H), 7.02 (dd, 2 H, J = 8, 7 Hz), 2.48 (s, 3 H). MS: m/z 534 (M^+, 100), 504 (35), 366 (16), 203 (24). Exact mass 534.1581, calcd for $C_{35}H_{22}N_2O_4$ 534.1579.

9,14-Bis[4-(methylthio)phenyl]benzo[*b*]triphenylene (6). $NaSCH_3$ (51 mg, 0.73 mmol) was added to an argon-purged solution of compound 8 (72 mg, 0.12 mmol) in HMPA (5 mL), and the solution was heated at 80 °C for 13 h under an argon atmosphere. After cooling to room temperature, brine (15 mL) was added, and the mixture was extracted with ether (3 × 15 mL). The combined organic extracts were dried and concentrated to leave a brown oil. Purification by preparative TLC (1:1 hexane–benzene) gave 8.4 mg (13%) of the desired compound 6. Single crystals, mp 260–261 °C, were grown from solutions of 6 in CH_2Cl_2–MeOH. ^1H NMR ($CDCl_3$, 270 MHz): δ 8.27 (dd, 2 H, J = 8, 1 Hz), 7.95 (m, 2 H), 7.56 (dd, 2 H, J = 8, 1 Hz), 7.44 (m, 12 H), 7.02 (ddd, 2 H, J = 8, 8, 1 Hz), 2.59 (s, 6 H). MS: m/z 522 (M^+, 100), 474 (6), 426 (9), 352 (6), 350 (7). Exact mass 522.1480, calcd for $C_{36}H_{26}S_2$ 522.1476.

9,14-Bis(4-cyanophenyl)benzo[*b*]triphenylene (10). A solution of compound 8 (39 mg, 0.07 mmol) and cuprous cyanide (12 mg, 0.13 mmol) in DMF (15 mL) was refluxed under argon overnight. After cooling to room temperature, chloroform was added, and the solution was filtered and concentrated. The residue was purified by preparative TLC (benzene) to give 15 mg (47%) of the desired compound 10. Single crystals, mp >400 °C, were grown from solutions of 10 in CH_2Cl_2–acetone. ^1H NMR ($CDCl_3$, 270 MHz): δ 8.31 (dd, 2 H, J = 8, 1 Hz), 7.84 and 7.70 (AA'BB' system, 8 H), 7.78 and 7.52 (AA'BB' system, 4 H), 7.42 (ddd, 2 H, J = 8, 7, 1 Hz), 7.35 (dd, 2 H, J = 8, 1 Hz), 7.03 (ddd, 2 H, J = 8, 7, 1 Hz). MS: m/z 480 (M^+, 100), 377 (15). Exact mass 480.1626, calcd for $C_{28}H_{20}N_2$ 480.1635.

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Supplementary Material Available: Full details for the determination of the X-ray structures of compounds 3–12 and ^1H NMR spectra of compounds 3–16 (148 pages). Ordering information is given on any current masthead page.

Structure of a New Oligomer of Glutaraldehyde Produced by Aldol Condensation Reaction

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Glutaraldehyde (GA) was found to yield a new dimer when treated in an aqueous alkaline solution. This dimer was identified as a substance that had previously been known to be responsible for the high activity of certain immobilized enzymes prepared by using alkali-treated GA solution as a coupling agent. The dimer was isolated, and its structure was investigated by the various spectrometries. UV and IR spectra suggested the existence of an α,β-unsaturated formyl group and a hydroxyl group in its molecule, and GC-MS analysis indicated the molecular formula $C_{10}H_{14}O_3$ (MW 182). The existence of two formyl groups and one hydroxyl group was confirmed by GC-MS of the dimer derived to *O*-(pentafluorobenzyl) oxime (*O*-PFB oxime) and further to its TMS derivative, respectively. The structure of the *O*-PFB derivative was determined by two-dimensional NMR ^1H–^1H and ^1H–^{13}C spin-coupling networks in homonuclear shift correlation spectra and in proton detected heteronuclear multiple-bond connectivity spectra. Taking these results into account, we proposed the structure of the GA dimer.

