Synthesis of Optically Active 1,2,3-Substituted-1,4,5,6-tetrahydro-7*H*-indolones

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This manuscript is dedicated to Professor M. Tišler on the occasion of his seventieth birthday

Trisubstituted 1,4,5,6,-tetrahydro-7*H*-indolones are obtained in a one-pot synthesis from conjugated nitroolefins and α-ketoenamines derived from α-amino esters and cyclohexane-1,2-dione. In some cases bicyclo[3.2.1]octan-8-one and 1,2-oxazine *N*-oxide derivatives are isolated.

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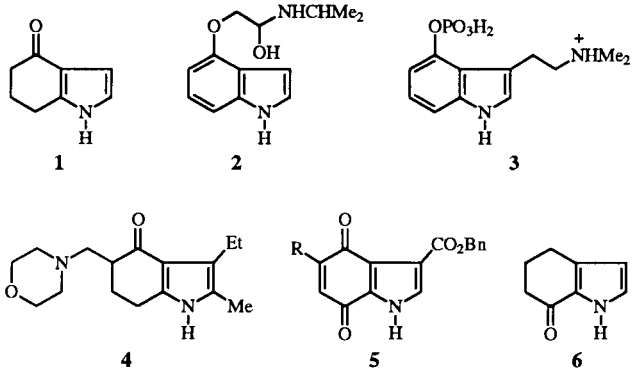
Derivatives of 4-oxo-1,4,5,6-tetrahydroindole **1** (Scheme 1) are studied in particular in relation with the synthesis of indoles bearing fuctionalities at the 4-position, which are important because of their wide variety of biological activities [1]. Examples are the pindolol **2** which belongs to the important family of compounds known as β adrenergic receptor antagonists [1d], the hallucinogenic psilocybine **3** [1e], the neurolectic molindone **4** and analogs [1f] and several other dehydrogenated derivatives [1a]. Whereas a synthesis of indoloquinones **5** present in important anticancer compounds such as mitomycin has been recently proposed by Edstrom [2], less is known about the synthesis of the simple 7-oxo-1,4,5,6-tetrahydroindole derivatives **6** [3], in particular as chiral compounds [4].

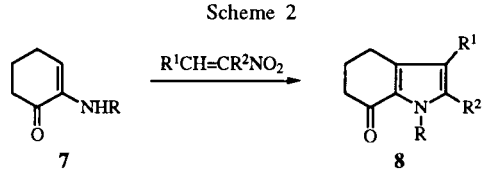
Scheme 1



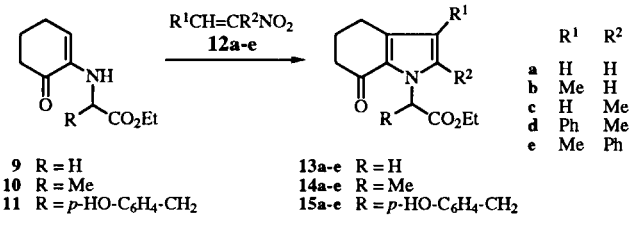
Secondary cross-conjugated α-ketoenamines **7** derived from cyclohexane-1,2-dione and alkyl and aryl amines have been shown to give 7-indolone derivatives **8** when reacted with conjugated nitroolefins (Scheme 2) [5].

As part of a program aimed at developing an approach to chiral heterocycles starting from α-ketoenamines [3], we investigated the reactivity of substrates in which the amino component was an amino acid ester residue [6]. Therefore the α-ketoenamines **9, 10** and **11** were prepared by Stork condensation [7] of cyclohexane-1,2-dione with glycine ethyl ester, alanine ethyl ester and tyrosine ethyl ester respectively (Scheme 3). This choice was made with the aim of studying the influence of an increasing bulkiness of the amine moiety on the reactivity of the substrate towards a series of conjugated nitroolefins **12a-e**. These latter compounds are listed in Scheme 3.

Scheme 2



Scheme 3



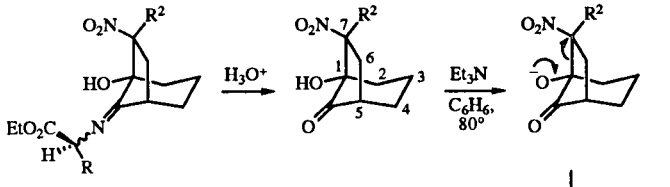
The tendency of the α-ketoenamines **9-11** to give the corresponding indolone derivatives **13-15** as the main reaction products was found in most cases with a few exceptions. They were characterized by the presence of strong band in the range 1625-1645 cm^{-1} for the ketone carbonyl group, while the heteroaromatic skeleton bands were at 1540-1550 cm^{-1}.

Among the other reactions observed, interesting is the behaviour of nitroethylene which reacted with all the substrates to give the bicyclo[3.2.1]octane derivative **19a** as the main product, after loss of the amino ester part from the imine intermediate **16a** occurring in the reaction medium and due to the presence of traces of water. With the α-keto enamines **9** and **10** the corresponding indolone derivatives **13a** and **14a** were also formed although in very small amount.

The stereochemistry of compound **19a**, which was formed as a single stereoisomer, was established by a combination of spectroscopic analysis and chemical reactivity. Under basic conditions, **19a** gave the product of ring opening, the 3-(2-nitroethyl)cyclohexane-1,2-dione **20a** in its tautomeric enol form (Scheme 4). The ir spectrum of **19a** contained absorptions at 3420 cm^{-1}, assigned to an OH

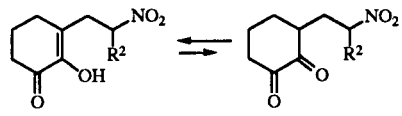
stretching band, and at 1750 cm^{-1}, consistent with a carbonyl group inserted in a five-membered ring. The nmr spectral data supported the stereochemistry of **19a**. A complete assignment was made by means of HH COSY and HC COSY techniques, followed by NOE difference measurements. The most significant result was that obtained irradiating 3ax-H at 1.70 ppm which produced a small enhancement (3%) of the nitromethine proton signal at 5.01 ppm, thus supporting the *exo* configuration of the nitro group.

Scheme 4



[16a] R = H, R^2 = H
[17a] R = Me, R^2 = H
[18a] R = *p*-HO-C_6H_4-CH_2, R^2 = H
18c R = *p*-HO-C_6H_4-CH_2, R^2 = Me

19a R^2 = H
19c R^2 = Me

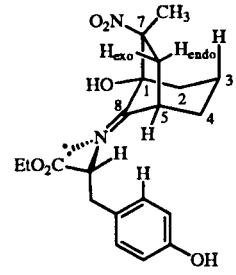


20a R^2 = H
20c R^2 = Me

Since compound **19a** derived from the chiral substrates **10** and **11** and nitroethylene showed a slight optical activity, both samples were converted into the corresponding trimethylsilyl derivative and analyzed by chiral high resolution gas chromatography. The enantiomeric excess was only 10 and 12% respectively.

