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Synthesis and Characterization of α,β-Unsaturated Hydroximoyl Chlorides and Hydroximates

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New α,β-unsaturated hydroximoyl chlorides (PhC(Cl)=CHC(Cl)=$NOCH_3$) and hydroximates (PhC(OCH_3)=CHC(OCH_3)=$NOCH_3$) were prepared. The *ZZ*-isomer of PhC(Cl)=CHC(Cl)=$NOCH_3$ was prepared in four steps from ethyl benzoylacetate. Ultraviolet irradiation of the *ZZ*-isomer gives a mixture of all four possible isomers. Sodium methoxide was reacted with these isomers to determine the configuration about the carbon–carbon double bond for each. The *Z*-isomers reacted with sodium methoxide to give the corresponding alkyne by elimination whereas the *E*-isomers gave the substitution product. The configuration about the carbon–nitrogen double bond was determined from the ^{1}H NMR chemical shift of the $NOCH_3$ group.

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Introduction

The imine functional group (>C=N–) is an important part of many therapeutic agents. For example, many third-generation cephalosporins (cefpodoxime, ceftriaxone, and ceftazidine)[1] contain an *O*-alkyloxime (*N*-alkoxyimine) functional group. These compounds are among the most commonly prescribed antibiotics. The antibiotic gemifloxacin (Factive),[2] developed by GlaxoSmithKline to help combat the problem of bacterial resistance to antibiotics, also contains an *O*-methyloxime group. Oximidines, which may act as selective antitumor drugs, contain an *O*-alkyloxime moiety (>C=$NOCH_3$).[3] Therefore the need for a fundamental understanding of the mechanisms of the reactions of compounds containing this functional group is apparent.

It is well known that compounds containing a carbon–nitrogen double bond undergo photochemical and acid-catalyzed *Z*/*E*-isomerization.[4–14] Athough much less common, base-catalyzed isomerization of imines have also been reported.[15–17] We have been particularly interested in mechanisms of acid- and base-catalyzed isomerization of imines. Although the mechanisms of these isomerizations have received some attention[6–17] they are still not completely understood. The high resistance of *O*-alkyloximes and their derivatives to thermal *Z*/*E*-isomerization makes these compounds ideally suited for studies on the acid- and base-catalyzed *Z*/*E*-isomerization mechanism.

In 1981 we reported[13a] experimental evidence that unambiguously demonstrated that *O*-methylbenzohydroximoyl chlorides (**1Ea** and **1Za**, Fig. 1) isomerize by nucleophilic

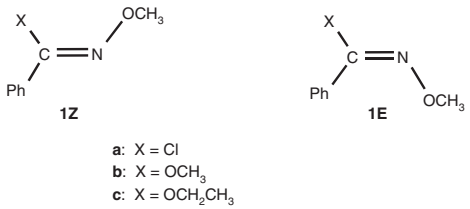

Fig. 1.

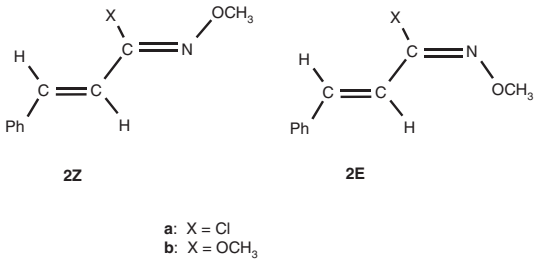

Fig. 2.

catalysis when the isomerization is carried out in H^{36}Cl/dioxane solution. Measurement of the rate of incorporation of radioactive chloride during the isomerization of **1Ea** to **1Za** demonstrated that the isomerization must take place by nucleophilic attack on carbon to give a tetrahedral intermediate (nucleophilic catalysis).