Glutaraldehyde (GA) has been widely used for tanning of leather, fixation of tissues for electron microscopy, immobilization of bioactive materials such as proteins, enzymes, and microorganisms, preservation of connective tissues for bioprostheses, chemical sterilization, and so on.[1-5] In these applications GA is often dissolved in an aqueous medium and exposed to the physiological pH for a relatively long period of time, during which GA tends to undergo a polymerization reaction. The polymers thus produced include α,β-unsaturated formyl groups in their molecules exhibiting strong UV absorption with maximum absorption at 235 nm, while GA itself shows only a weak absorption maximum at 280 nm.[6] The ratio of absorption at 235 nm to that at 280 nm, therefore, has been used as a purification index.[7] Margel and Rembaum[8] investigated aldol condensation of GA and found that high polymers (poly-GA) were precipitated from the aqueous solutions of pH 7–13.5. The poly-GA included hydroxyl and carboxyl groups in addition to α,β-unsaturated formyl groups in their molecules,[8] but the exact structure could not be determined. On the other hand, the formation of water-soluble GA oligomers has been left obscure because of difficulty in the precise separation and purification. These oligomers as well as the GA monomer, however, seem to play a significant role in the above-mentioned utilities of GA. It has been known that GA solutions including such types of oligomers show higher efficiency than pure GA solution in fixation of tissues[6] and immobilization of enzyme.[9] For instance, we found that certain enzymes im-

(1) Hayat, M. A. *Fixation for Electron Microscopy*; Academic Press: New York, 1981.
(2) Russell, A. D.; Hopwood, D. *Progr. Med. Chem.* **1976**, *13*, 271.
(3) Monsan, P. *Eur. J. Appl. Microbiol. Biotechnol.* **1978**, *5*, 1.
(4) Nimni, M. E.; Cheung, D.; Strates, B.; Kodama, M.; Sheikh, K. *J. Biomed. Mater. Res.* **1987**, *21*, 741.
(5) Gorman, S. P.; Scott, E. M. *J. Appl. Bacteriol.* **1980**, *48*, 161.
(6) Robertson, E. A.; Schultz, R. L. *J. Ultrastruct. Res.* **1970**, *30*, 275.
(7) Anderson, P. J. *J. Histochem. Cytochem.* **1967**, *15*, 652.
(8) Margel, S.; Rembaum, A. *Macromolecules* **1980**, *13*, 19.
(9) Makino, K.; Maruo, S.; Morita, Y.; Takeuchi, T. *Biotechnol. Bioeng.* **1988**, *31*, 617.

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mobilized to polymer gel by reaction with alkali-treated GA gave much higher activities than those prepared in a usual manner using untreated GA, though the amounts of protein immobilized were almost equal.[10] This finding suggests that the GA oligomers may be involved in a certain immobilization reaction in addition to the reaction between GA monomers and the enzymes. Several GA oligomers having λ_{max} at 235 nm were detected by the reversed phase HPLC of an alkali-treated GA solution. The aim of the present paper is to investigate the structure of the GA oligomer that was detected as the major peak (compound X) in the HPLC analysis.

Results

The compound X in aqueous solution showed two UV absorption peaks (235 and 302 nm). The peak at λ_{max} 235 nm (extinction coefficient 1.6×10^4 as $C_{10}H_{14}O_3$) is obviously due to the π–π^* transition of a C=C bond, whereas the peak at λ_{max} 302 nm (extinction coefficient 65.7 as $C_{10}H_{14}O_3$) is ascribable to the n–π^* transition of a C=O bond in an α,β-unsaturated formyl group.[10] The latter λ_{max} is known to undergo a red shift in a less polar solvent (e.g., 320 nm in methanol)[11,12] and to suffer a blue shift by substitution of an alkyl group to the C=C bond.[13]

The infrared spectrum of compound X in carbon tetrachloride showed the bands assignable to the C=O (1695 cm^{-1}) and C=C (1640 cm^{-1}) stretching vibrations of the α,β-unsaturated formyl group.[8,14] The spectrum also showed the bands that were assigned to the CH stretching vibration of the formyl group (2720 cm^{-1}) and to the OH stretching vibration of an isolated hydroxyl group (3630 cm^{-1}). High resolution EI-MS indicated the elemental composition of the compound to be $C_{10}H_{14}O_3$ (found 182.0932, calcd 182.0943). This result strongly suggests that compound X was formed by aldol condensation of two GA molecules followed by elimination of one water molecule.