The bicyclic derivative **19a** was surely formed by hydrolysis of the corresponding glycine, alanine, and tyrosine imine intermediates **16a**, **17a**, and **18a** which however, could not be isolated because under the reaction conditions used, they underwent easy hydrolysis, in spite of the use of classical anhydrous conditions. Actually, a bicyclo[3.2.1]octane derivative still containing the imine function, namely **18c**, was isolated in good yield as the only product from the reaction of the α-ketoenamine **11** and 2-nitropropene. In contrast to the previous cases, compound **18c** was less prone to hydrolysis than the glycine and alanine analogs, as it required acidic conditions and heating to be partially converted into the corresponding bicyclo[3.2.1]octanone derivative **19c**.

The stereochemistry of compound **18c** was assigned by means of DIFNOE measurements, after a complete interpretation of both the ^1H and ^{13}C nmr spectra. The most significant data are reported in the Table. Since the imine **18c** is optically active, its hydrolysis product **19c** is likely to be enantiomerically pure. Unfortunately, any attempt to purify it resulted in the formation of its fission product **20c**.

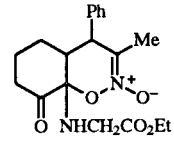


18c

Table
DIFNOE Data for Compound **18c**

Irradiated proton	Enhanced proton
2_{eq}-H	Me (6%)
5-H	CH_2Ar(14%), 6_{exo}-H (6%), *o*-H (4%)
6_{endo}-H	Me (4%)
Me	2_{eq}-H (6%), 6_{endo}-H (5%)

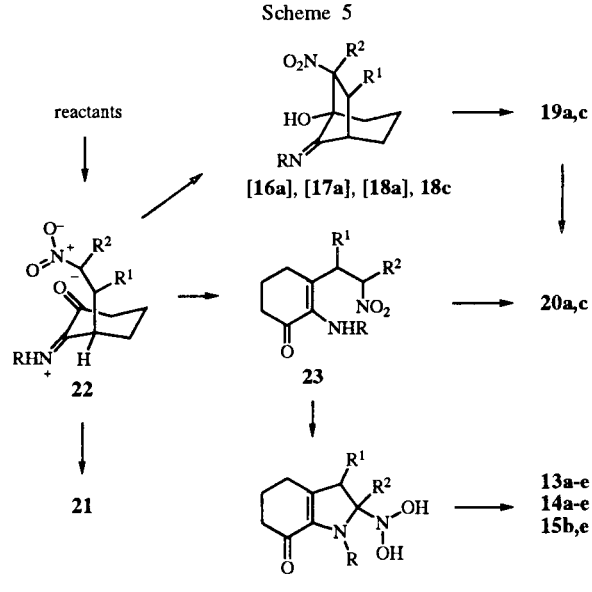
From the reaction of the ketoenamine **9** with 2-nitro-1-phenylpropene **12d**, a small amount of the 1,2-oxazine *N*-oxide derivative **21** was isolated (Figure). It could not be characterized by nmr spectroscopy because in solution it rapidly reverted to the reagents. It was possible, however, to measure its exact mass and its ir spectrum in the solid state showed the presence of the C=N^+-O^- stretching



Figure

band at 1630 cm^{-1} and the absence of NO_2 stretching bands. The formation of this heterocycle however gives support to the mechanism proposed for these reactions. Actually, the intermediacy of a zwitterion **22** must be envisaged which would also account for the formation of the other reaction products (Scheme 5). Nucleophilic attack of the carbanion onto either the iminium carbon atom or the carbonyl carbon atom led to the oxazine

Scheme 5



derivative **21** and the bicyclo[3.2.1]octane derivatives **16a**, **17a** and **18a,c** respectively, while the nucleophilic attack of the enamine nitrogen onto the *aci* nitro carbon atom would lead eventually to the indolone derivatives **13a-e**, **14a-e** and **15b,e**, after loss of water and nitrosyl [5].

EXPERIMENTAL

Melting points were determined on a Büchi apparatus and are uncorrected. The ir spectra were determined in nujol mulls with a Perkin Elmer 1320 spectrometer. The uv spectra were obtained on a Perkin Elmer Lambda 5 spectrophotometer. The ^1H and ^{13}C nmr spectra were scanned on a JEOL EX400 (400 MHz for proton and 100.4 MHz for carbon) using deuteriochloroform as the solvent and tetramethylsilane as the internal standard. All chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (J) are quoted in Hz. Mass spectra were determined with a VG 7070 spectrometer at 70 eV. Exact masses are given for those compounds for which the analyses were not satisfactory. Optical rotation was determined on a Perkin Elmer Model 241. CD spectra were registered on a Jasco J-700A spectropolarimeter for methanol solutions. Gas chromatographic analyses were performed on a C. Erba GC 8000 instrument, the capillary column being OV 1701, size 25 m x 0.32 mm. Chiral HRGC analyses were performed on a Chiraldex™ column, type GT-A, trifluoroacetyl γ-cyclodextrin, 40 m x 0.25 mm size. The tlc was performed on Merck 60F-254 glass-backed silica gel plates with visualisation by uv light (254 nm) or iodine. Flash chromatography was carried out using silica gel 230-400 mesh ASTM (Kieselgel 60, Merck 7385). Light petroleum refers to the fraction with b.p. 40-70° and ether to diethyl ether.

General Procedure for the Synthesis of the Ketoenamines **9-11**.

To a benzene solution (150 ml) of cyclohexane-1,2-dione (1.1 g, 10.0 mmoles) was added under nitrogen with stirring sodium dicarbonate (10.0 mmoles) and the aminoacid hydrochloride (10.0 mmoles). After the evolution of carbon dioxide had ceased, the flask was connected to a Dean-Stark apparatus and the water was eliminated by azeotropic distillation. The solvent was evaporated under reduced pressure to give the corresponding ketoenamine, which was purified by flash chromatography (light petroleum-ethyl acetate, gradient up to 3:2).

N-(6-Oxocyclohexenyl)glycine Ethyl Ester (**9**) [8].