More recently we have reported[14] on the kinetics and mechanism of acid-catalyzed *Z*/*E*-isomerization of *O*-methylbenzohydroximoyl chloride (**1Za** and **1Ea**), methyl

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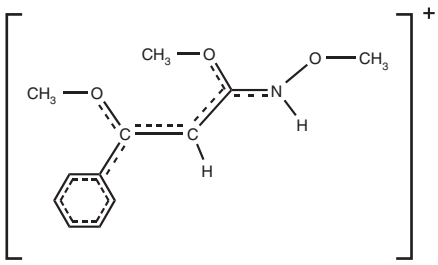


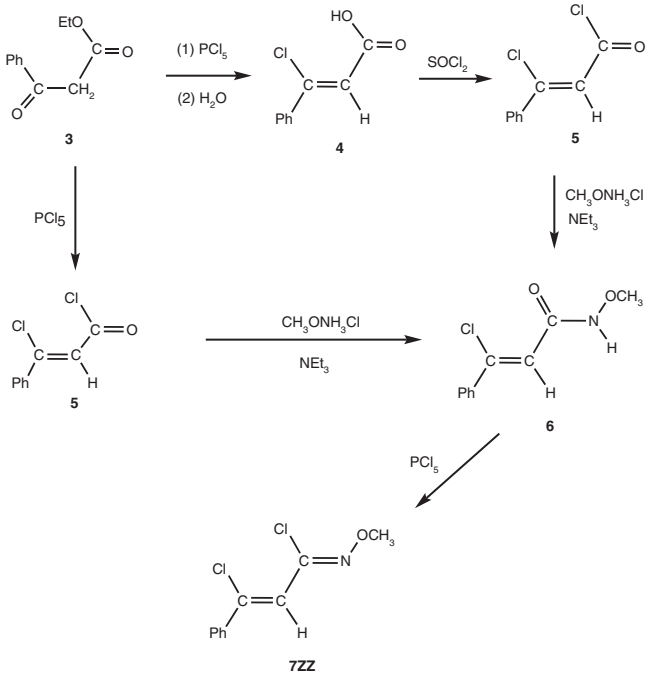
Fig. 3.

O-methylbenzohydroximate (**1Zb** and **1Eb**), ethyl *O*-methylbenzohydroximate (**1Zc** and **1Ec**), *O*-methylcinnamohydroximoyl chloride (**2Ea** and **2Za**, Fig. 2), and methyl *O*-methylcinnamohydroximate (**2Eb** and **2Zb**). The kinetics of *Z*/*E*-isomerization were studied in glacial acetic acid and in dioxane solutions containing hydrochloric, trifluoromethanesulfonic, or tetrafluoroboric acid. This study showed that the *O*-methylbenzohydroximoyl chlorides only isomerize by nucleophilic attack by chloride ion on the protonated imine (nucleophilic catalysis). Methyl *O*-methylbenzohydroximate (**1Zb** and **1Eb**) is capable of isomerizing by either nucleophilic catalysis or by rotation about the carbon–nitrogen double bond of the *N*-protonated intermediate (an iminium ion; protonation–rotation mechanism). Methyl *O*-methylcinnamohydroximate (**2Zb** and **2Eb**) isomerized only by the protonation–rotation mechanism. Theoretical calculations supported the notion that increased conjugation of protonated imines increases the rate of iminium ion rotation.

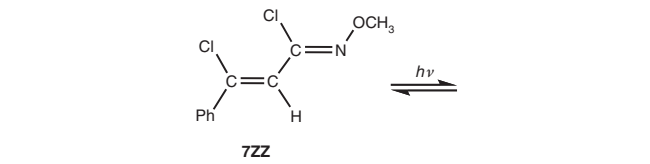
The purpose of this work was to synthesize and characterize new α,β-unsaturated hydroximoyl chlorides and hydroximates whose conjugate acids are expected to have lower rotational barriers than any compounds we have studied previously. We are especially interested in synthesizing compounds that contain a methoxy group in the β-position of cinnamohydroximoyl chlorides and hydroximates since iminium ions from these compounds should have low barriers to rotation (shown for a β-methoxycinnamohydroximate, Fig. 3).