O-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine (*O*-PFBHA) has been known to react with a formyl group and to yield a volatile oxime derivative.[15,16] This is favorable for GC and GC-MS analyses of compound X, in order to avoid thermal decomposition and to estimate the number of the formyl group. The capillary GC-MS analysis of *O*-PFB oxime of compound X showed two distinct GC peaks with retention times of 13.7 and 14.6 min. The TLC separation of these *O*-PFB oximes indicated the spots at R_f 0.62 and 0.70, which correspond, respectively, to the GC peaks with retention times of 13.7 and 14.6 min. Hereafter we call the former as compound XG (R_f 0.62) and the latter as compound XC (R_f 0.70). Since the compound X itself gave a single spot by TLC and a single peak by HPLC, the two GC peaks of the *O*-PFB oximes may be due to the isomeric *O*-PFB derivatives of compound X.[16] In fact, both products gave indistinguishable EI-MS spectra exhibiting a base ion peak at m/z 181 and an ion peak at m/z 572. The peak at m/z 181 is assignable to the PFB ion $(C_7H_2F_5)^+$ and the peak at m/z 572 could be due to the molecular ion formed by the reaction of two *O*-PFBHA molecules ($C_7H_4ONF_5$, molecular weight, 213) with compound X (molecular weight, 182) followed by elimination of two water molecules (i.e., $182 + (213 \times 2) - (18 \times 2) = 572$). The consistent result was also obtained from a CI-MS spectrum, which gave the peak at m/z 573 assignable to the protonated molecular ion. Thus, it follows that compound X includes two formyl groups in its molecule derivable to an *O*-PFB oxime.

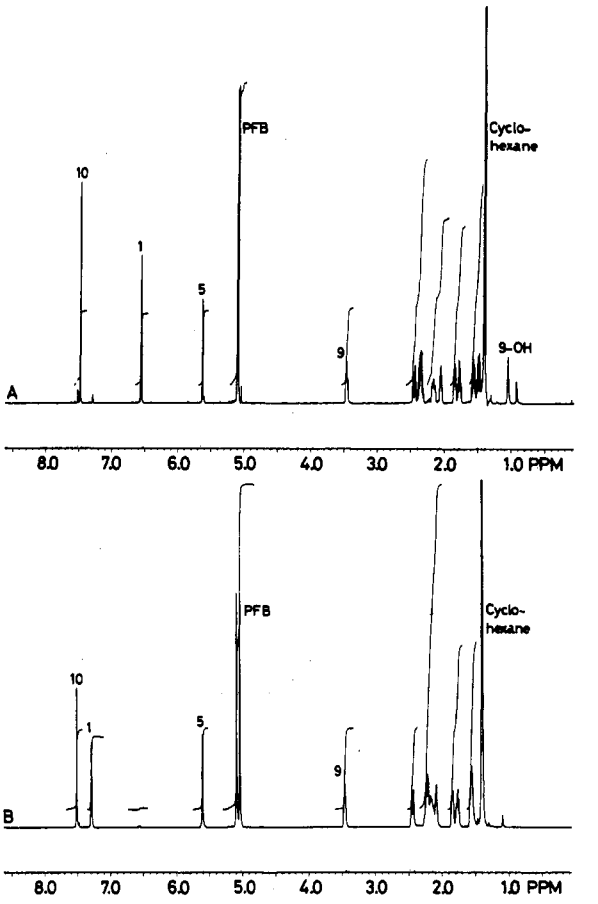


Figure 1. ^1H NMR spectra (600 MHz) of *O*-PFB oxime of compound X in cyclohexane-d_{12}: (A) compound XG; (B) compound XC.

