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Dioxopyrrolines. LX.[1] Cycloaddition Reaction of 4-Benzoyl-5-ethoxycarbonyl-1-phenyl-1*H*-pyrrole-2,3-dione to Olefins: An Inverse-Electron-Demand Hetero Diels–Alder Reaction[2]

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Thermal cycloaddition of 4-benzoyl-5-ethoxycarbonyl-1-phenyl-1*H*-pyrrole-2,3-dione (dioxopyrroline) 1 to electron-rich olefins smoothly proceeded in a highly regio- and stereoselective manner to give pyranopyrrole derivatives in excellent yields. The reaction is a typical inverse-electron-demand hetero Diels–Alder reaction, in which dioxopyrroline behaves as an electron-deficient diene.

Key words 1*H*-pyrrole-2,3-dione; dioxopyrroline; thermal cyloaddition reaction; hetero Diels–Alder reaction; pyranopyrrole

1*H*-Pyrrole-2,3-dione (dioxopyrroline) has been utilized as a versatile synthon for a variety of *N*-heterocycles. The double bond of this synthon is prone to undergo cycloaddition reactions such as [2+2] photocycloaddition[3] and Diels–Alder (D–A) reaction[4] to various olefins and dienes. In the D–A reaction, a dioxopyrroline usually acts as a dienophile, reacting with electron-rich 1,3-dienes to afford *cis*-hydroindoles. This reaction was used as a key step in the syntheses of *Amaryllidaceae*[5] and *Erythrina* alkaloids.[6]

This paper deals in detail with thermal cycloaddition reaction of 4-benzoyl-5-ethoxycarbonyl-1-phenyl-1*H*-pyrrole-2,3-dione **1**, (benzoyl-dioxopyrroline) to olefins, where **1** behaves, in contrast to the usual D–A reaction, as an enophile to undergo an inverse-electron-demand, hetero D–A reaction.[2]

Results and Discussion

Thermal Cycloaddition Reaction of 1 with Acyclic Olefins When a solution of **1** and ethoxyethylene (5 molar eq) in toluene was heated under reflux, a rapid reaction took place to give the adduct **2a** as a sole product in 95% yield within 3 min. Reactions of styrene, acetoxyethylene, and 1-hexene with **1**, though they required long reaction times, similarly gave the adducts **2b** (79% yield), **2c** (84% yield), and **2d** (38% yield) as sole products, respectively. In the reaction with 1-hexene, the yield of **2d** increased to 61% when the reaction was carried out using a large excess of the olefin.

The results (summarized in Table 1) suggest that the yield of the product is greatly affected by the electronic properties of the substituents on ethylenes, with order of reactivity being: OEt > Ph > OAc > Bu. In contrast, the olefins with electron-withdrawing substituents, such as methyl acrylate and 1,2-*cis*- and *trans*-dichloroethylene, did not give any adduct even on prolonged heating at elevated temperature (160 °C). In these cases, the product was a 4-quinolone derivative **3**, formed by pyrolysis of **1** *via* 6π-electrocyclic reaction of the iminoketene.[2,7]

The thermal cycloaddtion of **1** to 1,1-disubstituted olefins also proceeded with very high regio- and stereoselectivity. Thus, 1-acetoxy-1-methylethylene gave the adduct **2e** in a yield of 53% and 1-phenyl-1-trimethylsilyloxyethylene gave **2f** (28% yield), together with **4** (12% yield) and **5** (21% yield). The latter two products were presumably generated from the adduct **2f** during the purification procedure by silica gel column chromatography: opening of the pyran ring in **2f** by acid catalyzed β-elimination and subsequent acid hydrolysis would give **4** and **5**, respectively. In fact, treatment of **2f** in MeOH–CH_2Cl_2 (1 : 1) under reflux and of **4** with silica gel in CH_2Cl_2 at room temperature each gave **5** in quantitative yield.

The structures of adducts were elucidated from the spectral data as pyrano[4,3-*b*]pyrrole derivatives. For example, the adduct **2a** exhibited absorptions at 235 nm (ε 12700) and 323 nm (ε 15000) in the UV spectra. The IR spectrum exhibited carbonyl absorptions at 1730 and 1720 cm^{-1} due to an ester, a five-membered α,β-unsaturated ketone and a five-membered lactam. In addition to these signals a strong absorption band at 1620 cm^{-1}, attributed to the double bond of the enol ether, was observed. These data are consistent with the assigned conjugated diketopyrrole moiety. In the ^{1}H-NMR spectrum, signals of an ABX pattern due to protons on the dihydropyran ring were characteristic, with peaks at δ 1.98 (dd) and 3.06 (dd) as the AB components and at δ 5.86 (dd) as the X component. The former signals were attributable to the 4-methylene protons, and the latter one to the 3-methine proton. The large difference in chemical shifts between H_X and H_A clearly indicated that the adduct has the assigned structure **2a**, not the regio-isomeric structure **2a′**.

The stereochemistry of 3-OEt was deduced as follows. The appreciable difference in chemical shift between H_A and H_B indicated that the stereochemical situation of these protons is markedly different. The proton arranged *cis* to the vicinal ethoxycarbonyl group should be deshielded. Thus, the signals at δ 3.06 and δ 1.98 were attributable to H_B (β) and H_A (α), respectively. The coupling constants between H_B and H_X (4 Hz) and between H_A and H_X (10 Hz) indicated that the stereochemical relationship of the former was *cis*, while that of the latter was *trans*. Assuming that the dihydropyran ring adopts the most stable half-chair conformation, the configuration of the 3-OEt group was