Derivative **9** (1.30 g, 65%) was obtained as a yellow oil; ir (neat): ν NH 3400, ν CO_2Et 1740,ν CO 1670 and ν C=C 1630 cm^{-1}; ^1H nmr: δ 5.34 (t, J 4.6, 1H, vinyl-H), 4.73 (bs, 1H, NH), 4.18 (q, J 7.0, 2H, CH_2CH_3), 3.64 (bs, 2H, CH_2NH), 2.45 (t, 2H, CH_2), 2.33 (q, 2H, CH_2), 1.93 (quintet, 2H, CH_2), 1.25 (t, J 7.2, 3H, CH_3); ^{13}C nmr: δ 195.1 (s), 170.5 (s), 139.8 (s), 111.8 (d), 61.0 (t), 45.1 (t), 37.7 (t), 24.3 (t), 23.3 (t), 14.1 (q); ms: m/z 197.10721 (Calcd. for $C_{10}H_{15}NO_3$ 197.10518) ($M^{+\bullet}$,12%), 168 (5), 151 (M-EtOH, 3), 140 (1), 125 (10), 124 (M-$EtCO_2^\bullet$, 100), 96 (7), 95 (6), 94 (5), 67 (9), 55 (10); uv: 203 (ε 5300), 304 nm (ε 2900).

N-(6-Oxocyclohexenyl)-L-alanine Ethyl Ester (**10**).

The derivative **10** (1.90 g, 90%) was obtained as a yellow oil, ir (neat) ν NH 3390, ν CO_2Et 1735, ν CO 1670 and ν C=C 1630 cm^{-1}; ^1H nmr: δ 5.52 (t, J 4.7, 1H, vinyl-H), 4.71 (bd, J 7.1, 1H, NH), 4.30, 4.28 (2q, 2H, CH_2CH_3), 3.88 (quintet, J 7.1, 1H, CHNH), 2.59 (t, 2H, CH_2), 2.46 (q, 2H, CH_2), 2.05 (quintet, 2H, CH_2), 1.53 (d, J 7.1, 3H, CH_3), 1.37 (t, J 7.0, 3H, CH_3); ^{13}C nmr: δ 195.3 (s), 174.1 (s), 139.3 (s), 112.4 (d), 60.9 (t), 51.4 (d), 37.7 (t), 24.4 (t), 23.2 (t), 18.3 (q), 14.2 (q); ms: m/z 211.12137 (Calcd. for $C_{11}H_{17}NO_3$: 211.12083) ($M^{+\bullet}$, 12%), 182 (1), 165 (M-EtOH, 1), 154 (7), 139 (14), 138 (M-$EtCO_2^\bullet$, 100), 67 (9), 55 (10); uv 204 (ε 7100), 303 nm (ε 3400); $[\alpha]_D^{26}$ -66.2 (c 0.08 methanol); CD: $[\theta]_{225}$ +9260, $[\theta]_{291}$ -3560.

N-(6-Oxocyclohexenyl)-L-tyrosine Ethyl Ester (**11**).

Derivative **11** (1.95 g, 65%) was obtained as pale yellow crystals, mp 71-73°; ir: ν NH and OH 3400, ν CO_2Et 1730, ν CO 1670, ν C=C 1625, ν Ar 1610, 1590, 1510, 1480 cm^{-1}; ^1H nmr: δ 7.02 (d, J 8.5, 2H, Ar-H), 6.74 (d, J 8.5, 2H, Ar-H), 6.41 (bs, 1H, OH), 5.43 (t, J 4.6, 1H, vinyl-H), 4.68 (d, J 7.0, 1H, NH), 4.12 (q, J 7.1, 2H, CH_2CH_3), 3.90 (q, J 7.0, 1H, $CHCH_2$), 2.97 (part AB of an ABX system, J_{AB} 13.7, 2H, $CHCH_2$), 2.45 (t, 2H, CH_2), 2.31 (q, 2H, CH_2), 1.90 (quintet, 2H, CH_2), 1.19 (t, J 7.1, 3H, CH_2CH_3); ^{13}C nmr: δ 195.8 (s), 173.1 (s), 155.2 (s), 139.1 (s), 130.2 (d), 127.8 (s), 115.4 (d), 113.1 (d), 61.0 (t), 57.5 (d), 37.6 (2t), 24.3 (t), 23.1 (t), 14.1 (q); ms: m/z 304 (MH^+, 100%), 303.14840 (Calcd. for $C_{17}H_{21}NO_4$: 303.14705) (M^+, 7), 230 (M-$EtCO_2^\bullet$, 23), 196 (25), 122 (36), 107 (23), 91 (5), 77 (5), 55 (6); uv 205 (ε 12600), 224 (ε 7700), 285 (ε 2700) 307 nm (ε 2500); $[\alpha]_D^{26}$ -7.7 (c 0.26 methanol); CD: $[\theta]_{231}$ +7817, $[\theta]_{292}$ -2056.

General Procedure for the Reactions of the Ketoenamines **9-11** with the Nitroolefins.

To a solution of the ketoenamine in either ether or ethanol at 5° was added a solution of the nitroolefin in the same solvent. The mixture was stored at room temperature for the time indicated below, after which the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography.

Reaction of Ketoenamine **9** with Nitroethylene.

1,4,5,6-Tetrahydro-7*H*-indol-7-oxo-1-acetic Acid Ethyl Ester (**13a**), 1-Hydroxy-7-nitrobicyclo[3.2.1]octan-8-one (**19a**) and 3-(2-Nitroethyl)cyclohexane-1,2-dione (**20a**).

Compound **9** (1.0 g, 5.0 mmoles) and nitroethylene (0.37 g, 5.0 mmoles) were reacted in ether (25 ml) for 8 hours, at 5°. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (95:5) as eluent to give the bicyclo compound **19a** (0.65 g, 72%), mp 118-119°; ir: ν OH 3420, ν CO 1750, ν NO_2 1550 cm^{-1}; ^1H nmr: δ 5.01 (dd, J_1 8.8, J_2 2.9, 1 H, 7_{endo}-H), 3.22 (bs, 1H, OH), 2.78 (m, 1H, 5-H), 2.61 (ddd, J_1 14.8, J_2 7.7, J_3 2.9, 1 H, 6_{exo}-H), 2.35 (ddd, J_1 14.8, J_2 8.8, J_3 1.0, 1 H, 6_{endo}-H), 2.30 (1 H, m, 2_{eq}-H), 2.00 (m, 2H, 2 4-H), 1.93 (dt, 1H, 2_{ax}-H), 1.80 (m, 1 H, 3_{eq}-H), 1.70 (m, 1H, 3_{ax}-H); ^{13}C nmr: δ 213.7 (s, C=O), 85.3 (d, C-7), 79.1 (s, C-1), 41.7 (t, C-2), 41.3 (d, C-5), 34.9 (t, C-4), 28.7 (t, C-6), 17.6 (t, C-3); ms: m/z 185.0701 (Calcd. for $C_8H_{11}NO_4$: 185.0688) ($M^{+\bullet}$, 5%), 139 (M-$NO_2^\bullet$, 14), 138 (35), 137 (30), 111 (25), 110 (22), 109 (22), 95 (21), 93 (22), 91 (19), 81 (61), 79 (25), 77 (25), 67 (47), 65 (13), 57 (24), 55 (100); uv: 203 (ε 7500), 269 nm (ε 2900).