Results and Discussion

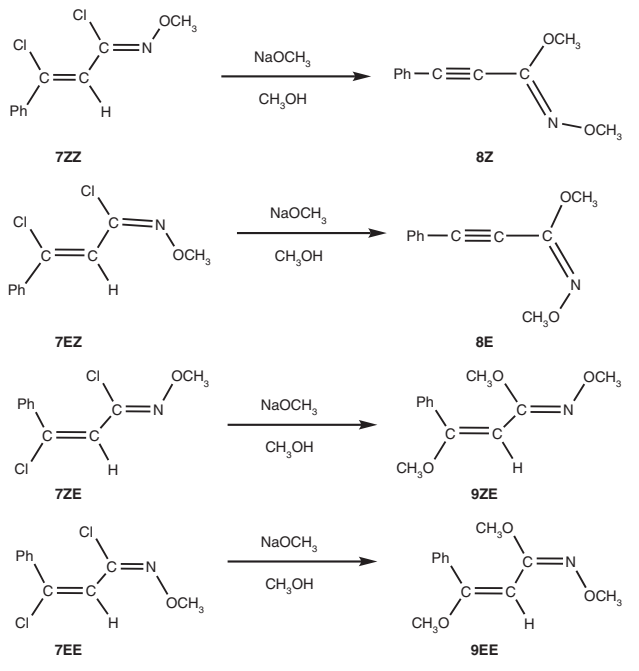
Methyl (*Z*)-β-chlorocinnamohydroxamate (**6**), *O*-methyl-β-chlorocinnamohydroximoyl chloride (**7ZZ**, **7ZE**, **7EE**, and **7EZ**), methyl *O*-methyl-β-phenylpropynohydroximate (**8E** and **8Z**), and methyl *O*-methyl-β-methoxycinnamohydroximate (**9ZE** and **9EE**) were synthesized according to Schemes 1–3. Methyl (*Z*)-β-chlorocinnamohydroxamate (**6**) was prepared by two different methods (Scheme 1). In the first method, ethyl benzoylacetate (**3**) was reacted with phosphorus pentachloride followed by hydrolysis.[18] The β-chlorocinnamic acid (**4**) produced in this reaction was a mixture of *Z*- and *E*-isomers. As described previously,[18] the *Z*-isomer selectively formed a precipitate of the barium salt when a mixture of the *E*- and *Z*-isomers was dissolved in aqueous ammonia followed by the addition of barium chloride. The barium salt of the *Z*-isomer was filtered and acidified with hydrochloric acid to give (*Z*)-β-chlorocinnamic acid (**4**).



Scheme 1.



Scheme 2.



Scheme 3.

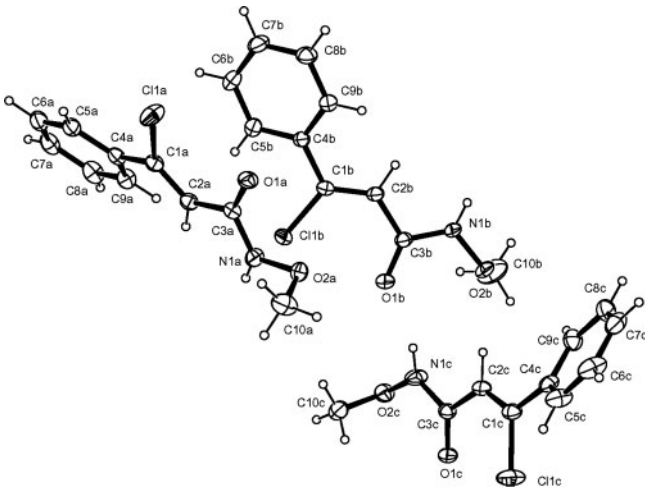


Fig. 4. The three independent molecules of **6**, with 50% ellipsoids. Mean bond distances are C1–Cl1 1.739, C1–C2 1.335, C2–C3 1.479, C3–O1 1.233, N1–C3 1.347, and N1–O2 1.390 Å.

