New Synthetic Method for Dehydrotryptophan Derivatives. Synthetic Studies on Indoles and Related Compounds. XXXIV1)

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Dehydrotryptophans (9) having various substituents on the indole ring were synthesized by vinylation of the corresponding indole derivatives (6) with N-acetyldehydroalanine methyl ester (7a) by the use of a stoichiometric amount of palladium salt in acetic acid (stoichiometric condition). Although vinylation of 4-, 5-, and 7-bromoindoles (6b, g, l, m) with 7a occurred chemoselectively at the C4-position to give the corresponding bromodehydrotryptophans (9b, g, l, m) under the stoichiometric condition, the palladium-catalyzed vinylation of 4-bromoindoles (6b, i) occurred at the bromine-bearing carbon at the C4-position [0.1 eq PdCl2(PPh3)2 in Et3N-dimethylformamide]. Vinylation of 3-bromoindoles (17a, b) with 7a, or ethoxycarbonyl- (7b) or tert-butoxycarbonyldehydroalanine methyl ester (7c) also gave the dehydrotryptophan (18a—d) in good yields under catalytic conditions. One of two possible regioisomers of the vinylated products was isolated in all cases, and the geometry was determined as Z based on the coupling constant of the ester carbonyl carbon and the olefinic proton in the 13C-NMR spectrum.

Keywords vinylation; palladium; dehydrotryptophan; indole; dehydroalanine

Tryptophan analogues (1) having various substituents on the indole ring are widely distributed in nature as free amino acids or as components of peptides,2) and play important roles in biological systems.3) Furthermore, 4-substituted tryptophans should be useful intermediates for the synthesis of indole alkaloids which have a tryptophan skeleton, such as clavicipitic acid (3), indolactam V (4), and echinuline (5). Several attempts to synthesize optically active 3 or 4 starting from L-tryptophan (1, X=H) have been reported,4) but satisfactory results have not been obtained because of difficulty in the cyclization of the α-carboxyl group of the side chain to its C4-position without racemization or in the selective introduction of a functional group at the benzene ring, which is less reactive than the pyrrole ring.

Although such tryptophan analogues (1) are readily available in racemic form by applying the known synthetic method for tryptophan itself (1, X=H),5) access to optically active analogs has been difficult.6) Asymmetric reduction of dehydroamino acids is a well established method for obtaining optically active amino acids.7) Thus, the dehydrotryptophans (2) having a functional group on the indole ring, can be regarded as good starting materials for the synthesis of optically active tryptophan analogues (1).8) The dehydrotryptophan derivatives were synthesized in good yields from 3-formylindole by the condensation of glycine oxazolones or of glycine phosphonates, but this method was applicable to the synthesis of only a few indole derivatives, and gave a mixture of E, Z-isomers in most cases.9)

Recently several methods for the preparation of dehydroamino acids utilizing a palladium-catalyzed vinylation have been reported,10) and those reactions give the Z-isomers exclusively. We have also reported11) the one-step synthesis of 4-bromodehydrotryptophan (8) from 4-bromoindole (6b) and ethoxycarbonyldehydroalanine

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1. asymmetric reduction
2. deprotection

Chart 1
methyl ester (7b) by the use of a stoichiometric amount of PdCl₂ (Chart 2). This reaction might have wide applicability for the synthesis of dehydrotryptophan derivatives having various substituents on the indole ring, because the starting indoles having various substituents are easily prepared by known methods. In the present report, we wish to describe a new synthesis of dehydrotryptophan having various substituents on the indole ring by applying the above palladium-mediated vinylation.

**Results and Discussion**

Various indoles (6a—m) were allowed to react with N-acetyldihydroalanine methyl ester (7a) in the presence of 1.0 eq of PdCl₂ and 4 eq of AcONa in AcOH at 120—130°C, and the results are summarized in Table 1 (Chart 3). N-₃-Toluene sulfonyl(tosyl)indole (6a) and ethyl indole-2-carboxylate (6h), which has been utilized as a stable synthetic equivalent of indole itself by our group, gave the desired products (9a, 9h) in 50% and 59% yields, respectively (runs 1 and 8). It is noteworthy that the protection of indole nitrogen was not necessary in the case of 6h, whereas the protection of nitrogen on indole itself (6, R¹ = R² = X = H) was essential in the palladium-mediated vinylation.