Further elution gave the indolone derivative **13a** (0.10 g, 10%) as an oil; ir, ν CO_2Et 1740, ν CO 1635, ν C=C 1545 cm^{-1}; ^1H nmr: δ 6.76 (d, J 2.4, 1H, vinyl-H), 6.05 (d, J 2.4, 1H, vinyl-H), 5.01 (s, 2H, CH_2N), 4.21 (q, J 7.1, 2H, CH_2CH_3), 2.74 (t, 2H, CH_2), 2.45 (t, 2H, CH_2), 2.07 (quintet, 2H, CH_2), 1.28 (t, J 7.1, 3H, CH_3); ^{13}C nmr: δ 189.2 (s), 168.9 (s), 138.2 (s), 130.3 (d), 126.8 (s), 107.7 (d), 61.5 (t), 50.2 (t), 38.8 (t), 25.1 (t), 23.8 (t), 14.2 (q); ms: m/z 221.10532 (Calcd. for $C_{12}H_{15}NO_3$: 221.10519) ($M^{+\bullet}$, 99%), 175 (M-EtOH, 94), 148 (M-$EtCO_2^\bullet$, 100), 118 (23), 92 (29), 65 (11).

To a solution of the bicyclo derivative **19a** (0.050 g, 0.27 mmole) in benzene were added a few drops of triethylamine and the mixture refluxed for 1.5 hours. Product **20a** (0.040 g, 80%) was isolated, mp 69-70°, from light petroleum, ir: ν OH 3452, ν CO 1677, ν C=C 1656, ν NO_2 1554 cm^{-1}, ^1H nmr: δ 6.23 (bs, 1H, OH), 4.61 (t, J 7.0, 2H, CH_2NO_2), 2.94 (t, J 7.0, 2H, $CH_2CH_2NO_2$), 2.50 (t, 2H, CH_2), 2.40 (t, 2H, CH_2), 1.99 (quintet, 2H, CH_2); ^{13}C nmr: δ 194.2 (s), 144.9 (s), 126.3 (s), 72.7 (t), 35.6 (t), 29.2 (t), 29.0 (t), 22.4 (t); ms: m/z 185 ($M^{+\bullet}$, 17%), 149 (12), 139 (M-$NO_2^\bullet$, 33), 138 (M-HNO_2, 100), 137 (63), 123 (10), 122 (20), 111 (29), 110 (54), 109 (24), 97 (12), 96 (24), 95 (38), 93 (17), 91 (15), 84 (16), 83 (20), 82 (17), 81 (53), 79 (13), 77 (12), 69 (12), 68 (18), 67 (45), 57 (22), 55 (62); uv: 202 (ε 5240), 270 nm (ε 8944).

Anal. Calcd. for $C_8H_{11}NO_4$: C, 51.99; H, 5.99; N, 7.56. Found: C, 51.90, H, 6.04; N, 7.63.

Reaction of Ketoenamine **9** with 1-Nitropropene.

3-Methyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-acetic Acid Ethyl Ester (**13b**).

Compound **9** (0.30 g, 1.5 mmoles) and 1-nitropropene (0.13 g, 1.5 mmoles) were reacted neat for 1 hour. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (9:1) as eluent to give compound **13b** (0.021 g, 60%), mp 74-76°, from light petroleum; ir: ν CO_2Et 1749, ν CO 1630, ν C=C 1558, 1510 cm^{-1}; ^1H nmr: δ 6.58 (s, 1H, vinyl-H), 4.96 (s, 2H, CH_2N), 4.20 (q, J 7.1, 2H, CH_2CH_3), 2.62 (t, 2H, CH_2), 2.42 (t, 2H, CH_2), 2.05 (quintet, 2H, CH_2), 1.99 (s, 3H, CH_3), 1.27 (t, J 7.1, 3H, CH_2CH_3); ^{13}C nmr: δ 188.9 (s), 169.0 (s), 136.8 (s), 128.9 (d), 126.5 (s), 116.6 (s), 61.3 (t), 49.7 (t), 38.5 (t), 24.7 (t), 21.8 (t), 14.1 (q), 9.4 (q); ms: m/z 235 ($M^{+\bullet}$, 47), 189 (M-EtOH, 53), 162 (M-$EtCO_2^\bullet$, 100), 149 (16), 138 (22), 134 (16), 132 (16), 126 (11), 125 (17), 123 (14), 122 (15), 106 (28), 95 (26), 89 (47), 81 (47), 79 (23), 77 (26), 67 (37), 55 (41); uv: 202 (ε 5600), 273 (ε 11000), 291 nm (ε 13000).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.10; H, 7.25; N, 5.78.

Reaction of Ketoenamine **9** with 2-Nitropropene.

2-Methyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-acetic Acid Ethyl Ester (**13c**).

Compound **9** (0.40 g, 2.0 mmoles) and 2-nitropropene (0.175 g, 2.0 mmoles) were reacted neat for 24 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (85:15) as eluent to give compound **13c** (0.070 g, 15%), mp 91-92°; from ligroin-ethyl acetate; ir: ν CO_2Et 1735, ν CO 1645, 1638, ν C=C 1550 cm^{-1}; ^1H nmr: δ 5.85 (s, 1H, vinyl-H), 5.10 (s, 2H, CH_2N), 4.22 (q, J 7.1, 2H, CH_2CH_3), 2.70 (t, 2H, CH_2), 2.44 (t, 2H, CH_2), 2.18 (s, 3H, CH_3), 2.04 (quintet, 2H, CH_2), 1.29 (t, J 7.1, 3H, CH_2CH_3); ^{13}C nmr δ 188.1 (s), 168.9 (s), 138.5 (s), 138.1(s), 126.5 (s), 107.7 (d), 61.4 (t), 46.4 (t), 38.8 (t), 24.9 (t), 23.7 (t), 14.2 (q),11.7 (q); ms: m/z 235 ($M^{+\bullet}$, 86), 207 (12), 190 (M-EtO, 20), 188 (52), 178 (16), 163 (24),162 (M-$EtCO_2^\bullet$, 100), 161 (60), 134 (30), 133 (16), 132 (22), 122 (18), 107 (16), 106 (42), 78 (22), 65 (22); uv: 203 (ε 1100), 294 nm (ε 3950).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 65.92; H, 7.22; N 5.86.

Reaction of Ketoenamine **9** with 2-Nitro-1-phenylpropene.

2-Methyl-3-phenyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-acetic Acid Ethyl Ester (**13d**) and *N*-(4a,5,6,7,8,8a-Hexahydro-3-methyl-4-phenyl-8-oxo-4*H*-1,2-benzoxazin-8a-yl)glycine Ethyl Ester 2-Oxide (**21**).