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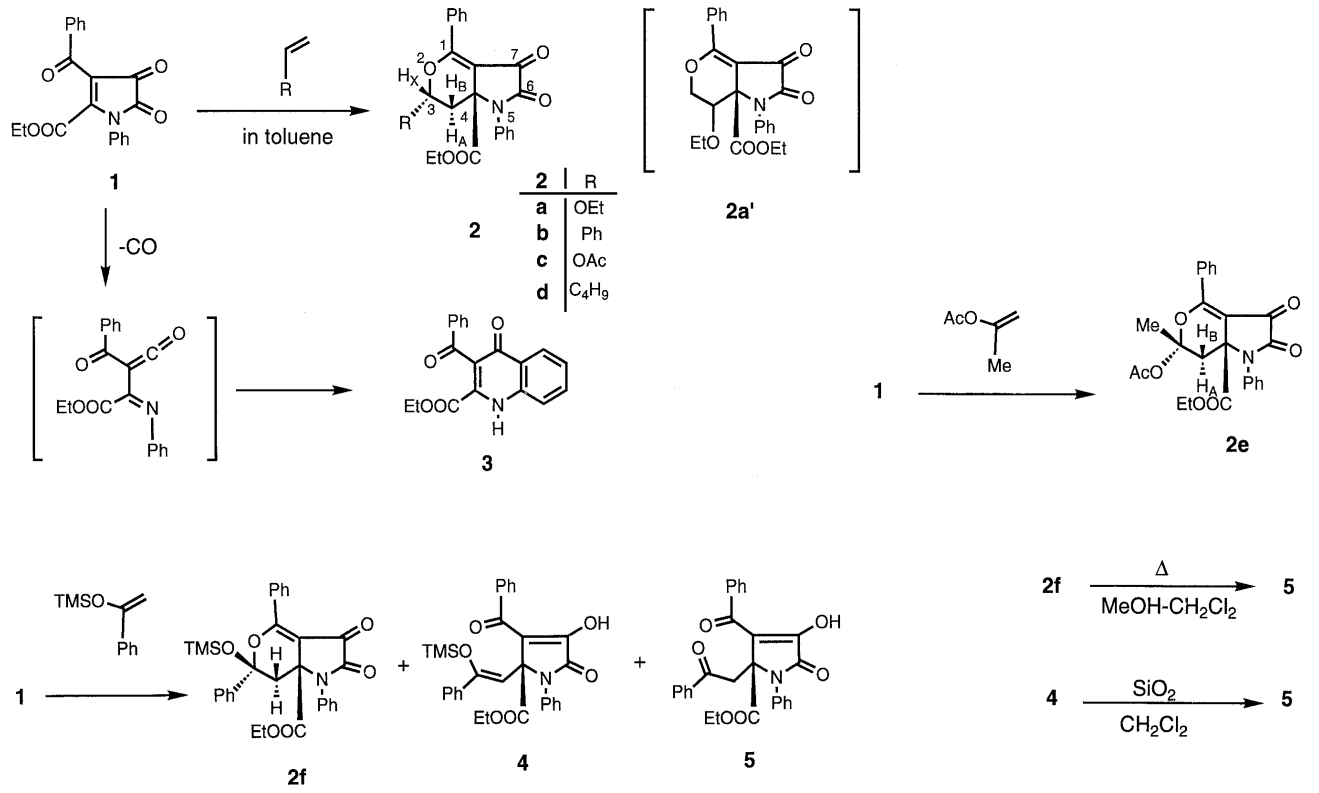

Chart 1

Table 1. Thermal Cycloaddition Reaction of **1** with Acyclic Olefins

Olefin	mol eq	Temp. (°C)	Time	Yields (%)	
				2	Others
Ethoxyethylene	5	120	3 min	95 (**2a**)	
Styrene	5	120	6 h	79 (**2b**)	
Acetoxyethylene	5	120	16 h	84 (**2c**)	
1-Hexene	5	120	40 h	38 (**2d**)	
	10	120	40 h	61 (**2d**)	
1-OAc-1-Me-ethylene	5	120	16 h	53 (**2e**)	
1-OTMS-1-Ph-ethylene	5	100	1 h	28 (**2f**)	12 (**4**) 21 (**5**)

Table 2. ^{1}H-NMR Spectra of H_A, H_B and H_X of Adducts **2**

Adduct	H_A (δ)	H_B (δ)	H_X (δ)	J_{A-B} (Hz)	J_{A-X} (Hz)	J_{B-X} (Hz)
2a	1.98	3.06	5.86	13	10	4
2b	2.05	3.06	5.79	13	12	3
2c	2.10	3.11	6.94	13	10	5
2d	1.73	2.84	4.74	13	13	3
2e	2.67	3.55	—	14	—	—

concluded to be equatorial (α).

The structure of the adducts **2b**, **2c**, and **2d** was similarly determined from their spectral data (see Experimental) and the stereochemistry of the 3-substituent was assigned as equatorial (α) (Table 2).

Pyranopyrrole structures of **2e** and **2f** were readily assigned from their spectral data. The stereochemistry at C_3 in **2e** was determined as β-Me and α-OAc, since a nuclear Overhauser effect (NOE) between the 3-Me (δ 2.04) and H_B (δ 3.55) signals was observed in the two dimensional nuclear Overhauser effect spectroscopy (2D-NOESY) spectrum, revealing that they are in *cis*-relationship. The stereochemistry of **2f**, though no informative spectroscopic evidence could be obtained, was deduced to be as depicted by analogy with that of the 1-trimethylsilyloxycyclohexene adduct **8b** (see below).

The structures of the adducts **2** indicate that in this cycloaddition reaction the conjugated enone of the 4-benzoyl moiety and the double bond in dioxopyrroline act as a heterodiene and the olefins as dienophiles.

Thermal Cycloaddition Reaction with Cyclic Olefins

Thermal cycloaddition reaction of **1** with five- and six-membered cyclic olefins (dihydrofuran, dihydropyran, cyclopentene, cyclohexene, 1-trimethylsilyloxycyclopentene, 1-trimethylsilyloxycyclohexene) proceeded in a highly regio- and stereoselective manner to give the pyranopyrrole derivatives as single products. Among cycloolefins, dihydropyran and dihydrofuran were the most reactive, giving the adducts **6a** and **6b** in quantitative yield, respectively, on heating at 120 °C for a short time (10—20 min). Cyclopentene, on heating for 40 h at 120 °C, gave the adduct **7a** in 74% yield. Cyclohexene was the least reactive olefin and gave the adduct **7b** in only 18% yield on heating at 120 °C for 40 h (Table 3).

The structures of these adducts **6a**, **6b**, **7a** and **7b** as pyranopyrrole derivatives were supported by the spectroscopic data. The stereochemistry of the ring juncture was elucidated as *cis* based on the coupling constant of the ring juncture protons (H_B and H_X, J=3—5 Hz). The *endo* configuration (α) of the newly introduced ring was deduced from the chemical shift of H_B, which appeared at relatively low field (δ 4.48—2.75) (Table 4), since the proton *trans* to H_X would exhibit a signal at around δ 2.0 (see Table 2).