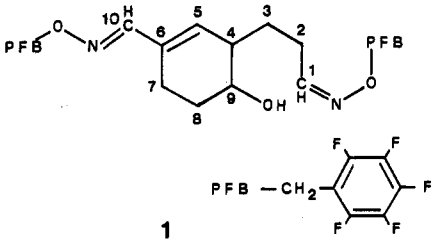
It is expected that if the *O*-PFB oxime of compound X has a hydroxyl group, it will give a TMS derivative by reaction with *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA). The GC-MS analysis of the TMS derivative showed two major GC peaks with retention times of 12.3 and 13.2 min. The CI-MS spectra of these peaks were similar with each other. They showed the ion peaks at m/z 645 and m/z 555. The peak at m/z 645 can be assigned to the protonated TMS derivative, $(572 + TMS)^+$. The elimination of TMS-OH molecule, which is often observed with TMS derivatives, seems to be responsible for the formation of the ion peak at m/z 555. These results confirmed that compound X possesses one hydroxyl group, which can yield a TMS derivative when treated with BSTFA.

Figures 1A and 1B show ^1H NMR spectra of compounds XG and XC in cyclohexane-d_{12}, respectively. In both spectra, the two strong singlet peaks at about 5.1 ppm are due to the methylene protons of *O*-PFB; this observation also gives evidence that there are two *O*-PFB in the *O*-PFB oxime of compound X. In both spectra, expected chemical shifts imply that the peaks labeled 10 and 1 are due to the methine protons of a Schiff base (—CH=N—) and the peak labeled 5 is due to an olefinic proton. The peak labeled 1 showed a triplet splitting and thus the —CH=N— proton is adjacent to a CH_2 group (i.e., —CH_2CH=

(10) Nakagawa, T.; Izawa, K.; Yagi, S.; Shibukawa, A.; Tanaka, H.; Tashima, T.; Imai, M. *Chem. Pharm. Bull.* **1989**, *37*, 2463.
(11) McConnell, H. *J. Chem. Phys.* **1952**, *20*, 700.
(12) Evans, L. K.; Gillam, A. H. *J. Chem. Soc.* **1943**, 565.
(13) Cookson, R. C.; Dandegaonker, S. H. *J. Chem. Soc.* **1955**, 1651.
(14) Margel, S. *J. Polym. Sci. Polym. Chem. Ed.* **1984**, *22*, 3521.
(15) Kobayashi, K.; Tanaka, M.; Kawai, S. *J. Chromatogr.* **1980**, *187*, 413.
(16) Kuijk, F. J. G. M.; Thomas, D. W.; Stephens, R. J.; Dratz, E. A. *Biochem. Biophys. Res. Commun.* **1986**, *139*, 144.

N—); consequently the remaining peak labeled 10 can be ascribed to the —CH=N— proton, which originates from an α,β-unsaturated formyl group. The peak labeled 9 may be assigned to a -CH(OH)- methine proton from its chemical shift. The peaks between 2.5 and 1.0 ppm can be assigned to aliphatic methine and methylene protons in addition to an exchangeable hydroxyl proton.

Both compounds XG and XC in cyclohexane-d_{12} gave 10 carbon peaks besides those due to the *O*-PFB in their complete proton-decoupled ^{13}C NMR spectra. The corresponding DEPT (distorsionless enhancement by polarization transfer)[17] spectra classified these 10 carbons into 4 CH_2, 5 CH, and 1 quaternary carbons. By considering the above-mentioned results, the 3 CH groups and 1 quaternary carbon atom are due to the two formyl groups and one olefin group (—CH=C—). In order to obtain information on connectivities among the 4 CH_2 and 5 CH groups, we observed various two-dimensional spectra, which include ^1H–^1H COSY,[18] NOESY,[19,20] ^{13}C–^1H COSY,[21] and ^1H–^{13}C HMBC[22,23] spectra. The connectivities obtained are summarized in Table I. The C–H COSY spectra gave clear one-bond correlations between proton(s) and a carbon atom; hence, in Table I we used the same numbering scheme for both ^1H and ^{13}C resonances. The numbering scheme was finally ascribed to the structural formula 1. For obtaining unambiguous spin-coupling connectivities from the COSY spectra, it was necessary to assign the methylene protons that belong to the same CH_2 group; this information could also be easily supplied by the C–H COSY spectra and the two methylene protons were distinguished with each other by denoting a and b for the above-mentioned numbering scheme. The connectivities obtained from the COSY and NOESY spectra inform us that both compounds XG and XC have the following two sequences starting from the proton labeled 1 and also from that labeled 7: PFB-ON=CH(1)CH_2-(2)CH_2(3)CH(4)CH(5)=C(6)CH(10)=NO-PFB and -CH_2(7)CH_2(8)CH(9)OHCH(4)-. Interestingly both sequences involve the -CH(4)- group; thus we can easily construct a candidate for the structure of compounds XG and XC by attaching the -CH_2(7)- group of the latter sequence to the quarternary carbon =C(6)- of the former sequence as shown in 1. The ^1H–^{13}C connectivities obtained from the HMBC spectra were due to ^1JCH, ^2JCH, and ^3JCH couplings for the structure of 1, which give strong support to this structure.