Compound **9** (0.40 g, 2.0 mmoles) and 2-nitro-1-phenylpropene (0.33 g, 2.0 mmoles) were reacted neat at room temperature for 30 minutes, after which the reaction mixture was treated with ether. Product **21** (0.17 g, 24%) was isolated as a solid, mp 110° dec; ir: ν NH 3340, ν CO_2Et 1730, ν C=N 1630 cm^{-1}; ms: m/z 360.15841 (Calcd. for $C_{19}H_{24}N_2O_5$: 360.16851) ($M^{+\bullet}$, 3), 342 (23), 327 (21), 311 (100), 297 (29), 286 (36), 283 (28), 271 (36), 269 (38), 265 (24), 253 (27), 238 (60), 224 (29), 210 (36), 198 (40), 182 (26), 168 (28), 153 (26), 141 (33), 128 (38), 115 (93), 105 (33), 91 (66), 77 (46). The mother liquors were treated with absolute ethanol and compound **13d** separated as a white solid (0.37 g, 60%), mp 143°; ir: ν CO_2Et 1735, ν CO 1630, ν Ar 1550 cm^{-1}; ^1H nmr: δ 7.41 (m, 2H, Ar-H), 7.27 (m, 3H, Ar-H), 5.19 (2s, H, CH_2N), 4.25 (q, 2H, J 7.0, CH_2CH_3), 2.71 (t, 2H, CH_2), 2.49 (t, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.05 (quintet, 2H, CH_2), 1.31 (t, J 7.0, 3H, CH_2CH_3); ^{13}C nmr: δ 188.6 (s), 168.9 (s), 136.0 (s), 135.7 (s), 134.5 (s), 129.6 (d), 128.3 (d), 126.3 (d), 125.8 (s), 121.7 (s), 61.5 (t), 46.7 (t), 38.9 (t), 24.8 (t), 22.9 (t), 14.2 (q), 10.3 (q); ms: m/z 311.14615 (Calcd. for $C_{19}H_{21}NO_3$ 311.15213) ($M^{+\bullet}$, 100%), 283 (10), 265 (M-EtOH, 19), 255 (14), 239 (14), 238 (M-$EtCO_2^\bullet$, 52), 237 (24), 181 (14), 115 (10), 86 (16); uv: 203 (ε 16000), 251 (ε 14000), 305 nm (ε 15000).

Reaction of Ketoenamine **9** with 1-Nitro-1-phenylpropene (**12e**).

3-Methyl-2-phenyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-acetic Acid Ethyl Ester (**13e**).

Compound **9** (0.50 g, 2.5 mmoles) and 1-nitro-1-phenylpropene (0.41 g, 2.5 mmoles) were reacted neat for 5 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (gradient up to 4:1) as eluent to give compound **13e** (0.15 g, 20%) as an oil; ir: ν CO_2Et 1 740, ν CO 1630, ν Ar 1600, 1545 cm^{-1}; ^1H nmr: δ 7.36 (m, 3H, Ar-H), 7.21 (m, 2H, Ar-H), 4.76 (s, 2H, CH_2N), 4.14 (q, J 7.0, 2H, CH_2CH_3), 2.64 (t, 2H, CH_2), 2.43 (t, 2H, CH_2), 2.06 (quintet, 2H, CH_2), 1.87 (s, 3H, CH_3), 1.18 (t, J 7.0, 3H, CH_2CH_3); ^{13}C nmr: δ 187.7 (s), 168.5 (s), 139.0 (s), 135.7 (s), 129.4 (s), 129.2 (d), 127.6 (d), 127.5 (d), 126.0 (s), 114.6 (s), 60.2 (t), 46.8 (t), 37.8 (t), 23.5 (t), 21.1 (t), 13.1 (q), 8.4 (q); ms: m/z 311.15225 (Calcd. for $C_{19}H_{21}NO_3$: 311.15213) ($M^{+\bullet}$, 98%), 266 (M-EtO$^\bullet$, 16), 265 (53), 239 (21), 238 (M-$EtCO_2^\bullet$, 100), 237 (14), 210 (11), 182 (31), 117 (36), 115 (34), 105 (19), 91 (34), 77 (23); uv: 203 (ε 12000), 251 (ε 5200), 308 nm (ε 12800).

Reaction of Ketoenamine **10** with Nitroethylene (**12a**).

(*S*)-1,4,5,6-Tetrahydro-7*H*-indol-7-oxo-1-(2-methyl)acetic Acid Ethyl Ester (**14a**).

Compound **10** (0.50 g, 2.4 mmoles) and nitroethylene (0.175 g, 2.4 mmoles) were reacted in ether (2.0 ml) for 5 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (4:1) as eluent to give the bicyclo compound **19a** (0.275 g, 62%). The indolone derivative **14a** could only be detected in the ^1H nmr of the crude reaction mixture: δ 7.01 (d, J 2.7, 1H, vinyl-H), 6.06 (d, J 2.7, 1H, vinyl-H), 5.89 (q, J 7.4, 1H, $CHCH_3$), 4.18 (q, J 7.1, 2H, CH_2CH_3), 2.73 (t, 2H, CH_2), 2.45 (t, CH_2, 2H), 2.04 (quintet, 2H, CH_2), 1.69 (d, J 7.4, 3H, $CHCH_3$), 1.25 (t, J 7.1, 3H, CH_3).

Reaction of Ketoenamine **10** with 1-Nitropropene (**12b**).

(*S*)-3-Methyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(2-methyl)-acetic Acid Ethyl Ester (**14b**).

Compound **10** (0.50 g, 2.4 mmoles) and 1-nitropropene (0.21 g, 2.4 mmoles) were reacted neat for 24 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (85:15) as eluent to give compound **14b** (0.18 g, 30%) as an oil; ir: ν CO_2Et 1743, ν CO 1643, ν C=C 1560, 1510 cm^{-1}; ^1H nmr: δ 6.84 (s, 1H, vinyl-H), 5.88 (q, J 7.2, 1H, C*H*CH_3), 4.18 (q, J 7.1, 2H, C*H*$_2$$CH_3$), 2.62 (t, 2H, CH_2), 2.43 (t, 2H, CH_2), 2.06 (m, 2H, CH_2), 2.01 (s, 3H, CH_3), 1.67 (d, J 7.2, 3H, CHC*H*$_3$), 1.26 (t, J 7.1, 3H, CH_2C*H*$_3$); ^{13}C nmr: δ 188.8 (s), 171.8 (s), 136.9 (s), 126.2 (s), 125.5 (d), 116.6 (s), 61.3 (t), 54.9 (d), 38.9 (t), 24.5 (t), 21.9 (t), 17.9 (q), 14.1 (q), 9.6 (q); ms: m/z 249 ($M^{+\bullet}$, 36), 204 (M-EtO$^\bullet$, 31), 176 (M-$EtCO_2^\bullet$, 100), 148 (18), 147 (18), 134 (13), 133 (16), 132 (18), 121 (16), 120 (28), 119 (16), 118 (15), 108 (10), 107 (10), 106 (11), 93 (15), 91 (18), 79 (14), 78 (10), 77 (22), 67 (10), 66 (16), 65 (21); uv: 201 (ε 5330), 274 (ε 11000), 292 nm (ε 12500); $[\alpha]_D^{22}$ -77.2 (c 0.14 methanol); CD: $[\theta]_{219}$ +4455, $[\theta]_{264}$ +5569, $[\theta]_{297}$ -16861.

Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.12; H, 7.35; N, 5.36.

Reaction of Ketoenamine **10** with 2-Nitropropene (**12c**).

(*S*)-2-Methyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(2-methyl)-acetic Acid Ethyl Ester (**14c**) and 3-(2-Nitropropyl)cyclohexan-1,2-dione (**20c**).

Compound **10** (0.50 g, 2.4 mmoles) and 2-nitropropene (0.21 g, 2.4 mmoles) were reacted neat for 24 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (9:1) as eluent to give compound **14c** (0.080 g, 13%) as an oil; ir: ν CO_2Et 1737, ν CO 1640, ν C=C 1550 cm^{-1}; ^1H nmr: δ 5.83 (s, 1H, vinyl-H), 5.56 (bm, 1H, C*H*CH_3), 4.20 (m, 2H, C*H*$_2$$CH_3$), 2.70 (t, 2H, CH_2), 2.42, (t, 2H, CH_2), 2.22 (s, 3H, CH_3), 2.03 (quintet, 2H, CH_2), 1.65 (d, J 6.8, 3H, CHC*H*$_3$), 1.24 (t, J 7.1, 3H, CH_2C*H*$_3$); ^{13}C nmr: δ 187.3 (s), 170.6 (s), 138.4 (s), 138.1 (s), 125.8 (s), 108.1 (d), 61.3 (t), 53.6 (d), 38.9 (t), 24.8 (t), 123.8 (t), 17.4 (q), 14.1 (q), 12.7 (q); ms: m/z 249 ($M^{+\bullet}$, 44%), 204 (20), 203 (M-EtOH, 31), 176 (M-$EtCO_2^\bullet$, 100), 175 (49), 174 (25), 150 (16), 149 (28), 148 (44), 147 (34), 146 (16), 136 (16), 135 (20), 134 (21), 133 (39), 132 (33), 131 (16), 121 (41), 120 (97), 119 (38), 118 (29), 117 (20), 108 (15), 107 (20), 106 (20), 105 (28), 104 (21), 103 (15), 95 (15), 94 (20), 93 (38), 92 (20), 91 (47), 81 (21), 80 (18), 79 (47), 78 (29), 77 (70), 69 (24), 68 (16), 67 (33), 66 (38), 65 (61), 57 (24), 56 (25), 55 (69); uv: 202 (ε 8200), 266 (ε 6200), 292 nm (ε 13540); $[\alpha]_D^{22}$ -46.1 (c 0.13 methanol); CD: $[\theta]_{208}$ +4463, $[\theta]_{268}$ +2898, $[\theta]_{305}$ -5475.

Anal. Calcd. for $C_{14}H_{19}NO_3$: C: 67.45; H, 7.68; N, 5.62. Found: 67.31; H, 7.96; N, 5.85%.

Further elution gave the dione **20c** (0.085 g, 18%) as a white solid, mp 62°, from light petroleum; ir: ν OH 3452, ν C=O 1675, ν C=C 1654, ν NO_2 1551 cm^{-1}; ^1H nmr: δ 6.22 (s, 1H, OH), 4.89 (sextet, J 7.2, 1H, $CHNO_2$), 2.82 (2 *pseudo* q, part AB of an ABX, system, J_{AB} 13.7, 2H, C*H*$_2$$CHNO_2$), 2.49 (t, 2H, CH_2), 2.34 (q, 2H, CH_2), 1.96 (quintet, 2H, CH_2), 1.58 (d, J 6.7, 3H, CH_3); ^{13}C nmr: δ 194.3 (s), 145.1 (s), 126.4 (s), 80.9 (d), 36.7 (t), 35.7 (t), 29.0 (t), 22.4 (t), 19.3 (q); ms: m/z 199 ($M^{+\bullet}$, 2%), 153 (M-$NO_2^\bullet$, 30), 152 (M-HNO_2, 27), 151 (16), 137 (76), 124 (13), 123 (20), 109 (11), 97 (14), 95 (26), 91 (19), 81 (43), 79 (23), 77 (18), 69 (22), 67 (37), 57 (31), 55 (100); uv: 203 (ε 5700), 272 nm (ε 10600).

Anal. Calcd. for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.03; H, 6.75; N, 6.91.

Reaction of Ketoenamine **10** with 2-Nitro-1-phenylpropene (**12d**).

(*S*)-2-Methyl-3-phenyl- 1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(2-methyl)acetic Acid Ethyl Ester (**14d**).

To a solution of compound **10** (0.50 g, 2.4 mmoles) in ethanol (10 ml) 2-nitro-1-phenylpropene (0.39 g, 2.4 mmoles) was added and the mixture was heated at 80° for 2 hours. The mixture was purified by flash chromatography (light petroleum-ethyl acetate) and furnished the indolone **14d** (0.30 g, 40%) as a solid mp 110°, from absolute ethanol; ir: ν CO_2Et 1730, ν CO 1640, ν Ar 1600, 1550 cm^{-1}; ^1H nmr: δ 7.41 (m, 2H, Ar-H), 7.28 (m, 3H, Ar-H), 5.70 (bs, 1H, C*H*CH_3), 4.24 (m, 2H, C*H*$_2$$CH_3$), 2.70 (t, 2H, CH_2), 2.50, (m, 2H, CH_2), 2.24 (s,3H, CH_3), 2.05 (quintet, 2H, CH_2), 1.71 (d, J 7.0, 3H, CHC*H*$_3$), 1.28 (t, J 7.0, 3H, CH_2C*H*$_3$); ^{13}C nmr: δ 187.7 (s), 170.6 (s), 136.4 (s), 135.3 (s), 134.5 (s), 129.8 (d), 128.3 (d), 126.3 (d), 125.1 (s), 122.1 (s), 61.4 (t), 53.9 (d), 39.0 (t), 24.7 (t), 23.1 (t), 17.6 (q), 14.2 (q), 11.1 (q); ms: m/z 325.16779 (Calcd. for $C_{20}H_{23}NO_3$ 325.16746)($M^{+\bullet}$, 72%), 279 (M-EtOH, 29), 252 (M-$EtCO_2^\bullet$, 100), 251 (34), 224 (36), 196 (20), 115 (14), 91 (15),77 (10); uv: 204 (ε 19000), 252 (ε 16000), 306 nm (ε 16000); $[\alpha]_D^{26}$ -81.2 (c 0.08 methanol); CD: $[\theta]_{246}$ -9258, $[\theta]_{302}$ -12128.