Reaction of (*Z*)-β-chlorocinnamic acid with thionyl chloride gave (*Z*)-β-chlorocinnamoyl chloride (**5**, not isolated) that was reacted with methoxylamine hydrochloride and triethylamine to give methyl (*Z*)-β-chlorocinnamohydroxamate (**6**). Since **5** is likely to be formed as an intermediate in this method, an alternate method of synthesizing **6** was developed (Scheme 1). In this procedure ethyl benzoylacetate was reacted with phosphorus pentachloride followed by addition of methoxylamine hydrochloride and triethylamine. In this method column chromatography was necessary to prepare pure **6**.

The configuration of **6** was established by a single crystal X-ray structure determination. Three independent molecules are present in the asymmetric unit, as shown in Fig. 4. There is good agreement in bond distances among the three molecules, and mean values are given in the Fig. 4 caption. There is some variability, however, in the conformations of the three. The C1–C2–C3–O1 torsion angle varies from −2.4(2) to −14.7(2)°, Cl1–C1–C4–C5 from −21.73(16) to −36.63(17)°, and C3–N1–O2–C10 from 88.58(15) to 96.79(14)°. All N–H groups are involved in intermolecular hydrogen bonds, with carbonyl O1 atoms as acceptors. The N1···O1 distances range 2.7904(15)–2.8798(14) Å, and N1–H–O1 angles range 161.3(16)–168.9(16)°.

(*Z*,*Z*)-*O*-Methyl-β-chlorocinnamohydroximoyl chloride (**7ZZ**) was synthesized (Scheme 1) by the reaction of **6** with phosphorus pentachloride. All of the isomers (**7ZE**, **7EZ**, and **7EE**) of (*Z*,*Z*)-*O*-methyl-β-chlorocinnamohydroximoyl chloride (**7ZZ**) were prepared (Scheme 2) by prolonged ultraviolet irradiation of a hexane solution of **7ZZ**. GC-MS analysis of the crude mixture indicated that the mixture contained only three isomers. It was subsequently determined that **7EZ** and **7EE** have identical retention times on the GC column that we were using (J & W DB-5MS). The ^{1}H NMR spectrum of the crude product clearly showed that the photostationary mixture contained all four isomers **7ZZ**, **7EZ**, **7ZE**, and **7EE** in a 1.8:2.1:2.3:1.0 ratio. The isomers were separated by column chromatography. Among those four isomers, the **7EE** isomer was the most difficult to isolate. It was formed in the smallest amount in the photoisomerization of **7ZZ**. Also, it partially overlapped with **7ZZ** when the mixture was separated by column chromatography.

The four isomers of **7** were reacted with sodium methoxide (1:2 mol ratio of **7** to methoxide ion, Scheme 3). Two of the isomers (**7ZZ** and **7EZ**) underwent elimination of HCl to give the corresponding methyl *O*-methyl-β-phenylpropynohydroximate (**8Z** and **8E**). The other two isomers (**7ZE** and **7EE**) underwent substitution to give methyl β-methoxy-*O*-methylcinnamohydroximate (**9ZE** and **9EE**). Small sample sizes made isolation of the hydroximates **9ZE**, **9EE**, and **8E** impractical, so these compounds were identified only from their mass spectra obtained during GC-MS analysis of the crude reaction products.

In our earlier work[19–24] it was found that the NMR spectra of hydroximoyl halides,[19,22,23] hydroximates[25] thiohydroximates,[24] hydroximoyl cyanides,[20] and amidoximes[21] were sufficiently different to make the assignment of the configuration as long as both isomers were available. In the halogen derivatives, the most stable isomers have always been found to have the *Z*-configuration,[19,22,23] while with hydroximates[15,25] the *E*-isomers predominate in DMSO solution and an equilibium mixture of equal proportions of *Z*- and *E*-isomers is produced in glacial acetic acid.[14] The *N*-methoxy absorption in the ^{1}H NMR spectrum of a *Z*-isomer is further downfield than the absorption in the corresponding *E*-isomer.