Indoles with an electron-withdrawing or -donating group on the C₅⁺ or Cₗ-positions (6e—g or 6j—m) gave the products (9e—g or 9j—m) in almost the same yields as unsubstituted indoles (6a, 6h) (runs 5—7, 10—13). However, 4-substituted indoles (6b—d, 6i) did not react smoothly, and the products were obtained in low yields or not at all (runs 2—4, 9). Those data show that this reaction was not affected by the electron density of the indole ring but was greatly influenced by steric hindrance.

The selective formation of bromodehydrotryptophan derivatives (6b, g, l, m) is especially interesting, because these results indicated that selective palladation occurred at the C₅⁺-position to form the σ-complex (10) in spite of the presence of a carbon–bromine bond. It is well known that the aryl palladium σ-complex (14) is formed either by direct palladation of an aromatic hydrocarbon (12) with Pd(II) salt or by the oxidative addition of Pd(0) species to an aryl halide (13) (Chart 4). The former process requires a stoichiometric amount of Pd(II) (stoichiometric condition) and the latter, known as Heck arylation, requires a catalytic amount of Pd(0) (catalytic condition).

Since the vinylations under the stoichiometric condition were accomplished as above, we next tried vinylation of
Various bromoindoles under catalytic condition [0.1 eq. PdCl₂(PPh₃)₂] in dimethylformamide (DMF)–Et₃N at 120 °C] in order to confirm the formation of the σ-complex (11) by oxidative addition of Pd(0) to the carbon–bromine bond. Vinylation of 4-bromoindoles (6b, 6i) gave the C₄-vinylated products (16a, 16b) in very good yields (Chart 5). It was interesting that the C₃-vinylated products (bromodehydrotryptophans, 9b, 9i) were not detected in the case of the catalytic condition. Vinylation of 5- or 7-bromoindoles (6g or 6m) with 7a did not give the C₅ or C₇-vinylated products but a mixture of starting material and debrominated product (6, X = H), while on vinylation of 3-bromoindole (17a, 17b) with 7a or alkoxy-carbonyldehydroalanine (7b, 7c), the dehydrotryptophans (18a–d) were obtained in good yields (Chart 6, Table II).

Although the reactivities in the vinylation varied irregularly with the position of the bromine on the indole ring and with the reaction conditions (stoichiometric or catalytic), the reacted position was completely differentiated between the stoichiometric and catalytic conditions. The selective vinylation at the C₃-position of bromoindoles is considered to be synthetically useful, because bromine on an aromatic ring might be easily converted to carbon functionalities by various methods including organo-transition metal-catalyzed reactions. We have reported[17] that such chemoselectivity appeared more clearly when vinylation of various bromoindoles or some bromobenzene derivatives was carried out by the use of ethyl acrylate instead of 7 as an olefin; Et₃N and PPh₃ played an important role in the appearance of such chemoselectivity.

### Table II. Vinylation of 3-Bromoindoles (17) under the Catalytic Condition

<table>
<thead>
<tr>
<th>Run</th>
<th>Indole 17</th>
<th>Olefin 7</th>
<th>Reaction time (h)</th>
<th>Product yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17a</td>
<td>7a</td>
<td>5</td>
<td>66 (18a)</td>
</tr>
<tr>
<td>2</td>
<td>17a</td>
<td>7b</td>
<td>2.5</td>
<td>53 (18b)</td>
</tr>
<tr>
<td>3</td>
<td>17a</td>
<td>7c</td>
<td>5</td>
<td>61 (18c)</td>
</tr>
<tr>
<td>4</td>
<td>17b</td>
<td>7a</td>
<td>5</td>
<td>53 (18d)</td>
</tr>
</tbody>
</table>

a) Molar ratio; 17∶7∶PdCl₂(PPh₃)₂∶AcONa = 1∶2∶0.1∶2. b) Molar ratio; 17∶7∶PdCl₂(PPh₃)₂∶AcONa = 1∶1.5∶0.05∶1.5.
Hegedus reported that the 4-bromodehydrotryptophan (9b), used as a key intermediate for the total synthesis of clavicipitic acid (2), was prepared from 6b by a three-step sequence of reactions including a hazardous mercuration–iodination reaction and selective vinylation of the resultant 3-iodo-4-bromoinodole (20) with 7a (route A in Chart 7). Although we obtained the same compound (9b) in one step from the same starting material (6b), the yield was only 17% (route B in Chart 7). The reason for the low yield was considered to be that Pd(II) was consumed by the reaction with 7a to produce Pd(0). So we tried to change the reactivity of 7a toward Pd(II) by changing the protecting group on nitrogen from an acetyl group to an ethoxycarbonyl group. The reaction of 7b with 4-bromoinodole (6b) smoothly proceeded to give the desired product (8) in 51% yield (route C in Chart 7). Our method proved to be greatly superior to the reported method. We are now trying to synthesize optically active indole alkaloids by using this compound as a starting material.