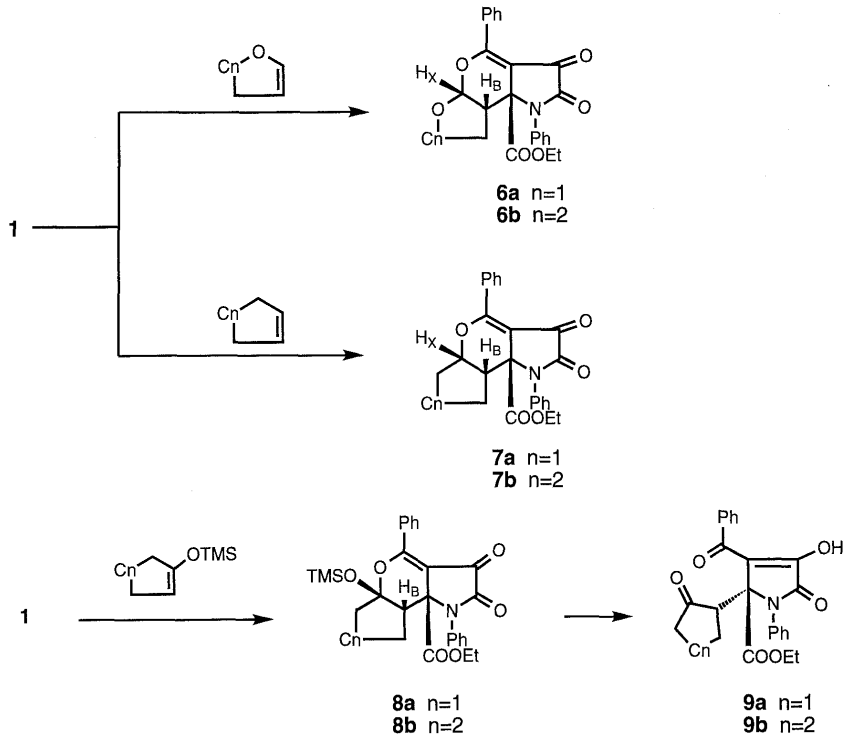

Chart 2

1-Trimethylsilyloxycyclopentene, on heating with **1** at 100 °C for 1 h, gave a Michael product **9a** as the sole adduct in 78% yield. This compound should be formed by hydrolysis of the adduct **8a**, although **8a** could not be detected in the reaction mixture even by TLC. The instability of **8a** to hydrolysis is attributable to the steric strain of the fused cyclopentane ring.

The reaction of **1** with 1-trimethylsilyloxycyclohexene also proceeded smoothly at 120 °C to give the normal adduct **8b** in 68% yield. The stereochemical relationship between the 5a-OTMS, 9a-H, and 9b-COOEt groups in the adduct was assigned as *β-cis* from the chemical shift of 9a-H (δ 3.10), which appeared at relatively lower field. Treatment of **8b** with silica gel caused hydrolysis of the silylether followed by concomitant ring opening to give **9b** in a quantitative yield.

In summary, the cycloaddition reaction of **1** with olefins under thermal conditions is concluded to be a D–A reaction with inverse electronic demand, where the benzoyl dioxopyrroline behaves as an electron-deficient heterodiene and the olefin as an electron-rich dienophile. The addition reaction of these addends proceeds in an *endo* fashion, as in the usual D–A reaction, with very high regio- and stereo-selectivity. Besides its theoretical interest, the reaction presented here provides a synthetic approach to the pyranopyrrole (5-oxahydroindole) ring system.

Experimental

Unless otherwise stated, the following procedures were adopted. All melting points were taken on a Yanagimoto micro hot-stage melting point apparatus (Yanagimoto MP type) and are uncorrected. IR spectra were measured with a JASCO FT/IR-5000 as KBr disks or Nujol mulls and values are given in cm^{-1}. UV spectra were measured with a Hitachi U-3200 spectrophotometer in dioxane and values are given in λ_{max} nm (ε). NMR spectra were taken on a JEOL JNM-α500 (^{1}H, 500 MHz; ^{13}C, 125 MHz), a JNM-GX270 (^{1}H, 270 MHz; ^{13}C, 67.5 MHz) or an EX-90 (^{1}H, 90 MHz; ^{13}C, 22.5 MHz) NMR spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. The chemical shifts are given in δ values. Low-resolution mass spectra (LRMS) and high-resolution mass spectra (HRMS) were determined with a JEOL JMS-HX110A spectrometer at 30 eV by using a direct inlet system. Elemental analyses were recorded on a Yanaco CHN-corder MT-3. For column chromatography, silica gel (Mallinkrodt type 150A or Wako-gel C-200) was used. Thin layer chromatography (TLC) was performed on Merck precoated Silica gel 60 F_{254} plates.

Table 3. Thermal Cycloaddition Reaction of **1** with Cyclic Olefins

Olefin	Temp. (°C)	Time	Yield (%) of products
Dihydrofuran	120	20 min	98 (**6a**)
Dihydropyran	120	10 min	95 (**6b**)
Cyclopentene	120	40 h	74 (**7a**)
Cyclohexene	120	40 h	18 (**7b**)
1-OTMS-cyclopentene	100	1 h	78 (**9a**)
1-OTMS-cyclohexene	120	10 h	68 (**8b**)

Table 4. ^{1}H-NMR Spectra of H_B and H_X in the Adducts of Cyclic Olefins

Product	H_X (δ)	H_B (δ)	J_{B-X}
6a	6.75	4.48	5.5
6b	6.29	2.97	3.5
7a	5.38	3.11	5
7b	5.05	2.75	3
8b	—	3.10	—

Cycloaddition of 1 with Acyclic Olefins (General Procedure) A toluene (10—25 ml) solution of **1** (2 mmol) and an olefin (10 mmol) was heated in a sealed tube under the conditions described in Table 1. After removal of the solvent *in vacuo*, the residue was purified by crystallization from CH_2Cl_2–Et_2O or by silica gel column chromatography (eluting with CH_2Cl_2), followed by crystallization from CH_2Cl_2–Et_2O, to give adduct **2** in the yields shown in Table 1.