The four isomers of **7** were identified using the following methods. The configuration about the carbon–carbon double bond was determined from results of the reaction of each isomer with sodium methoxide in methanol (Scheme 3). The *Z*-isomers underwent an *anti*-elimination to give methyl *O*-methyl-β-phenylpropynohydroximate. Because it is well known that *anti*-elimination in vinyl halides is much faster than *syn*-elimination,[26,27] it is reasonable to assume that it is the *Z*-isomers (about the carbon–carbon double bond, **7ZZ** and **7EZ**) that underwent elimination to give **8Z** and **8E** (identified only by their MS spectra). The structure of **7ZZ** is also consistent with the X-ray structural analysis of **6**, which shows that the carbon–carbon double bond in this compound has the *Z*-configuration. Thus the reaction of **6** with PCl_5 gives the expected hydroximoyl chloride (**7ZZ**) with retention of configuration at the carbon–carbon double bond. The configuration about the carbon–nitrogen double bond was determined by ^{1}H NMR spectroscopy. In the closely related *Z*- and *E*-isomers of *O*-methylcinnamohydroximoyl chloride (**2Za** and **2Ea**), and in all of the other hydroximoyl chlorides that we have synthesized, the chemical shift of $NOCH_3$ group is further downfield in the *Z*-isomer. Table 1 gives a list of the isomers with the order of retention time on a GC column (J & W DB-5MS), retention on a column chromatography column (silica gel), and the proton chemical shift of the $NOCH_3$ group.

Conclusions

The structures of all four isomers of β-chlorocinnamohydroximoyl chloride have been deduced. It is clear that improved

Table 1. ^{1}H NMR chemical shifts, relative retention times, and reactivity of the stereoisomers of 7

Configuration	Retention order in gas chromatography (J & W DB-5MS)	Elution order in column chromatography (silica gel)	Reaction with excess sodium methoxide	^{1}H NMR chemical shift of $NOCH_3$
EZ	1	1	Elimination to form alkyne	3.89
EE	1	2	Substitution	3.84
ZZ	3	3	Elimination to form alkyne	4.07
ZE	2	4	Substitution	3.97

yields for the synthesis β-methoxy-*O*-methylcinnamohydroximates will require replacing the α-hydrogen with an alkyl or aryl substituent in order to prevent the elimination reaction observed in this work.

Experimental

General Procedures

Melting points were determined in a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra of solids were determined from Nujol mulls. Proton and carbon NMR spectra were determined on a Varian Mercury 300 MHz spectrometer. Unless otherwise noted, all NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard. Low resolution mass spectra were determined on Varian Saturn 3 ion-trap GC/MS spectrometer. Midwest Microlab (Indianapolis, IN) performed the elemental analysis of the new compounds. Photoisomerization was carried out using a Rayonet Photochemical Reactor Model RPR-100 equipped with five lamps (254 nm) and a merry-go-round rack. Separation of mixture of isomers was accomplished by column chromatography using silica gel (MN-Kieselgel 60, 70–130 mesh) that had been dried at 95°C for ~1 h before packing the column. The progress of the chromatography was followed by thin-layer chromatography.

Crystal Structure Determination

The structure of **6** was determined, using data collected at T 110 K with $Mo_{K\alpha}$ radiation (λ 0.71073 Å) on a Nonius Kappa CCD diffractometer. Crystal data: $C_{10}H_{10}ClNO_2$, M 211.64, triclinic, space group $P\bar{1}$, a 10.8798(15), b 11.3640(10), c 13.0891(14) Å, α 104.466(6), β 101.454(5), γ 95.672(7)°, V 1516.9(3) Å^3, Z 6, D_x 1.390 g cm^{-3}, μ 3.50 cm^{-1}, colourless crystal with dimensions 0.33 × 0.25 × 0.23 mm, transmission coefficients 0.893–0.924, 38244 measured data with $\theta < 30.5°$, 9143 unique data used in refinement, R 0.038 for 7229 observed data, 392 refined parameters. The X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre as deposition no. 297168.