All of the dehydrotryptophans (8, 9, 18) and Cα-vinylated products (16) were isolated as single geometrical isomers from the present reaction, but a trace amount of the other isomer was sometimes detected in the reaction mixture on thin layer chromatography (TLC). Most of those minor isomers were not isolated in a pure form. However, in the case of the reaction of 17b with 7a under the catalytic condition, the minor isomer of 18d was isolated as a pure form (ca. 2%). The determination of the geometry of those isomers was accomplished by consideration of the 13C-NMR coupling constant of ester carbonyl carbon and olefinic hydrogen. It was reported that the Z-isomer has a larger coupling constant (ca. 10 Hz) than that of E-isomer (ca. 4 Hz). The coupling constants of both isomers were measured by low-power selective decoupling of the ester methyl protons and amide proton simultaneously to eliminate the effect of these protons. Since the major isomer had a smaller coupling constant (4.4 Hz) than that of the minor isomer (11.7 Hz), the former isomer was concluded to be the Z-isomer (Z-18d) while the latter was the E-isomer (E-18d). The coupling constants (4.4—5.1 Hz) observed for some analogous dehydrotryptophans (8, 9b, 18b) and Cα-vinylated products (16a, b) showed all these isomers to have Z-configuration. Since asymmetric reduction of Z-dehydroamino acids or esters was shown to give better results than that of E-isomer, the present method has an advantage over other known methods for dehydrotryptophan synthesis.

Experimental
All melting points were determined on a Yanagimoto micro-melting point hot-stage apparatus and are uncorrected. IR spectra were recorded in Nujoil mulls (unless otherwise stated) on a Shimadzu IR-400 spectrometer. NMR spectra were recorded in CDCl3 on a Hitachi R-24 spectrometer (1H-NMR, 60 MHz; unless otherwise stated) or a JEOL GX-400 spectrometer (1H-NMR, 400 MHz; 13C-NMR, 100 MHz) with tetramethylsilane as an internal reference. Mass spectra were measured with a JEOL JMS-01SG-2 spectrometer using a direct inlet system. For column chromatography, Kieselgel 60 (70—230 mesh, Merck), and for TLC, Kieselgel GF254, were used. The abbreviations used are as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; dt, double triplet; q, quartet; m, multiplet; br, broad; d, diff., diffused; Ar, aromatic.

General Procedure for the Synthesis of Dehydroalanine Derivatives (7a—e)
According to the reported method for the preparation of N-benzylxoxycarbonyldehydroalanine methyl ester, a mixture of methyl pyruvate and 2.0 eq of acetamide for 7a (1.0 eq of ethyl carbamate for 7b or 0.5 eq of tert-butyl carbamate for 7c) in benzene was refluxed for 2—5h in the presence of a catalytic amount of p-toluenesulfonic acid (TsOH, 0.1 eq) and hydroquinone (0.05 eq) with a Dean—Stark apparatus for continuous removal of H2O. After the reaction was completed, the solution was directly passed through a short dry Al2O3 column (benzene—AcOEt or benzene—hexane) without any work-up. Since the obtained dehydroalanines (7a—e) were relatively unstable and pure enough, they were isolated by 1H-NMR to use for the next step, further purification was not carried out.

N-Acetylderalanine Methyl Ester (7a): Yield 61%. Colorless needles, mp 49—51°C. IR : 3330 (NH), 1695, 1660 (C=O)cm⁻¹. 1H-NMR (CDCl3) δ: 2.11 (3H, s, NHCOC2H5), 5.87 (1H, d, J=2 Hz, one of CH2=C), 6.57 (1H, s, one of CH2=C), 7.8 (1H, brs, NH). MS m/z: 143 (M⁺, 84%), 101 (100%).
N-Butyrylcarbonylhydrodeanaline Methyl Ester (7b): Yield 98%. Colorless oil. IR (neat): 3400 (NH), 1720 (C=O) cm⁻¹. 1H-NMR (CDCl₃): δ 2.09 (3H, s, CH₃), 2.30 (3H, s, Ar-CH₃), 2.32 (3H, s, Ar-CH₃), 2.73 (3H, s, CO₂H), 7.35 (1H, d, J=8 Hz, Ar-H), 7.43 (1H, t, J=1.6 Hz, Ar-H), 7.53 (1H, t, J=8 Hz, Ar-H), 7.65 (1H, d, J=8 Hz, Ar-H), 7.77 (1H, t, J=1.6 Hz, Ar-H), 7.94 (1H, m, Ar-H, CH=CH=C=NH). MS m/z: 422 (M⁺, 100%).