(3*R**,4a*R**)-3-Ethoxy-4a-ethoxycarbonyl-4,4a,6,7-tetrahydro-6,7-

dioxo-1,5-diphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2a**): Yellow prisms, mp 188—190 °C. IR (Nujol): 1730, 1720, 1620, 1600. UV: 235 (12700), 323 (15000). ^{1}H-NMR: 1.28 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 1.32 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.98 (1H, dd, J=10, 13 Hz, H-4), 3.06 (1H, dd, J=4, 13 Hz, H-4), 3.79 (1H, dq, J=9.5, 7 Hz, $OC\underline{H}_2CH_3$), 4.16 (1H, dq, J=9.5, 7 Hz, $OC\underline{H}_2CH_3$), 4.28 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.86 (1H, dd, J=4, 10 Hz, H-3), 7.2—7.6 (8H, m, Ph), 7.9—8.0 (2H, m, Ph). ^{13}C-NMR: 14.2 ($COOCH_2C\underline{H}_3$), 15.3 ($OCH_2C\underline{H}_3$), 35.1 (C4), 62.6 (C4a), 63.3 ($OC\underline{H}_2CH_3$), 66.4 ($COOC\underline{H}_2CH_3$), 102.0 (C3), 105.3 (C7a), 125.5 (2C, Ph), 128.1 (2C, Ph), 128.4 (Ph), 129.8 (2C, Ph), 130.3 (2C, Ph), 130.9 (Ph), 133.0 (Ph), 135.1 (Ph), 162.8 (C6), 164.5 ($\underline{C}OOCH_2CH_3$), 170.7 (C1), 177.6 (C7). *Anal.* Calcd for $C_{24}H_{23}NO_6$: C, 68.39; H, 5.51; N, 3.32. Found: C, 68.24; H, 5.50; N, 3.25.

(3*R**,4a*R**)-4a-Ethoxycarbonyl-4,4a,6,7-tetrahydro-6,7-dioxo-1,3,5-triphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2b**): Yellow prisms, mp 240—243 °C. IR (Nujol): 1730, 1720, 1590. UV: 230 (12600), 320 (13000). ^{1}H-NMR: 1.32 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.05 (1H, dd, J=12, 13 Hz, H-4), 3.06 (1H, dd, J=3, 13 Hz, H-4), 4.34 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$) 5.79 (1H, dd, J=3, 12 Hz, H-3), 7.3—7.5 (13H, m, Ph), 7.9—8.0 (2H, m, Ph). ^{13}C-NMR: 14.0 ($COOCH_2\underline{C}H_3$), 36.1 (C4), 62.0 (C4a), 63.2 ($COO\underline{C}H_2CH_3$), 78.7 (C3), 104.7 (C7a), 125.2 (2C, Ph), 126.1 (2C, Ph), 127.7 (2C, Ph), 128.1 (Ph), 129.0 (3C, Ph), 129.5 (2C, Ph), 130.0 (2C, Ph), 130.7 (Ph), 132.5 (Ph), 134.9 (Ph), 138.4 (Ph), 162.4 (C6), 165.2 ($\underline{C}OOCH_2CH_3$), 170.7 (C1), 177.9 (C7). *Anal.* Calcd for $C_{28}H_{23}NO_5$: C, 74.15; H, 5.12; N, 3.09. Found: C, 74.10; H, 5.20; N, 2.89.

(3*S**,4a*R**)-3-Acetoxy-4a-ethoxycarbonyl-4,4a,6,7-terahydro-6,7-dioxo-1,5-diphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2c**): Yellow prisms, mp 209—213 °C. IR (Nujol): 1759, 1730, 1610, 1592. UV: 235 (13300), 325 (15400). ^{1}H-NMR: 1.28 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.10 (1H, dd, J=10, 13 Hz, H-4), 2.20 (3H, OAc), 3.11 (1H, dd, J=5, 13 Hz, H-4), 4.31 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 6.94 (1H, dd, J=5, 10 Hz, H-3), 7.3—7.5 (8H, m, Ph), 7.9—8.0 (2H, m, Ph). ^{13}C-NMR: 13.9 ($COOCH_2\underline{C}H_3$), 20.7 ($OCO\underline{C}H_3$), 33.2 (C4), 61.9 (C4a), 63.4 ($COO\underline{C}H_2CH_3$), 91.8 (C3), 105.3 (C7a), 125.1 (2C, Ph), 127.8 (2C, Ph), 128.4 (Ph), 129.6 (2C, Ph), 130.0 (2C, Ph), 133.0 (Ph), 133.0 (Ph), 134.6 (Ph), 162.0 (C6), 163.1 ($\underline{C}OOCH_2CH_3$), 168.4 ($O\underline{C}OCH_3$), 169.8 (C1), 177.4 (C7). *Anal.* Calcd for $C_{24}H_{21}NO_7$: C, 66.19; H, 4.87; N, 3.22. Found: C, 65.99; H, 4.93; N, 3.11.

(3*S**,4a*R**)-3-Butyl-4a-ethoxycarbonyl-4,4a,6,7-terahydro-6,7-dioxo-1,5-diphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2d**): Yellow prisms, mp 195—196 °C. IR (Nujol): 1730, 1700, 1602, 1590. UV: 233 (13500), 332 (13900). ^{1}H-NMR: 0.95 (3H, t, J=7 Hz, $C\underline{H}_3$ $(CH_2)_3$), 1.28 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.41 (2H, q, J=7 Hz, CH_3–$C\underline{H}_2$–$(CH_2)_2$), 1.45—1.53 (1H, m, CH_2), 1.55—1.63 (1H, m, CH_2), 1.73 (1H, t, J=13 Hz, H-4), 1.80—1.91 (2H, m, CH_2), 2.84 (1H, dd, J=3, 13 Hz, H-4), 4.27 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 4.72—4.77 (1H, m, H-3), 7.22—7.28 (2H, m, Ph), 7.31—7.37 (1H, m, Ph), 7.43—7.50 (4H, m, Ph), 7.54—7.57 (1H, m, Ph), 7.86—7.88 (2H, m, Ph). ^{13}C-NMR: 13.9 ($\underline{C}H_3(CH_2)_3$), 14.1 ($COOCH_2\underline{C}H_3$), 22.5 (CH_3–$\underline{C}H_2$–$(CH_2)_2$), 27.1 (CH_3–CH_2–$\underline{C}H_2$–CH_2), 33.6 (C4), 35.1 (CH_3–CH_2–CH_2–$\underline{C}H_2$), 62.0 (C4a), 63.0 ($COO\underline{C}H_2CH_3$), 77.1 (C3), 104.7 (C7a), 125.3 (2C, Ph), 127.7 (2C, Ph), 128.1 (Ph), 129.6 (2C, Ph), 129.9 (2C, Ph), 131.0 (Ph), 132.4 (Ph), 135.1 (Ph), 162.8 (C6), 165.4 ($\underline{C}OOCH_2CH_3$), 170.9 (C1), 177.9 (C7). *Anal.* Calcd for $C_{26}H_{27}NO_5$: C, 72.04; H, 6.28; N, 3.23. Found: C, 71.80; H, 6.33; N, 3.08.