Synthetic Experimental Procedures

*(Z)-β-Chlorocinnamic Acid **4***

Ethyl benzoylacetate (**3**, 19.2 g, 0.1 mol) was added dropwise over a period of one hour with strong stirring to a solution of phosphorus pentachloride (50.30 g, 0.3 mol) in dry benzene (50 mL).[18] After the addition had been completed, the reaction mixture was kept at ambient temperature for 30 min and then it was refluxed for 30 min. After the reaction, the mixture was allowed to cool gradually to ambient temperature. Ice water (20 g) was added slowly. The benzene layer was separated and the aqueous layer was extracted with benzene (3 × 20 mL). The combined benzene solution was extracted with water (2 × 10 mL) and a saturated solution of sodium carbonate (3 × 20 mL) respectively. The sodium carbonate solution was collected and acidified with hydrochloric acid (10 mL) until the pH was less than 7. The crude product was obtained as a yellow solid. The crude product that contains *cis*- and *trans*-isomers was dissolved in 30% ammonium hydroxide solution (30 mL), which was followed by an addition of a saturated barium chloride solution (30 mL). The white precipitate that was formed was filtered in vacuo and the solid was collected. The precipitate was suspended in water and acidified with hydrochloric acid (30 mL). The solid residue was purified by recrystallization from carbon tetrachloride. Pure **4** (15.8 g, 88%) was obtained as a white microcrystalline solid. mp 146–147°C (lit.[18] 145–146°C). δ_H 6.61 (s, 1H), 7.43–7.46 (m, 3H), 7.70–7.13 (m, 2H). δ_C 115.4 (C), 127.4 (CH), 128.7 (CH), 131.1 (CH), 137.0 (C), 149.1(C), 168.8 (C).

*Methyl (Z)-β-Chlorocinnamohydroxamate **6** (Procedure 1)*

Compound **4** (3.65 g, 0.02 mol) was mixed with thionyl chloride (8.1 g, 0.06 mol) and chloroform (15 mL) and stirred for half an hour at ambient temperature. The solution was then refluxed for approximately 3 h. The solvent and the excess thionyl chloride were evaporated at room temperature at aspirator pressure. The residue was suspended in chloroform (10 mL). This mixture was added to a stirred ice-cold solution of methoxylamine hydrochloride (2.03 g, 0.024 mol) and triethylamine (5.22 g, 0.06 mol) over a period of ~30 min. The solution was then refluxed for 4 h. The reaction mixture was cooled to room temperature, washed with water, 0.2 N hydrochloric acid, saturated sodium bicarbonate, and water. The organic layer was dried over anhydrous magnesium sulfate overnight. The magnesium sulfate was removed by filtration and the solvent was removed by rotary evaporation to give the crude product. The crude product was purified by fractional crystallization from chloroform and ether solution. Pure **6** (3.85 g, 96%) was obtained as a white microcrystalline solid. mp 96–97°C. (Found: C 56.56, H 4.67, N 6.54, Cl 17.10. $C_{10}H_{10}O_2NCl$ requires C 56.74, H 4.73, N 6.62, Cl 16.78). δ_H 3.78 (s, 3H), 6.72 (s, 1H), 7.22–7.40 (m, 3H), 7.55–7.65 (m, 2H), 10.98 (s, 1H). δ_C 64.0 (CH_3), 116.0 (CH), 126.9 (CH), 128.3 (CH), 130.2 (CH), 136.9 (C), 142.6 (C), 162.2 (C).

*Methyl (Z)-β-Chlorocinnamohydroxamate **6** (Procedure 2)*

Ethyl benzoylacetate (9.6 g, 0.05 mol) was added dropwise to a cold suspension of phosphorus pentachloride (31.3 g, 0.15 mol) in dry benzene (35 mL) with strong stirring for 1 h. After the addition had been completed, the reaction mixture was stirred at ambient temperature for another 30 min, and then it was allowed to reflux for 30 min. After the reaction, the mixture was allowed to cool gradually to ambient temperature, and a precipitate was observable. The solvent was removed in vacuo quickly. The residue was suspended in chloroform (10 mL) and added dropwise to a stirred ice-cold solution of methoxylamine hydrochloride (2.51 g) and triethylamine (5.05 g) over a period of ~30 min. The solution was then refluxed for 4 h. The reaction mixture was allowed to cool gradually to ambient temperature, and then washed sequentially with water, 0.2 N hydrochloric acid (2 × 15 mL), saturated sodium bicarbonate (2 × 15 mL), and water (2 × 15 mL). The organic layer was dried over anhydrous magnesium sulfate overnight and filtered, and the filtrate was concentrated in vacuo to give a 3.50 g of crude product. The crude product was purified via column chromatography on 70 g silica gel by elution with 10% ethyl acetate and hexane. Pure **6** (4.5 g, 39%) was obtained as a colorless microcrystalline solid. mp 96–97°C.