Reaction of Ketoenamine **10** with 1-Nitro-1-phenylpropene (**12e**).

(*S*)-3-Methyl-2-phenyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(2-methyl)acetic Acid Ethyl Ester (**14e**).

Compound **10** (0.50 g, 2.4 mmoles) and 1-nitro-1-phenylpropene (0.39 g, 2.4 mmoles) were reacted neat at room temperature for 5 days. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (4:1) as eluent to give compound **14e** (0.23 g, 30%) as an oil; ir: ν CO_2Et 1735, ν CO 1640, ν Ar 1600, 1550 cm^{-1}; ^1H nmr: δ 7.37 (m, 3H, Ar-H), 7.22 (m, 2H, Ar-H), 4.72 (q, J 7.0, 1H, C*H*CH_3), 4.11 (m, 2H, C*H*$_2$$CH_3$), 2.63 (t, 2H, CH_2), 2.42 (m, 2H, CH_2), 2.04 (m, 2H, CH_2), 1.83 (s, 3H, CH_3), 1.47 (d, J 7.0, 3H, CHC*H*$_3$), 1.17 (t, J 7.3, 3H, CH_2C*H*$_3$); ^{13}C nmr: δ 187.3 (s), 170.7 (s), 140.1 (s), 137.4 (s), 130.8 (s), 130.3 (d), 128.6 (2d), 125.2 (s), 115.4 (s), 61.2 (t), 54.8 (d), 38.8 (t), 24.4 (t), 22.2 (t), 17.9 (q), 14.1 (q), 9.4 (q); ms: m/z 325 ($M^{+\bullet}$, 57%), 280 (12), 279 (M-EtOH, 34), 252 (M-$EtCO_2^\bullet$, 100), 251 (21), 250 (39), 236 (10), 225 (12), 224 (10), 196 (22), 194 (10), 115 (12), 91 (12), 77 (12); uv: 203 (ε 25000), 309 nm (ε 24500); $[\alpha]_D^{26}$ -154.5 (c 0.10 methanol); CD: $[\theta]_{218}$ -3931, $[\theta]_{243}$ -2557, $[\theta]_{310}$ -16619

Anal. Calcd. for $C_{20}H_{23}NO_3$: C: 73.82; H, 7.12; N, 4.30. Found: C, 73.33; H, 7.42; N, 4.05%.

Reaction of Ketoenamine **11** with Nitroethylene (**12a**).

The reaction carried out under the same conditions as for the ketoenamines **9** and **10** furnished the same bicyclo derivative (**19a**) in 20% yield.

Reaction of Ketoenamine **11** with 1-Nitropropene (**12b**).

(*S*)-3-Methyl-1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(4-hydroxybenzyl)acetic Acid Ethyl Ester (**15b**).

Compound **11** (0.75 g, 2.5 mmoles) and 1-nitropropene (0.22 g, 2.5 mmoles) were reacted neat for 3 days. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (4:1) as eluent to give compound **15b** (0.38 g, 36%) as a crystalline product, mp 184-185°, from light petroleum; ir: ν

OH 3600, 3200, ν CO_2Et 1734, ν CO 1625, ν C=C and Ar 1616, 1594, 1554, 1517 cm^{-1}; ^1H nmr: δ 6.97 (d, J 8.3, 2H, Ar-H), 6.96 (s, 1H, vinyl-H), 6.73 (d, J 8.3, 2H, Ar-H), 6.28 (bs, 1H, CHN), 4.14 (m, 2H, CH_2CH_3), 3.34 (dd, J_1 7.0, J_2 14.0, 1H, CHAr), 3.11 (dd, J_1 8.5, J_2 14.0, 1H, CHAr), 2.62 (m, 2H, CH_2), 2.40 (m, 2H, CH_2), 2.04 (m, 2H, CH_2), 1.98 (s, 3H, CH_3), 1.18 (t, J 7.3, 3H, CH_2CH_3); ^{13}C nmr: δ 189.7 (s), 170.8 (s), 155.3 (s), 137.9 (s), 130.2 (d), 127.6 (s), 127.4 (d), 125.9 (s), 117.2 (s), 115.3 (d), 61.5 (t), 60.4 (d), 38.9 (t), 38.7 (t), 24.4 (t), 22.0 (t), 14.0 (q), 9.6 (q); ms: m/z 341 ($M^{+\bullet}$, 8%), 339 (5), 268 (M-$EtCO_2^{\bullet}$, 29), 266 (15), 249 (10), 235 (16), 234 (M-CH_2-C_6H_4-OH, 19), 210 (13), 192 (24), 189 (28), 178 (15), 176 (20), 162 (37), 150 (100), 149 (57), 147 (28), 134 (21), 132 (25), 121 (38), 120 (33), 119 (22), 118 (21), 107 (62), 106 (31), 94 (26), 93 (33), 91 (30), 84 (16), 79 (20), 78 (22), 77 (31); uv: 223 (ε 9060), 279 (ε 11100), 284 (ε 11150), 294 nm (ε 10900); $[\alpha]_D^{22}$ -78.4 (c 0.19 methanol); CD: $[\theta]_{213}$ -16510, $[\theta]_{263}$ +6659, $[\theta]_{299}$ -9787

Anal. Calcd. for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.13; H, 6.77; N, 3.96.

Reaction of Ketoenamine **11** with 2-Nitropropene (**12c**).

[Anti,7-exo]-*N*-(1-hydroxy-7-methyl-7-nitro-bicyclo[3.2.1]-octane-8-ylidene-L-tyrosine Ethyl Ester (**18c**) and [7-Exo]-1-hydroxy-7-methyl-7-nitro-bicyclo[3.2.1]octan-8-one (**19c**).