(3*S**,4a*R**)-3-Acetoxy-4a-ethoxycarbonyl-4,4a,6,7-terahydro-3-methyl-6,7-dioxo-1,5-diphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2e**): Yellow prisms, mp 180—182 °C. IR (Nujol): 1723, 1610, 1590. UV: 233 (13000), 335 (15700). ^{1}H-NMR: 1.24 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.04 (3H, s, CH_3), 2.04 (3H, s, $OCOC\underline{H}_3$), 2.67 (1H, d, J=14 Hz, H-4), 3.55 (1H, d, J=14 Hz, H-4), 4.26 (2H, qq, J=11, 7 Hz, $COOC\underline{H}_2CH_3$), 7.25—7.27 (2H, m, Ph), 7.37 (1H, t, J=8 Hz, Ph), 7.46 (2H, t, J=8 Hz, Ph), 7.52 (2H, t, J=8 Hz, Ph), 7.61 (1H, t, J= 8 Hz, Ph), 8.07—8.09 (2H, m, Ph). ^{13}C-NMR: 14.0 ($COOCH_2\underline{C}H_3$), 21.9 ($\underline{C}H_3$), 26.4 ($OCO\underline{C}H_3$), 40.7 (C4), 62.6 (C4a), 63.4 ($COO\underline{C}H_2CH_3$), 106.1 (C7a), 109.2 (C3), 125.0 (2C, Ph), 128.2 (2C, Ph), 128.3 (Ph), 129.7 (2C, Ph), 130.3 (Ph), 130.6 (2C, Ph), 133.7 (Ph), 134.7 (Ph), 161.9 (C6), 163.3 ($\underline{C}OOCH_2CH_3$), 169.0 ($O\underline{C}OCH_3$), 169.9 (C1), 177.7 (C7). *Anal.* Calcd for $C_{25}H_{23}NO_7$: C, 66.80; H, 5.17; N, 3.12. Found: C, 66.88; H, 5.15; N, 2.96.

Cycloaddition of 1 with 1-Trimethylsilyloxy-1-phenylethylene A benzene (10 ml) solution of **1** (698 mg, 2 mmol) and 1-trimethylsilyoxy-1-phenylethylene (1.8 g, 10 mmol) was heated in a sealed tube at 100 °C for 1 h. After removal of the solvent *in vacuo*, the residue was crystallized from CH_2Cl_2–Et_2O to give **2f** (303 mg, 28%) as yellow prisms. The mother liquor was chromatographed over SiO_2. Elution with benzene–CH_2Cl_2 (1 : 1) gave **4** (134 mg, 12%) and elution with CH_2Cl_2 gave **5** (200 mg, 21%).

(3*S**,4a*R**)-4a-Ethoxycarbonyl-4,4a,6,7-tetrahydro-3-trimetylsilyloxy-6,7-dioxo-1,3,5-triphenyl-5*H*-pyrano[4,3-*b*]pyrrole (**2f**): Yellow prisms, mp 159—161 °C. IR (KBr): 1725, 1595. UV: 230 (14700), 315 (12300). ^{1}H-NMR: −0.19 (9H, s, OTMS), 1.23 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 2.11 (1H, d, J=13 Hz, H-4), 3.32 (1H, d, J=13 Hz, H-4), 4.19 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 7.11—7.15 (2H, m, Ph), 7.36—7.50 (6H, m, Ph), 7.52—7.62 (5H, m, Ph), 8.04—8.08 (2H, m, Ph). ^{13}C-NMR: 0.7 (OTMS), 13.9 ($COOCH_2\underline{C}H_3$), 42.2 (C4), 62.1 ($COO\underline{C}H_2CH_3$), 62.4 (C4a), 101.4 (C3), 106.9 (C7a), 125.2 (2C, Ph), 127.7 (2C, Ph), 127.8 (2C, Ph), 128.6 (2C, Ph), 128.8 (Ph), 129.1 (Ph), 129.3 (2C, Ph), 130.1 (2C, Ph), 130.9 (Ph), 132.3 (Ph), 134.8 (Ph), 142.1 (Ph), 161.4 (C6), 162.4 ($\underline{C}OOCH_2CH_3$), 168.3 (C1), 178.4 (C7). *Anal.* Calcd for $C_{31}H_{31}NO_6Si$: C, 68.74; H, 5.77; N, 2.59. Found: C, 68.60; H, 5.61; N, 2.70.

(5*R**)-4-Benzoyl-5-ethoxycarbonyl-1,5-dihydro-3-hydroxy-5-(2-trimethylsilyloxy-2-phenylethenyl)-2*H*-pyrrol-2-one (**4**): Colorless prisms from CH_2Cl_2–Et_2O, mp 149—151 °C. IR (KBr): 3200, 1746, 1682, 1649, 1601. UV: 258 (21600), 306 sh (7200). ^{1}H-NMR: −0.10 (9H, s, OTMS), 1.12 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 4.17 (2H, qq, J=11, 7 Hz, $COOC\underline{H}_2CH_3$), 5.75 (1H, s, H-1′), 7.09 (2H, d, J=7 Hz, Ph), 7.20—7.29 (4H, m, Ph), 7.40 (2H, t, J=8 Hz, Ph), 7.48 (2H, t, J=8 Hz, Ph), 7.57—7.61 (3H, m, Ph), 7.90 (2H, d, J=8 Hz, Ph). ^{13}C-NMR: 1.14 (OTMS), 13.9 ($COOCH_2\underline{C}H_3$), 62.8 ($COO\underline{C}H_2CH_3$), 69.3 (C5), 102.1 (C1′), 119.8 (C4), 123.85 (3C, Ph), 127.0 (Ph), 127.5 (2C, Ph), 128.0 (2C, Ph), 128.2 (2C, Ph), 128.8 (Ph), 129.0 (3C, Ph), 132.9 (Ph), 136.1 (Ph), 137.4 (Ph), 138.8 (Ph), 154.2 (C2′), 155.0 (C3), 165.7 (C2), 169.0 ($\underline{C}OOCH_2CH_3$), 188.8 ($\underline{C}OPh$). *Anal.* Calcd for $C_{31}H_{31}NO_6Si$: C, 68.74; H, 5.77; N, 2.59. Found: C, 68.50; H, 5.81; N, 2.68.