*(Z,Z)-β-Chlorocinnamohydroximoyl Chloride **7ZZ***

Compound **6** (2.02 g, 0.01 mol) was mixed with phosphorus pentachloride (6.26 g, 0.03 mol) with strirring in an ice bath.[19] The mixture was then stirred for 22 h at room temperature. Hexane (20 mL) was

added to the reaction mixture, and it was poured into an ice-water mixture. The organic layer was separated and washed with a saturated sodium bicarbonate solution and water respectively. The organic layer was dried with anhydrous magnesium sulfate for 3 h. The mixture was filtered and the solvent was evaporated. The crude product was purified by column chromatography (silica gel, with 0.5% chloroform/hexane until the product started to elute; the solvent was then changed to pure hexane) to give a colorless liquid. (Found: C 52.27, H 4.00, N 6.07, Cl 30.80. $C_{10}H_9ONCl_2$ requires C 52.20, H 3.94, N 6.09, Cl 30.82). δ_H 4.07 (s, 3H), 6.56 (s, 1H), 7.32–7.43 (m, 3H), 7.55–7.68 (m, 2H). δ_C 63.1 (CH_3), 118.5 (CH), 126.8 (CH), 128.4 (CH), 129.9 (CH), 132.7 (C), 137.2 (C), 138.8 (C). ν_{max}/cm^{-1} (neat) 1620. *m/z* 233 (4), 232 (14), 231 (16), 230 (53), 229 (22), 228 (69), 198 (84), 179 (21), 165 (57), 164 (32), 163 (53), 162 (100), 128 (85).

*(*E,*Z)*-O-*Methyl-β-chlorocinnamohydroximoyl Chloride* ***7EZ****,*
*(*E,E*)*-O-*Methyl-β-chlorocinnamohydroximoyl Chloride* ***7EE****, and*
*(*Z,E*)*-O-*Methyl-β-chlorocinnamohydroximoyl Chloride* ***7ZE***

A solution of (*Z*,*Z*)-*O*-methyl-β-chlorocinnamohydroximoyl chloride (**7ZZ**, 2.01 g) in hexane (44 mL) was placed in 4 quartz tubes. The test tubes were irradiated in a Rayonet photochemical reactor (254 nm) for 6 h. After irradiation, the hexane solution was immediately extracted with saturated solution of sodium carbonate (2 × 15 mL). The hexane extracts were dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated in vacuo. The residue was analyzed by ^{1}H NMR, and it was found to contain **7ZZ**, **7EZ**, **7ZE**, and **7EE** in a 1.8:2.1:2.3:1.0 ratio. The mixture was separated via column chromatography on silica gel by eluting with chloroform in hexane. The percentage of chloroform was increased from 1.1% to 1.8% to 2.0% to 3.3% during the chromatography. The isomers eluted from the column in the order **7EZ**, **7EE**, **7ZZ**, and **7ZE**.

7EZ (0.03 g, 1.5%) was obtained as a colorless liquid. (Found: C 52.49, H 4.09, N 6.06, Cl 30.83. $C_{10}H_9ONCl_2$ requires C 52.20, H 3.94, N 6.09, Cl 30.82). δ_H 3.89 (s, 3H), 6.77 (s, 1H), 7.30–7.47 (m, 5H). δ_C 63.0 (CH_3), 121.2 (CH), 128.0 (CH), 129.0 (CH), 129.7 (CH), 132.8 (C), 136.5 (C), 141.9 (C). *m/z* identical to **7ZZ**.