Compound **11** (0.75 g, 2.5 mmoles) and 2-nitropropene (0.22 g, 2.5 mmoles) were reacted neat at 5° for 3 days. The reaction mixture was purified by flash chromatography with light-petroleum-ethyl acetate (7:3) as eluent to give compound **18c** (0.38 g, 39%) as a white solid, mp 141°, from light petroleum; ir: ν OH 3600, 3400, ν CO_2Et 1729, ν C=N 1615, ν Ar 1594, 1543, 1513 cm^{-1}; ^1H nmr: δ 7.05 (d, J 8.3, 2H, *o*-Ar-H), 6.73 (d, J 8.3, 2H, *m*-Ar-H), 4.29 (dd, part X of an ABX system, J_{AX} 3.8, J_{BX} 10.4, 1H, N-CH), 4.23 (dq, 2H, CH_2CH_3), 3.20, 3.11 (2 *pseudo* q, part AB of an ABX system, J_{AB} 13.7, J_{AX} 3.8, J_{BX} 10.4, 2H, CH_2Ar), 3.04 (bm, 1H, 5-H), 2.64 (dd, J_1 8.3, J_2 15.1, 1H, 6_{exo}-H), 2.06 (bm, 1H, 2_{eq}-H), 1.73 (s, 3H, CH_3), 1.68 (d, J 15.1, 1H, 6_{endo}-H), 1.52 (m, 1H, 2_{ax}-H), 1.44 (m, 2H, 4_{eq}-H, 3-H), 1.29 (t and m, J 7.3, 4H, CH_2CH_3 and 3-H), 0.44 (m, 1H, 4_{ax}-H); ^{13}C nmr: δ 181.3 (COO, s), 171.1 (s, C=O), 154.7 (s, *p*-C), 130.9 (2 d, 2 *o*-C), 129.8 (s, C-1'), 115.1 (2 d, 2 *m*-C), 92.6 (s, C-7), 80.0 (s, C-1), 66.2 (d, N-CH), 61.4 (t, OCH_2CH_3), 39.0 (t, C-2), 38.5 (t, CH_2Ar), 38.0 (t, C-6), 34.3 (d, C-5), 32.3 (t, C-4), 17.7 (t, C-3), 16.6 (q, CH_3 at C-7), 14.0 (q, OCH_2CH_3); ms: m/z 344 (M-EtOH, 8%), 317 (M-$EtCO_2^{\bullet}$, 6), 283 (M-CH_2-C_6H_4-OH, 20), 275 (20), 270 (16), 238 (14), 237 (22), 236 (33), 208 (16), 207 (20), 202 (17), 196 (27), 192 (18), 168 (46), 164 (20), 162 (27), 150 (31), 149 (32), 147 (26), 137 (29), 136 (53), 135 (36), 134 (37), 133 (35), 123 (48), 121 (37), 109 (52), 108 (100), 107 (57), 95 (52), 92 (48), 85 (41), 80 (49), 78 (60), 77 (66); uv: 223 (ε 10000), 277 (ε 1700), 283 nm (ε 1500); $[\alpha]_D^{22}$ -62.0 (c 0.05 methanol); CD: $[\theta]_{224}$ -25304, $[\theta]_{242}$ -21127, $[\theta]_{281}$ +15410.

Anal. Calcd. for $C_{20}H_{26}N_2O_6$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.37; H, 6.55; N, 7.01.

Compound **18c** was hydrolysed in ethanol-water, at *p*H 2, under reflux for 2 hours, to give the corresponding ketone **19c**; ir: ν OH 3420, ν CO 1750, ν NO_2 1550 cm^{-1}; ^1H nmr: δ 2.96 (bs, 1H, OH), 2.87 (m, 1H, 5-H), 2.71 (dd, J 8.5, 14.9, 6_{endo}-H), 2.22 (m, 1H, 2_{eq}-H), 2.06 (m, 2H, 2 4-H), 1.90 (dd, J 0.9, 14.9, 6_{exo}-H), 1.86 (m, 1H, 2_{ax}-H), 1.80 (s, 3H, CH_3), 1.74 (m, 2H, 2 3-H); ^{13}C nmr: δ 215.5 (s, C-8), 91.1 (s, C-7), 82.0 (s, C-1), 42.0 (d, C-5), 40.2 (t, C-2), 36.3 (t, C-6), 35.4 (t, C-4), 17.6 (t, C-3), 16.1 (q, CH_3); ms: m/z 199 ($M^{+\bullet}$, 0.7), 153 (M - NO_2, 31), 152 (24), 151 (14), 137 (M- HNO_2, 100), 123 (14), 105 (10), 95 (21), 91 (18), 81 (39), 79 (28), 77 (15), 67 (27), 65 (10), 57 (17), 55 (46), 53 (20). Any attempt to purify the ketone by flash chromatography resulted in opening of the system into the corresponding dione **20c**.

Reaction of Ketoenamine **11** with 1-Nitro-1-phenylpropene (**12e**).

(*S*)-3-Methyl-2-phenyl- 1,4,5,6-tetrahydro-7*H*-indol-7-oxo-1-(4-hydroxybenzyl)acetic Acid Ethyl Ester (**15e**).

Compound **11** (0.50 g, 1.65 mmoles) and 1-nitro-1-phenylpropene (0.27 g, 1.65 mmoles) were reacted neat at 5° for 24 hours. The reaction mixture was purified by flash chromatography with light petroleum-ethyl acetate (gradient up to 4:1) as eluent to give compound **15e** (0.47 g, 68%) as a solid, mp 141-144°, from light petroleum; ir: ν OH 3400, ν CO_2Et 1733, ν CO 1633, ν C=C 1514 cm^{-1}; ^1H nmr: δ 7.26 (m, 5H, Ph), 6.54 (d, J 8.5, 2H, Ar-H), 6.41 (d, J 8.5, 2H, Ar-H), 4.92 (bs, 1H, OH), 4.66 (bd, J 7.6, 1H, CHN), 4.26 (m, 2H, CH_2CH_3), 3.29 (2 *pseudo* q, AB part of an ABX system, J_{AB} 14.3, 2H, CH_2Ar), 2.74-2.49 (m, 4H), 2.16 (m, 2H, CH_2), 1.74 (s, 3H, CH_3), 1.28 (t, J 7.0, 3H, CH_2CH_3); ^{13}C nmr: δ 187.5 (s), 170.0 (s), 154.2 (s), 142.0 (s), 138.0 (s), 130.4 (s), 130.2 (s), 129.9 (d), 128.3 (d), 128.1 (d), 125.1 (s), 114.9 (s), 114.8 (d), 61.5 (t), 61.2 (d), 36.9 (t), 29.2 (t), 24.7 (t), 22.4 (t), 14.3 (q), 9.2 (q), ms: m/z 417 ($M^{+\bullet}$, 3%), 345 (M-$EtCO_2H$, 7), 237 (10), 227 (56), 226 (100), 198 (10), 155 (13), 108 (19), 91 (12), 77 (12); uv: 202 (ε 22640), 221 (ε 11380), 286 (ε 7113), 313 nm (ε 10710); $[\alpha]_D^{22}$ -180.0 (c 0.01 methanol); CD: $[\theta]_{216}$ -1939, $[\theta]_{227}$ +3234, $[\theta]_{242}$ -2935, $[\theta]_{274}$ +5600, $[\theta]_{311}$ -24804.

Anal. Calcd. for $C_{26}H_{27}NO_4$: C, 74.80; H, 6.52; N, 3.35. Found: C, 75.12; H, 6.48; N, 3.63.

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