(5*R**)-4-Benzoyl-5-ethoxycarbonyl-1,5-dihydro-3-hydroxy-5-(2-oxo-2-phenylethyl)-2*H*-pyrrol-2-one (**5**): Colorless prisms from CH_2Cl_2–Et_2O, mp 190—192 °C. IR (KBr): 3200, 1742, 1719, 1680, 1630, 1599. UV: 249 (19400), 293 (11700). ^{1}H-NMR: 1.31 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 3.56 (1H, d, J=18 Hz, H-1′), 4.08 (1H, d, J=18 Hz, H-1′), 4.30 (1H, dq, J=11, 7 Hz, $COOC\underline{H}_2CH_3$), 4.40 (1H, dq, J=11, 7 Hz, $COOC\underline{H}_2CH_3$), 7.20—7.22 (2H, m, Ph), 7.30—7.41 (7H, m, Ph), 7.43—7.46 (1H, m, Ph), 7.50—7.53 (1H, m, Ph), 7.75—7.77 (4H, m, Ph). ^{13}C-NMR: 14.1 ($COOCH_2\underline{C}H_3$), 35.7 (C1′), 62.9 ($COO\underline{C}H_2CH_3$), 69.4 (C5), 118.7 (C4), 126.5 (2C, Ph), 127.9 (2C, Ph), 128.2 (2C, Ph), 128.5 (Ph), 128.6 (2C, Ph), 129.2 (2C, Ph), 129.6 (2C, Ph), 133.0 (Ph), 133.4 (Ph), 134.2 (Ph), 136.8 (Ph), 137.6 (Ph), 150.2 (C3), 166.7 (C2), 169.3 ($\underline{C}OOCH_2CH_3$), 189.7 ($\underline{C}OPh$), 195.9 (C2′$\underline{C}O$). *Anal.* Calcd for $C_{28}H_{23}NO_6 \cdot H_2O$: C, 68.98; H, 5.17; N, 2.87. Found: C, 68.70; H, 4.91; N, 3.01.

Hydrolysis of 2f and 4 1) A solution of **2f** (260 mg) in MeOH–CH_2Cl_2 (1 : 1) (2 ml) was refluxed for 1 min and the product was cystallized from MeOH–CH_2Cl_2–Et_2O to give **5** (220 mg, 98%).

2) A solution of **4** (15 mg) in CH_2Cl_2 (10 ml) was treated with SiO_2 (2 g) at room temperature for 2 h. The mixture was passed through a short SiO_2 column to give **5** (12 mg, 92%).

Cycloaddition of 1 with Cyclic Olefins (General Procedure) A toluene (10—25 ml) solution of **1** (2 mmol) and an olefin (5 mmol) was heated in a sealed tube under the conditions shown in Table 3. After removal of the solvent *in vacuo*, the residue was purified by crystallization from CH_2Cl_2–Et_2O or by silica gel column chromatography (eluting with CH_2Cl_2) to give the adducts **6** and **7** in the yields shown in Table 3.

(3a*R**,8a*R**,8b*S**)-8a-Ethoxycarbonyl-1,2,6,7,8a,8b-hexahydro-6,7-dioxo-8*H*-furo[2′,3′ : 6,5]pyrano[4,3-*b*]pyrrole (**6a**): Yellow prisms, mp 207—210 °C, IR (KBr): 1729, 1595. UV: 232 (13100), 334 (15800). ^{1}H-NMR: 1.27 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 1.64—1.72 (1H, m, CH_2), 1.79—1.86 (1H, m, $C\underline{H}_2$), 3.48 (1H, td, J=10, 5.5 Hz, H-8b), 4.03 (1H, dd, J=16.5, 8 Hz, OCH_2), 4.10 (1H, td, J=9, 5 Hz, $OC\underline{H}_2$), 4.32 (2H, qq, J=11, 7 Hz, $COOC\underline{H}_2CH_3$), 6.37 (1H, d, J=5.5 Hz, H-3a), 7.31—7.36 (3H, m, Ph), 7.44—7.51 (4H, m, Ph), 7.58—7.61 (1H, m, Ph), 8.00—8.02 (2H, m, Ph). ^{13}C-NMR: 13.9 ($COOCH_2\underline{C}H_3$), 24.1 ($\underline{C}H_2$), 42.0 (C8b), 63.4 ($COO\underline{C}H_2CH_3$), 64.4 (C8a), 68.5 ($O\underline{C}H_2$), 105.2 (C3a), 123.2 (2C, Ph), 127.7 (Ph), 128.0 (2C, Ph), 129.6 (2C, Ph), 130.2 (2C, Ph), 133.4 (Ph), 135.0 (2C, Ph), 162.3 (C7), 165.2 ($\underline{C}OOCH_2CH_3$), 170.6 (C5), 177.4 (C6). HRMS Calcd for $C_{24}H_{21}NO_6$: 419.1366. Found: 419.1356.

(5a*R**,9a*S**,9b*R**)-9b-Ethoxycarbonyl-2,3,8,9,9a,9b-hexahydro-2,3-dioxo-1,4-diphenyl-1*H*-pyrano[2′,3′ : 6,5]pyrano[4,3-*b*]pyrrole (**6b**): Yellow prisms, mp 232—235 °C. IR (Nujol): 1730, 1720, 1603, 1598. UV: 228 (9200), 325 (10300). ^{1}H-NMR: 1.23 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$),

1.41—1.46 (1H, m, CH_2), 1.63—1.73 (3H, m, CH_2), 2.97 (1H, ddd J=10, 4.5, 3.5 Hz, H-9a), 3.88—3.90 (2H, m, OCH_2), 4.30 (2H, qq, J=11, 7 Hz, $COOCH_2CH_3$), 6.29 (1H, d, J=3.5 Hz, H-5a), 7.29—7.32 (1H, m, Ph), 7.36—7.38 (2H, m, Ph), 7.43—7.47 (2H, m, Ph), 7.49—7.52 (2H, m, Ph), 7.57—7.61 (1H, m, Ph), 7.95—7.97 (2H, m, Ph). ^{13}C-NMR: 13.9 ($COOCH_2CH_3$), 18.1 (CH_2), 23.3 (CH_2), 33.2 (C9a), 61.5 (OCH_2), 63.4 ($COOCH_2CH_3$), 65.2 (C9b), 97.9 (C5a), 102.0 (C3a), 121.9 (2C, Ph), 127.1 (Ph), 127.9 (2C, Ph), 129.6 (2C, Ph), 129.7 (2C, Ph), 130.4 (Ph), 132.9 (Ph), 135.5 (Ph), 162.6 (C2), 164.0 ($COOCH_2CH_3$), 171.2 (C4), 177.6 (C3). *Anal.* Calcd for $C_{25}H_{23}NO_6$: C, 68.40; H, 5.50; N, 3.33. Found: C, 68.65; H, 5.44; N, 3.40.