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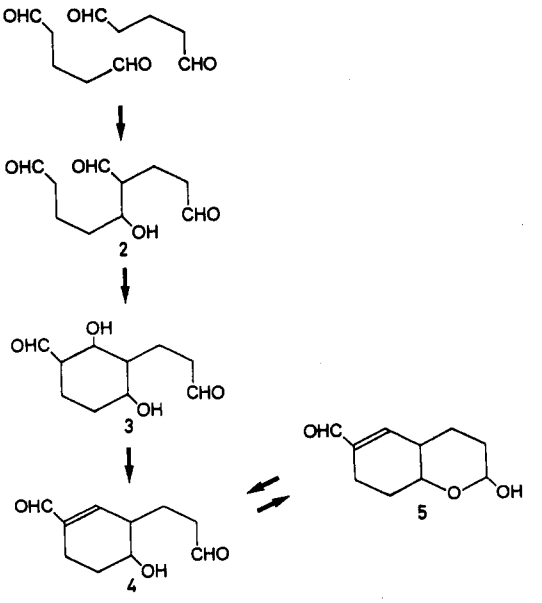
As described thus far, MS and NMR spectroscopic data of compounds XG and XC closely resembled each other. This finding suggests that the two compounds are isomers

Scheme I



produced at the time of the formation of an oxime. One might expect that if the compounds XG and XC are syn–anti isomers concerning the nitrogen atom of the oxime, each of the two compounds would isomerize to the other in solution. This was, in fact, observed in the ^1H NMR spectra of the compounds dissolved as $CDCl_3$ solutions. Both compounds XG and XC gave the same overlapped ^1H NMR spectrum, which consists of an approximately 1:2 ratio of the peaks due to compound XG and those due to compound XC. In cases of aldoxime (RCH=NOH), it is reported that the methine proton of the anti isomer resonates at a higher field (6.65 ppm) than its syn counterpart (7.25 ppm).[24] Accordingly, inspection of chemical shifts of the peaks labeled 10 and 1 in Figures 1A and 1B allows us to conclude that in compound XG the oxime that involves C-1 is anti and the oxime that involves C-10 is syn, as shown in 1; while in compound XC, both oximes take a syn configuration.

Discussion

From the UV, IR, and MS spectra, compound X was indicated to have molecular formula $C_{10}H_{14}O_3$ (molecular weight, 182), which was assignable to a dimer produced by aldol condensation of two GA molecules followed by dehydration. This compound was suggested to bear two formyl groups derivable to *O*-PFB oxime and one hydroxyl group derivable to TMS ether, one of the two formyl groups being substituted to an unsaturated carbon atom. Taking these results and NMR spectroscopic investigations on *O*-PFB oxime into account, we may assume structure 4 as a candidate of compound X (Scheme I). This structure has not so far been proposed as an aldol condensate of GA. Whipple and Ruta reported that GA exists in aqueous solution in equilibrium with its hydrates and hemiacetal.[25] By analogy we conclude that compound X can also take cyclic hemiacetal form (structure 5) in the aqueous solution in equilibrium with structure 4. In the presence of *O*-PFBHA, the equilibrium deviated to 4, yielding di-PFB oxime, which was further derived to the