**General Procedure for the Vinylation of the Indoles (6) with N-Acetylcysteinehydrodeanaline Methyl Ester (7a) under the Stoichiometric Condition**

Methyl ester 7a (1.0 mmol), PdCl₂ (0.05 mmol), and AcONa (2.0 mmol) in AcOH (2.5 ml) was heated at 100°C for 2 h in a sealed tube. Then the reaction mixture was diluted with AcOEt and filtered through a Celite pad. The Celite pad was thoroughly washed with AcOEt and H₂O, and the separated aqueous layer was extracted with AcOEt. The combined organic layer was washed successively with 5% aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl, and dried over MgSO₄. After evaporation of the solvent, the residue was separated by silica gel column chromatography (benzene or benzene- AcOEt) to give the desired dehydrothiophene derivative (9a—m) and the corresponding starting material. The yields of the products and the recovery of the starting materials are listed in Table I, and the physical and spectral data are as follows.

(Z)-N-Acetyl-1-tosylhydrodeanaline Methyl Ester (9a): Colorless needles (benzene-AcOEt-EtOH), mp 227–230°C. Anal. Calc. for C₁₅H₁₂N₂O₄S·C₂H₅OH: C, 54.33; H, 5.63; N, 7.56; S, 10.19. Found: C, 54.5; H, 5.62; N, 7.57; S, 10.21. 1H-NMR (CDCl₃): δ 6.83, 6.76 (2H, d, J=10 Hz, Ar-H), 7.09 (1H, t, J=9 Hz, Ar-H), 7.28 (2H, d, J=10 Hz, Ar-H), 7.63 (1H, t, J=9 Hz, Ar-H), 7.82 (1H, d, J=8 Hz, Ar-H), 7.84 (1H, d, J=9 Hz, Ar-H), 7.93 (1H, m, Ar-H, CH=CH=C=NH). MS m/z: 355 (M⁺, 100%).

(Z)-N-Acetyl-5-nitro-2-ethoxythiophene-3-carboxylic acid Methyl Ester (9k): Colorless prisms (EtOH-AcOEt), mp 254–256°C. Anal. Calc. for C₁₅H₁₂N₂O₄S·C₂H₅OH: C, 49.99; H, 5.59; N, 7.77. Found: C, 50.14; H, 5.56; N, 7.80. 1H-NMR (CDCl₃): δ 6.77–6.84 (2H, m, Ar-H), 7.08 (1H, d, J=8 Hz, Ar-H), 7.31 (1H, t, J=7 Hz, Ar-H), 7.45 (1H, d, J=8 Hz, Ar-H), 7.58 (1H, d, J=8 Hz, Ar-H), 7.67 (1H, d, J=8 Hz, Ar-H), 7.78 (1H, d, J=8 Hz, Ar-H), 7.81 (1H, t, J=7 Hz, Ar-H), 7.93 (1H, m, Ar-H, CH=CH=C=NH). MS m/z: 360 (M⁺, 100%), 272 (62%).

(Z)-N-Acetyl-5-bromo-2-ethoxythiophene-3-carboxylic acid Methyl Ester (9l): Pale yellow fine needles (hexane-AcOEt), mp 155–157°C. Anal. Calc. for C₁₅H₁₂BrN₂O₄S·C₂H₅OH: C, 49.89; H, 4.19; N, 6.83. Found: C, 50.02; H, 4.26; N, 6.77. IR: δ 3310, 3250 (NH), 1710, 1690 (C=O) cm⁻¹. 1H-NMR (CDCl₃-d₅): δ 1.35 (3H, t, J=7 Hz, OCH₂CH₃), 1.85 (3H, s, CO₂H), 2.35 (3H, s, CO₂H), 3.41 (2H, q, J=7 Hz, OCH₂CH₃), 4.30 (2H, q, J=7 Hz, OCH₂CH₃), 7.36–7.45 (2H, m, Ar-H), 7.52 (1H, d, J=0.9 Hz, C₆H₅), 7.60 (1H, s, C₆H₅), 9.51 (1H, s, CN), 9.66 (1H, s, CN). MS m/z: 410 (M⁺, 2 +, 29%), 408 (M⁺, 29%), 366 (100%).

