developed by a convergent method that uses two kinds of trialkylsilyl groups. The method presented here may be applied to the synthesis of metal–acetylide dendrimers other than platinum, since several stable transition metal–acetylide complexes are already known.[9, 11]

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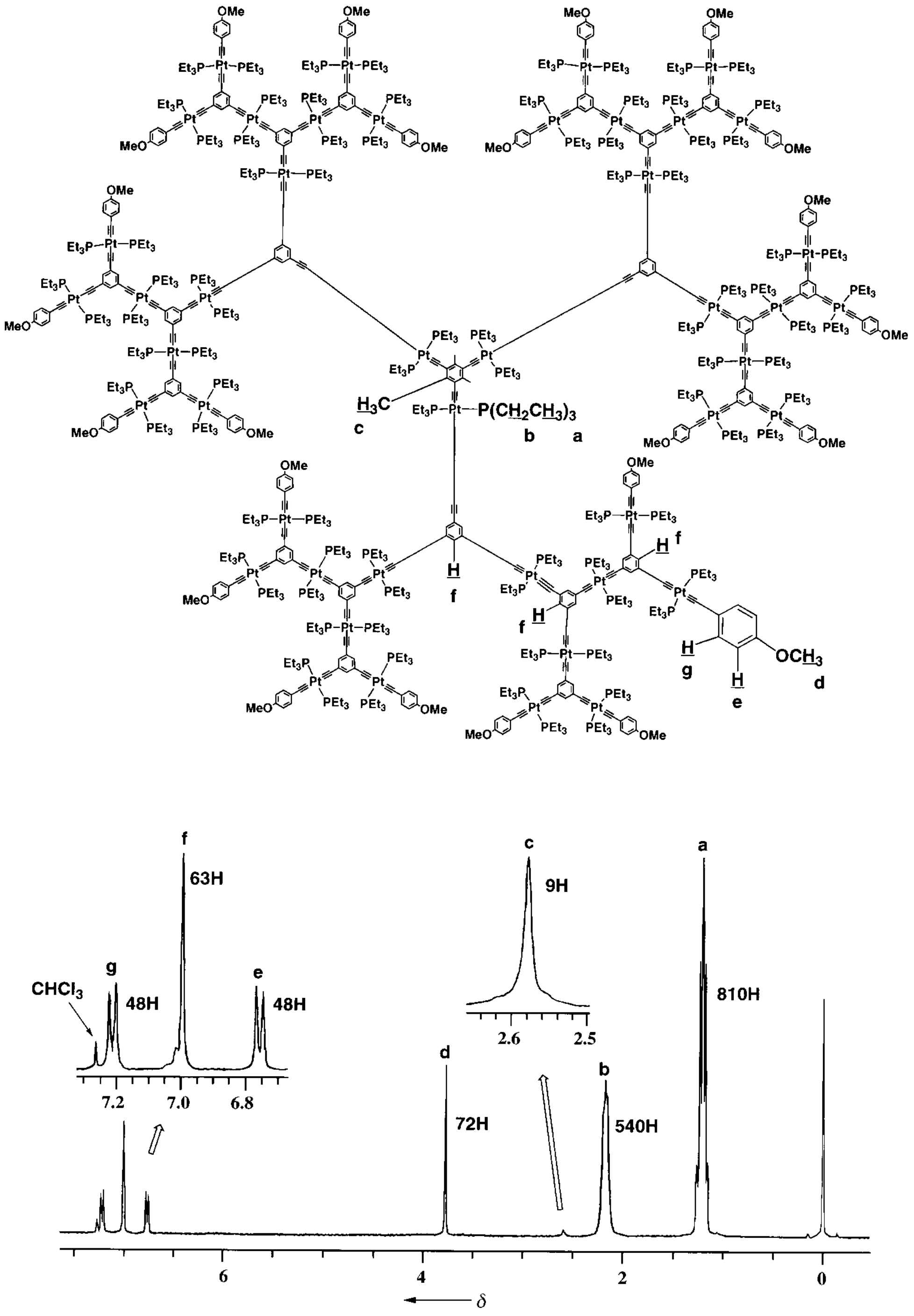

Figure 2. Structure and ^1H NMR spectrum (in $CDCl_3$) of the third-generation dendrimer **14**.

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[10] Crystallographic data for **7**: $C_{54}H_{78}O_2P_4Pt_2$ ($M_r = 1273.28$), monoclinic, space group $P2_1/c$ (No. 14), $a = 24.461(3)$, $b = 10.286(3)$, $c = 22.814(4)$ Å, $\beta = 106.50(1)^\circ$, $V = 5503(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.536$ g cm^{-3}, $\mu(\mathrm{Mo}_{K\alpha}) = 52.10$ cm^{-1}, $-75\,^\circ$C, $\omega - 2\theta$ scan, $6 < 2\theta < 55^\circ$, R (R_w) = 0.051 (0.061) determined by full-matrix least-squares method for 559 parameters against 6391 reflections with $I > 3.0\sigma(I)$ from 12638 unique reflections ($R_{int} = 0.037$), GOF = 1.07. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102875. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-011; e-mail: deposit@ccdc.cam.ac.uk).

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