(17) Doddrell, D. M.; Pegg, D. T.; Bendall, M. R. *J. Magn. Reson.* **1982**, *48*, 323.
(18) Jeener, J. Ampere International Summer School, Basko Polje, Yugoslavia, 1981.
(19) Macura, S.; Ernst, R. R. *Mol. Phys.* **1980**, *41*, 95.
(20) Bodenhausen, G.; Kogler, H.; Ernst, R. R. *J. Magn. Reson.* **1984**, *58*, 370.
(21) Bax, A.; Morris, G. A. *J. Magn. Reson.* **1981**, *42*, 501.
(22) Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285.
(23) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093.
(24) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*; John Wiley & Sons: New York, 1981; p 233.
(25) Whipple, E. B.; Ruta, M. *J. Org. Chem.* **1974**, *39*, 1666.

Table I. Observed ^1H and ^{13}C NMR Chemical Shifts and Connectivities Obtained from COSY, NOESY, C-H COSY, and HMBC of Compounds XG and XC in Cyclohexane-d_{12}

	chemical shift (ppm)				connectivities		
	^1H		^{13}C				
assign[a]	XG	XC	XG	XC	COSY (^1H)	NOESY (^1H)	C-H COSY, HMBC (^{13}C)
1	6.55	7.29	153.4	152.6	2ab	2ab, 3a, 3b, 4	1, 2, 3
2ab	2.34	2.22	24.8	28.8	1, 3a, 3b	3a, 3b, 4	1, 2, 3, 4
3a	1.77	1.76	31.0	31.0	2ab, 3b, 4	2ab, 4	1, 2, 3, 4, 5, 9
3b	1.48	1.56			2ab, 3a, 4	2ab, 4	1, 2, 3, 4, 5, 9
4	2.04	2.08	46.4	46.1	3a, 3b, 5, 9	3a, 3b, 5, 8a,[b] 9, 9-OH[b]	4
5	5.62	5.60	137.7	137.9	4, 7a, 7b	2ab, 3a, 3b, 4, 10	3, 4, 5, 7, 9, 10
6			135.3	135.4			
7a	2.44	2.44	24.2	24.2	7b, 8a, 8b	7b, 8b	5, 6, 7, 8, 9
7b	2.15	2.14			7a, 8a, 8b	7a, 8a	5, 6, 8[b]
8a	1.84	1.84	32.9	32.6	7a, 7b, 8b	7b, 8b, 9-OH[b]	4, 6, 7, 8, 9
8b	1.56	1.55			7a, 7b, 8a	4,[b] 7a, 8a, 9-OH[b]	4, 6, 7, 8, 9
9	3.45	3.45	72.7	72.8	4, 8a, 8b, 9-OH	2ab,[b] 3a, 3b,[b] 4, 7b, 8a, 8b,[c] 9-OH[b]	3, 7,[c] 9[c]
10	7.47	7.51	153.1	153.2	5, 7a, 7b[b]	5	5, 6, 7, 10

[a] The numbering scheme is shown in structural formula 1. [b] Observed only in compound XG. [c] Observed only in compound XC.

TMS ether by reaction with BSTFA.

The mechanism for the formation of **5** from GA can be explained by the dimolecular aldol condensation (Scheme I). The reaction is initiated by the attack of a carbon α to a formyl group in one GA molecule on the formyl group of another GA molecule. The dimer **2** thus formed can undergo intramolecular aldol condensation to form saturated six-membered ring **3**, followed by dehydration to yield α,β-unsaturated aldehyde **4**. This compound readily forms cyclic acetal structure **5**.

Experimental Section[26]