(Vinylation of 4-Bromo-1-tosylindole (6b) with 7a under the Catalytic Condition)

A mixture of 4-tosyl-4-bromomidine (6b, 88 mg, 0.25 mmol), N-acetylcysteinehydrodeanaline methyl ester (7a, 91 mg, 0.60 mmol), PdCl₂ (PPh₃)₂ (16 mg, 0.023 mmol), and AcONa (82 mg, 0.98 mmol) in Et₅N (0.8 ml)-DMF (0.4 ml) was heated at 120°C for 2 h in a sealed tube. Then the reaction mixture was diluted with AcOEt and filtered through a Celite pad. The Celite pad was thoroughly washed with AcOEt and H₂O and the separated aqueous layer was extracted with AcOEt. The combined organic layer was washed successively with 10% aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl, and dried over MgSO₄. After evaporation of the solvent, the residue (147 mg) was separated by silica gel column chromatography (benzene:AcOEt=10:1) to give methyl 2-(1-tosylindole-4-yl)acetamidoacrylate (16a) as a pale yellow solid (93 mg, 90% yield), which was recrystallized from benzene.

For colorless needles, mp 171–173°C. Anal. Calc. for C₁₅H₁₇NO₃S·C₂H₅OH: C, 61.15; H, 4.89; N, 6.79. Found: C, 61.45; H, 4.98; N, 6.62. IR: δ 3320 (NH), 1720, 1660 (C=O) cm⁻¹. 1H-NMR (CDCl₃-d₅): δ 1.91 (3H, s, CH₃CO₂), 3.96 (3H, s, CO₂CH₃), 3.85 (3H, s, Ar-CH₃), 3.97 (3H, s, Ar-CH₃), 7.10 (4H, m, Ar-H, CH=CH=C=NH). MS m/z: 492 (M⁺, 2 +, 36%), 490 (M⁺, 35%), 293 (100%).

(Z)-N-Acetyl-5-bromo-2-ethoxythiophene-3-carboxylic acid Methyl Ester (9l): Pale yellow needles (EtOH-AcOEt), mp 200–205°C. Anal. Calc. for C₁₅H₁₂BrN₂O₄S·C₂H₅OH: C, 49.89; H, 4.19; N, 6.83. Found: C, 50.02; H, 4.26; N, 6.77. IR: δ 3310, 3250 (NH), 1710, 1690 (C=O) cm⁻¹. 1H-NMR (CDCl₃-d₅): δ 1.35 (3H, t, J=7 Hz, OCH₂CH₃), 1.85 (3H, s, CO₂H), 2.35 (3H, s, CO₂H), 3.41 (2H, q, J=7 Hz, OCH₂CH₃), 4.30 (2H, q, J=7 Hz, OCH₂CH₃), 7.36 (3H, s, CO₂H), 4.41 (2H, q, J=7 Hz, OCH₂CH₃), 7.62 (1H, s, C₆H₅), 7.68 (1H, d, J=9 Hz, C₆H₅), 8.19 (1H, dd, J=9, 2.2 Hz, C₆H₅), 8.40 (1H, d, J=2.2 Hz, C₆H₅), 9.67 (1H, s, NHCOC₃), 12.19 (1H, brs, indole-NH). MS m/z: 375 (M⁺, 44%), 333 (M⁺, 20%), 301 (M⁺, 100%).
Vinylation of Ethyl 4-Bromomido-2-carboxylate (66) with N-Acetyldihydroalanine Methyl Ester (7a) under the Catalytic Condition A mixture of ethyl 4-bromomido-2-carboxylate (66, 137 mg, 0.51 mmol), N-acetyldihydroalanine methyl ester (7a, 145 mg, 1.09 mmol), PdCl₂(PPh₃)₂ (26 mg, 0.037 mmol), and AcOEt (87 mg, 1.1 mmol) in Et₂N·(0.50 mL)-DMF (0.5 mL) was heated at 130 °C for 3.5 h in a sealed tube. The reaction mixture was diluted with AcOEt and filtered through a Celite pad. The celite pad was thoroughly washed with AcOEt and H₂O, and the separated aqueous layer was extracted with AcOEt. The combined organic layer was washed successively with 10% aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl, and dried over MgSO₄. After evaporation of the solvent, the residue (191 mg) was triturated with benzene to give pure methyl 2-(2-ethylcorylenidio-4)-acetycamoacrylate (16b) as a pale yellow solid (105 mg, 62%), which was recrystallized from AcOEt-ether to give colorless needles, mp 229°232 °C. Anal. Calcd for C₁₅H₂₀N₂O₄: C, 51.8; H, 6.2; N, 7.5. Found: C, 51.8; H, 6.2; N, 7.5. 