(5a*S**,8a*R**,8b*R**)-8b-Ethoxycarbonyl-2,3,8a,8b-tetrahydro-2,3-dioxo-1,4-diphenyl-1*H*-cyclopenta[1′,2′:5,6]pyrano[4,3-*b*]pyrrole (**7a**): Yellow prisms, mp 172—174 °C. IR (KBr): 1720, 1593. UV: 230 (14700), 330 (14800). ^{1}H-NMR: 1.26 (3H, t, J=7 Hz, $COOCH_2CH_3$), 1.26—1.33 (1H, m, CH_2), 1.48—1.56 (1H, m, CH_2), 1.68—1.79 (2H, m, CH_2), 2.06—2.14 (1H, m, CH_2), 2.25 (1H, ddd, J=15, 8, 3 Hz, CH_2), 3.11 (1H, td, J=10, 5 Hz, H-8a), 4.30 (2H, qq, J=11, 7 Hz, $COOCH_2CH_3$), 5.38 (1H, t, J=5 Hz, H-5a), 7.28—7.32 (3H, m, Ph), 7.43 (2H, t, J=8 Hz, Ph), 7.47 (2H, t, J=8 Hz, Ph), 7.57 (1H, t, J=7 Hz, Ph), 7.86 (1H, d, J=7 Hz, Ph). ^{13}C-NMR: 14.0 ($COOCH_2CH_3$), 21.9 (CH_2), 24.6 (CH_2), 33.9 (CH_2), 41.1 (C8a), 63.0 ($COOCH_2CH_3$), 64.0 (C8b), 84.9 (C5a), 101.7 (C3a), 123.1 (2C, Ph), 127.3 (Ph), 127.9 (2C, Ph), 129.5 (3C, Ph), 130.0 (Ph), 130.9 (Ph), 132.8 (Ph), 135.6 (Ph), 162.7 (C2), 165.8 ($COOCH_2CH_3$), 171.4 (C4), 177.9 (C3). *Anal.* Calcd for $C_{25}H_{23}NO_5$: C, 71.93; H, 5.55; N, 3.36. Found: C, 71.84; H, 5.71; N, 3.23.

(5a*S**,9a*R**,9b*R**)-9b-Ethoxycarbonyl-2,3,9a,9b-tetrahydro-2,3-dioxo-1,4-diphenyl-1*H*-cyclohexa[1′,2′:5,6]pyrano[4,3-*b*]pyrrole (**7b**): Yellow prisms, mp 156—158 °C. IR (KBr): 1725, 1593. UV: 229 (14800), 325 (14800). ^{1}H-NMR: 0.98 (1H, ddd, J=26, 13, 4 Hz, CH_2), 1.17—1.26 (1H, m, CH_2), 1.23 (3H, t, J=7 Hz, $COOCH_2CH_3$), 1.33—1.36 (1H, m, CH_2), 1.53—1.61 (2H, m, CH_2), 1.66—1.78 (2H, m, CH_2), 2.33 (1H, br d, J=14 Hz, CH_2), 2.75 (1H, ddd, J=13, 4, 3 Hz, H-9a), 4.27 (2H, qq, J=11, 7 Hz, $COOCH_2CH_3$), 5.05 (1H, br d, J=3 Hz, H-5a), 7.27—7.30 (1H, m, Ph), 7.37—7.39 (2H, m, Ph), 7.41—7.45 (2H, m, Ph), 7.48—7.50 (2H, m, Ph), 7.54—7.58 (1H, m, Ph), 7.86—7.90 (2H, m, Ph). ^{13}C-NMR: 13.9 ($COOCH_2CH_3$), 20.0 (CH_2), 20.5 (CH_2), 24.0 (CH_2), 30.1 (CH_2), 34.2 (C9a), 63.0 ($COOCH_2CH_3$), 65.0 (C9b), 75.4 (C5a), 102.5 (C3a), 122.3 (2C, Ph), 126.9 (Ph), 127.7 (2C, Ph), 129.4 (2C, Ph), 129.6 (2C, Ph), 131.0 (Ph), 132.3 (Ph), 135.9 (Ph), 162.8 (C2), 164.8 ($COOCH_2CH_3$), 171.8 (C4), 178.2 (C3). *Anal.* Calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 72.29; H, 5.92; N, 3.24.