Preparation of GA Oligomer (Compound X). An aqueous 20% solution of GA was diluted twice with water and alkalized to pH 8.5 with sodium bicarbonate (final concentration 0.3 mol dm^{-3}) and, if necessary, with an appropriate volume of 1 mol dm^{-3} of sodium hydroxide. The alkalized solution was kept at 60 °C for 1 h, cooled to room temperature, and neutralized to pH 7.0 with 1 mol dm^{-3} of hydrochloric acid. A 250-mL portion of the solution was fed at a flow rate of 5 mL/min to a glass column (160 mm × 30 mm i.d.) packed with 90 g of octylsilyl silica. The column was washed with 200 mL of water to remove GA monomer, and the GA oligomers remaining in the column were eluted out with 10% acetonitrile. The first 300 mL of eluant was discarded, and the following 400-mL portion was collected and extracted three times with each 400 mL of ethyl acetate. The organic layers were combined and the solvent was evaporated to dryness under reduced pressure at room temperature. The residue was submitted to flash chromatography (eluent, hexane/ethyl acetate = 2:8). The eluent was fractionated, the fractions exhibiting a single spot (R_f 0.6) on silica gel TLC were collected, and the solvent was completely removed. The residue was distilled under highly reduced pressure (2×10^{-3} mmHg) at 110 °C using a glass tube oven. The distillate, a white solid with a melting point of 85 °C (uncorrected), gave single peak by reversed phase HPLC. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74; O, 26.34. Found: C, 64.39; H, 7.61; O, 26.69.

Preparation of *O*-(Pentafluorobenzyl)oxime (*O*-PFB Oxime) of Compound X (Compounds XG and XC). A 520-mg sample of compound X was dissolved in 20 mL of water and added gradually to 50 mL of an aqueous solution containing 3 g of *O*-PFBHA hydrochloride. The mixture was stirred for 4 h at room temperature and then extracted with 50 mL of a hexane/ethyl ether (1:1) mixed solvent. The organic layer was washed three times with equal volume of water, and the solvent was evaporated under reduced pressure at 40 °C to given the *O*-PFB oxime of compound X as a pale yellow oil. The *O*-PFB oximes of compound X consisting of compounds XG and XC were separated by flash chromatography (hexane/ethyl acetate = 6:4). After evaporating the eluent under the reduced pressure at 40 °C, each residue was dissolved in cyclohexane and cooled to 4 °C; compound XG was obtained as needle crystals (mp 77.5–79.5 °C) and compound XC as amorphous powders (mp 63.0–65.0 °C). The purity of the title compounds was judged to be >95% by ^1H and ^{13}C NMR spectral determinations.

Preparation of Trimethylsilyl (TMS) Derivative of the *O*-PFB Oxime of Compound X. The *O*-PFB oxime derivative of compound X was dissolved in 1 mL of pyridine, added with 2 mL of BSTFA, and kept at room temperature for 2 days. Then, the mixture was evaporated under reduced pressure at 50 °C.

Registry No. 1, 130434-30-9; 4, 130434-31-0; GA, 111-30-8.

Supplementary Material Available: Reversed phase contour chromatogram, UV and IR spectra, and EI-MS spectrum of compound X, GC-MS spectra, COSY and HMBC NMR spectra of *O*-PFB oxime of compound X, and GC-MS spectra of TMS derivative of *O*-PFB oxime of compound X (8 pages). Ordering information is given on any current masthead page.

(26) The eluent in silica gel TLC was hexane/ethyl acetate (2:8, v/v) for compound X and hexane/ethyl acetate (6:4) for the *O*-PFB oxime of compound X. Reversed phase HPLC was performed by using an octadecylsilyl silica column (Inertsil ODS 5 μm, 15 cm × 4 mm) and on a liquid chromatograph equipped with a multichannel photodiode array detector. GC-MS analyses of compounds XG and XC and their TMS derivatives were carried out on a Model DX-303 GC-MS system (JEOL). The GC separation was done on a capillary column (25 m × 0.32 mm i.d., Model ULTRA #2, Hewlett Packard). The mass spectra of compound X were measured by the direct insertion method. NMR spectra were measured on a Bruker AM-600 (^1H, 600 MHz, ^{13}C, 150 MHz) or on a Bruker AC-300 (^1H, 300 MHz, ^{13}C, 75 MHz) spectrometer at 27 °C. ^1H chemical shifts were referenced to the peak due to the residual cyclohexane in cyclohexane-d_{12} as 1.4 ppm relative to TMS; ^{13}C chemical shifts were referenced to cyclohexane-d_{12} as 27.8 ppm relative to TMS. NOESY spectra were measured with mixing times of 0.8 and 1.0 s. In HMBC spectra, delay times for evolution of the heteronuclear multiple-quantum coherences due to long-range ^nJCH couplings were 30 and 60 ms.