General Procedure for the Vinylation of Ethyl 3-Bromomido-2-carboxylates (7a, b) with Dehydroalanine Methyl Esters (7a—c under the Catalytic Condition) A mixture of ethyl 3-bromomido-2-carboxylate (7a, 2.0 eq), PdCl₂(PPh₃)₂ (0.1 eq), and AcOEt (4.0 eq) in Et₂N-DMF (2:1) in a sealed tube was heated at 130 °C for the time indicated in Table II. After the reaction mixture was diluted with AcOEt and filtered through a Celite pad, the celite pad was thoroughly washed with AcOEt and H₂O, and the separated aqueous layer was extracted with AcOEt. The combined organic layer was washed successively with 5% aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl, and dried over MgSO₄. After evaporation of the solvent, the residue was washed with benzene to give the pure N-acetyldihydroalanine methyl ester (18a) or separated by silica gel column chromatography (benzene or benzene-AcOEt) to give the N-acetyldihydroalanine methyl ester (18b—d). The yields are listed in Table II and the analytical and spectral data are given below.

(2)-N-Ethoxybenzoyl-2-ethoxybenzoylhydroxydroprotophan Methyl Ester (18b) Pale yellow prisms (benzene), mp 168°171 °C. Anal. Calcd for C₁₅H₁₄O₄N₂: C, 61.8; H, 6.23; N, 7.21. Found: C, 61.6; H, 6.2; N, 7.2. IR: 3380 (N-M), 1680 (C=O). 1H-NMR (CDCl₃) δ: 1.28 (9H, s, C(CH₃)₃), 1.40 (3H, t, J=7.0 Hz, OCH₂CH₂), 3.37 (2H, q, J=7.0 Hz, OCH₂CH₂), 6.64 (s, H, OCH₃), 7.95 (d, J=7.0 Hz, Ar-CH₃), 7.69 (s, H, Ar-H), 7.75 (1H, s, CH=CH₂). MS m/z: 388 (M⁺, 90%), 358 (M⁺, 10%).

(2)-N-Acetyl-1-benzyl-2-ethoxybenzoylhydroxydroprotophan Methyl Ester (18b) Colorless needle (AcOEt-ether), mp 180°183 °C. Anal. Calcd for C₁₅H₁₄O₄N₂: C, 68.5; H, 5.75; N, 6.66. Found: C, 68.4; H, 5.69; N, 6.64. IR: 3310 (NH), 1720, 1670, 1650 (C=O) cm⁻¹. 1H-NMR (400 MHz, CDCl₃) δ: 1.30 (3H, t, J=8.0 Hz, OCH₂CH₂), 1.89 (3H, s, COS₂CH₂), 3.15 (3H, s, SO₂CH₂), 4.51 (2H, q, J=8.0 Hz, OCH₂CH₂), 5.50 (2H, s, CH₂Ph), 7.63 (4H, m, Ar-H), 4.17 (1H, s, NHC(O), 7.56 (5H, d, J=8.0 Hz, C₅H₆), 7.68 (2H, s, C₆H₄), 7.40 (2H, s, C₆H₄). MS m/z: 428 (M⁺, 90%), 398 (M⁺, 91%).
vinyl-(C), 161.3 (C\(\text{O}_2\)CH\(_2\)), 164.8 (C\(\text{O}_2\)CH\(_2\)), 167.8 (NH\(\text{CO}_2\)). Low-power selective double irradiation of the amide proton at 7.81 ppm and the methyl ester methyl at 3.33 ppm changed the signal of the ester carbon 164.8 ppm from multiplet to doublet (J = 11.7 Hz) in the \(^{13}\text{C}\)-nondecoupling spectrum. MS m/z: 420 (M*, 63%), 91 (100%). High-resolution-MS Found: 420.1721. Calcd for C\(_2\)\(\text{H}_4\)\(\text{N}_2\)\(\text{O}_2\): 420.1686. The second fraction gave the Z-isomer (186) as a pale yellow solid (22% mg, 53%).

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References and Notes