Cycloaddition of 1 with 1-Trimethylsilyloxycyclopentene A toluene (10 ml) solution of **1** (698 mg, 2 mmol) and an olefin (1.17 g, 7.5 mmol) was heated in a sealed tube at 100 °C for 1 h. After removal of the solvent *in vacuo*, the residue was crystallized from CH_2Cl_2–Et_2O to give (5*R**)-4-benzoyl-1,5-dihydro-3-hydroxy-5-(2-oxocyclopentyl)-2*H*-pyrrol-2-one (**9a**) 675 mg, 78% as colorless prisms, mp 203—205 °C. IR (Nujol): 1741, 1698, 1680, 1648, 1599. UV: 260 (11300), 300 sh (6000), 334 (3000). ^{1}H-NMR: 1.16 (3H, t, J=7 Hz, $COOCH_2CH_3$), 1.48 (1H, ddd, J=24, 12, 7 Hz, H-5′), 1.57—1.69 (1H, m, H-4′), 1.81—1.86 (1H, m, H-4′), 2.25 (1H, dd, J=14, 8 Hz, H-3′), 2.24 (1H, d, J=8 Hz, H-3′), 2.39—2.44 (1H, m, H-5′), 3.21 (1H, dd, J=12, 8 Hz, H-1′), 4.22 (1H, dq, J=11, 7 Hz, $COOCH_2CH_3$), 4.29 (1H, dq, J=11, 7 Hz, $COOCH_2CH_3$), 7.14—7.16 (2H, m, Ph), 7.36—7.49 (5H, m, Ph), 7.56—7.62 (1H, m, Ph), 7.81—8.00 (2H, m, Ph). ^{13}C-NMR: 13.7 ($COOCH_2CH_3$), 20.0 (C4′), 26.1 (C5′), 38.3 (C3′), 51.0 (C1′), 62.6 ($COOCH_2CH_3$), 72.3 (C5), 119.1 (C4), 128.0 (2C, Ph), 128.3 (2C, Ph), 129.0 (Ph), 129.6 (2C, Ph), 129.7 (2C, Ph), 133.3 (Ph), 135.2 (Ph), 137.3 (Ph), 148.1 (C3), 166.5 (C2), 168.0 ($COOCH_2CH_3$), 190.1 (COPh), 214.5 (C2′CO). *Anal.* Calcd for $C_{25}H_{23}NO_6$: C, 69.27; H, 5.35; N, 3.23. Found: C, 68.97; H, 5.30; N, 3.38.

Cycloaddition of 1 with 1-Trimethylsilyloxycyclohexene A toluene (10 ml) solution of **1** (698 mg, 2 mmol) and an olefin (1.26 g, 7.5 mmol) was heated in a sealed tube at 120 °C for 10 h. After removal of the solvent *in vacuo*, the residue was crystallized from CH_2Cl_2–Et_2O to give (5a*R**,9a*S**,9b*R**)-9b-ethoxycarbonyl-2,3,9a,9b-tetrahydro-2,3-dioxo-5a-trimethylsilyloxy-1,4-diphenyl-1*H*-cyclohexa[1′,2′:5,6]pyrano[4,3-*b*]pyrrole (**8b**) 698 mg, 68% as yellow prisms, mp 163—166 °C. IR (KBr): 1736, 1725, 1593. UV: 230 (15500), 322 (13600). ^{1}H-NMR: 0.03 (3H, s, OTMS), 1.00 (1H, td, J=13.5, 3.5 Hz, CH_2), 1.06 (3H, t, J=7 Hz, $COOCH_2CH_3$), 1.34 (1H, ddd, J=27, 13, 3.5 Hz, CH_2), 1.57 (1H, tt, J=13, 3.5 Hz, CH_2), 1.72—1.81 (2H, m, CH_2), 1.84—1.88 (2H, m, CH_2), 2.38 (1H, d, J=13.5 Hz, CH_2), 3.10 (1H, dd, J=13, 4 Hz, H-9a), 3.94 (1H, dq, J=11, 7 Hz, $COOCH_2CH_3$), 4.12 (1H, dq, J=11, 7 Hz, $COOCH_2CH_3$), 7.30—7.33 (1H, m, Ph), 7.40—7.51 (6H, m, Ph), 7.54—7.58 (1H, m, Ph), 7.88—7.90 (2H, m, Ph). ^{13}C-NMR: 1.5 (OTMS), 13.7 ($COOCH_2CH_3$), 23.5 (C8), 23.6 (C7), 23.7 (C9), 38.3 (C6), 40.7 (C9a), 61.9 ($COOCH_2CH_3$), 66.6 (C9b), 102.3 (C3a), 104.7 (C5a), 125.2 (2C, Ph), 127.6 (3C, Ph), 129.2 (2C, Ph), 129.8 (2C, Ph), 131.0 (Ph), 132.2 (Ph), 136.6 (Ph), 161.2 (C2), 163.3 ($COOCH_2CH_3$), 168.7 (C4), 178.5 (C3). *Anal.* Calcd for $C_{29}H_{33}NO_6Si$: C, 67.03; H, 6.40; N, 2.70. Found: C, 66.89; H, 6.19; N, 2.84.

Hydrolysis of 8b A solution of **8b** (50 mg) in CH_2Cl_2 (10 ml) was treated with SiO_2 (2 g) at room temperature for 2 h. The mixture was passed through a short SiO_2 column and the column was washed with the same solvent. After removal of the solvent *in vacuo*, the residue was crystallized from CH_2Cl_2–Et_2O–hexane to give (5*R**)-4-benzoyl-1,5-dihydro-3-hydroxy-5-(2-oxocyclohexyl)-2*H*-pyrrol-2-one (**9b**) 42 mg (98%) as colorless prisms, mp 189—192 °C. IR (KBr): 3068, 2946, 1734, 1715, 1698, 1651, 1599. UV: 257 (13500), 289 sh (6800). ^{1}H-NMR: 1.07 (3H, t, J=7 Hz, $COOCH_2CH_3$), 1.52—1.65 (1H, m, CH_2), 1.72—1.82 (2H, m, CH_2), 1.89—1.91 (1H, m, CH_2), 1.99—2.04 (1H, m, CH_2), 2.12—2.17 (1H, m, CH_2), 2.22—2.29 (1H, m, CH_2), 2.39—2.43 (1H, m, CH_2), 3.52 (1H, dd, J=12, 4.5 Hz, H-1′), 4.12 (1H, dq, J=11, 7 Hz, $COOCH_2CH_3$), 7.18—7.20 (2H, m, Ph), 7.38—7.49 (5H, m, Ph), 7.57—7.60 (1H, m, Ph), 7.97—7.99 (2H, m, Ph). ^{13}C-NMR: 13.7 ($COOCH_2CH_3$), 25.2 (CH_2), 26.5 (CH_2), 28.0 (CH_2), 42.4 (CH_2), 51.8 (C1′), 62.4 ($COOCH_2CH_3$), 73.5 (C5), 118.3 (C4), 128.1 (2C, Ph), 128.4 (2C, Ph), 129.0 (Ph), 129.6 (2C, Ph), 129.9 (2C, Ph), 133.5 (Ph), 135.3 (Ph), 137.1 (Ph), 147.5 (C3), 166.5 (C2), 168.1 ($COOCH_2CH_3$), 190.3 (COPh), 208.0 (C2′CO). *Anal.* Calcd for $C_{26}H_{25}NO_6$: C, 69.78; H, 5.63; N, 3.13. Found: C, 69.65; H, 5.71; N, 3.17.

References and Notes

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