7EE (0.005 g, 0.3%) was obtained as a colorless liquid. (Found: C 52.41, H 4.02, N 6.00, Cl 30.95. $C_{10}H_9ONCl_2$ requires C 52.20, H 3.94, N 6.09, Cl 30.82). δ_H 3.84 (s, 3H), 6.50 (1H), 7.32–7.45 (m, 5H). δ_C 63.5 (CH_3), 121.6 (CH), 128.5 (CH), 129.5 (CH), 130.2 (CH), 133.2 (C), 137.0 (C), 142.3 (CH). *m/z* identical to **7ZZ**.

7ZE (0.04 g, 2%) was obtained as a colorless liquid. (Found: C 52.53, H 4.12, N 5.80, Cl 30.83. $C_{10}H_9ONCl_2$ requires C 52.20, H 3.94, N 6.09, Cl 30.61). δ_H 3.97 (s, 3H), 6.88 (1H), 7.35–7.48 (m, 3H), 7.60–7.74 (m, 2H). δ_C 63.1 (CH_3), 114.9 (CH), 126.9 (CH), 128.4 (CH), 130.2 (CH), 136.6 (CH), 140.6 (C), 143.1 (CH). *m/z* identical to **7ZZ**.

*Methyl (*Z*)*-O-*Methyl-β-phenylpropynohydroximate* ***8Z***

Sodium metal (0.91 g, 0.040 mol) was reacted with methanol (15 mL). The mixture was cooled to room temperature and (*Z*,*Z*)-β-chlorocinnamohydroximoyl chloride **7ZZ** (4.59 g, 0.0200 mol) in methanol (6 mL) was added to the mixture. The solution was stirred and refluxed for about five hours. The solution was cooled to room temperature and the solid was separated by filtration. The solid was washed with methanol. The methanol was removed by rotary evaporation. Water (30 mL) and benzene (30 mL) were added to the residue. The water was separated and the organic layer was dried over anhydrous magnesium sulfate. The magnesium sulfate was removed by filtration and washed with benzene. The benzene was removed by rotary evaporation to give crude product (3.02 g). The product was purified by vacuum distillation to give product (2.9 g, 0.015 mol, 77%). bp 86.5–88.0°C/0.45 mmHg. (Found: C 69.97, H 6.00, N 7.37. $C_{11}H_{11}NO_2$ requires C 69.83, H 5.86, N 7.40). δ_H 3.99 (s, 3H), 3.92 (s, 3H), 7.30–7.45 (m, 3H), 7.50–7.60 (m, 2H). δ_C 58.8 (CH_3), 64.1 (CH_3), 77.8 (C), 99.8 (C), 121.7 (C), 129.7 (CH), 131.1 (CH), 133.2 (CH), 144.3 (C). ν_{max}/cm^{-1} (neat) 2210, 2920. *m/z* 189 (100), 174 (3), 158 (2), 143 (5), 129 (36), 115 (18), 102 (10), 89 (7).

*Methyl (*E*)*-O-*Methyl-β-phenylpropynohydroximate* ***8E***

7EZ (0.46 g) was reacted with sodium methoxide (from 0.092 g of sodium) in a similar manner to give a crude product with a different retention time than **8Z** and a mass spectrum identical to **8Z**.

*Methyl (*Z,E*)-β-Methoxy-O-methylcinnamohydroximate* ***9ZE***

7ZE (0.46 g) was reacted with sodium methoxide (from 0.092 g of sodium) in a similar manner to give a crude product. *m/z* 221 (8), 220 (36), 189 (100), 175 (9), 158 (9), 146 (9), 143 (12), 129 (49), 115 (36), 102 (18), 89 (17), 77 (19).

*Methyl (*E,E*)-β-Methoxy-O-methylcinnamohydroximate* ***9EE***

7EE (0.23 g) was reacted with sodium methoxide (from 0.069 g of sodium) in a similar manner to give a crude product with a GC retention time that was different than **9ZE** and a mass spectrum identical to **9ZE**.

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