Synthesis and 1,3-Dipolar Cycloaddition Reactions of *N*-Aryl-*C,C*-dimethoxycarbonylnitrones

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Arylnitroso compounds **1-3** easily reacted with dimethyl bromomalonate to give the corresponding *N*-aryl-*C,C*-dimethoxycarbonylnitrones (**4-6**). Treatment of *C,C*-dimethoxycarbonyl-*N*-(1-naphthyl)nitrone (**4**) with acetylene compounds (dimethyl acetylenedicarboxylate, methyl 2-butynoate or ethyl phenylpropiolate) caused 1,3-dipolar cycloaddition to furnish the corresponding 1*H*-benz[*g*]indolines (**7a-c**). In a similar manner, the reactions of nitrones **5** and **6** with acetylene compounds afforded the corresponding indolines **9a-c** and **11a-c** together with 4-oxazolines **13a-c** and **14a-c**.

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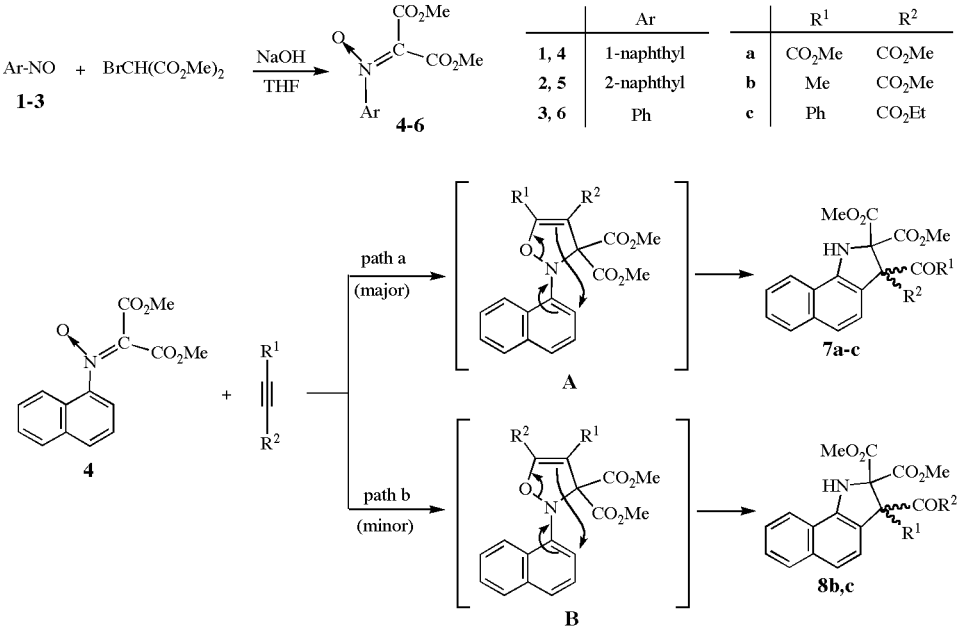
In recent years much attention has been focused on synthesis and reactions of nitrones because of their importance as synthetic tools in organic chemistry [1-4]. In fact, many reports have appeared, especially concerning 1,3-dipolar cycloaddition reactions. 1,3-Dipolar cycloaddition of nitrones occupies a uniquely important position due to their synthetic significance [5-10]. In general, nitrones react energetically with alkynes to form 2,3-dihydroisoxazoles as intermediates and products [11,12]. However, the situation is complicated by the instability of the isoxazoles produced and by the variety of different decomposition pathways. The 2,3-dihydroisoxazole system, which was associated with the presence of the weak nitrogen-oxygen bond and the carbon-carbon π system, goes through many types of rearrangements. In this respect, our interest in the chemistry of nitrone-alkyne cycloaddition stems from the exploitation of indolines and indoles showing biological interest [13-21]. This work presents an efficient method for the synthesis of *N*-aryl-*C,C*-dimethoxycarbonylnitrones from arylnitroso compounds. We also describe a new route to indolines from nitrones with acetylene compounds by their using 1,3-dipolar cycloaddition.

The starting compounds *N*-aryl-*C,C*-dimethoxycarbonylnitrones (**4-6**) were prepared by the reaction of the corresponding arylnitroso compounds **1-3** [22] with dimethyl bromomalonate and sodium hydroxide in moderate yields (**4**: 49%, **5**: 81%, **6**: 82%). When a mixture of **4** and acetylene compounds (dimethyl acetylenedicarboxylate, methyl 2-butynoate or ethyl phenylpropiolate) in benzene was refluxed, 1*H*-benz[*g*]indolines **7a-c** were obtained in good yields (**7a**: 89%, **7b**: 81%, **7c**: 92%). Fortunately, it was further found that dimethyl 3-methoxalyl(and 3-ethoxalyl)-1*H*-benz[*g*]indoline-2,2-dicarboxylates (**8b** and **8c**) were also obtained in 3 and 2% yield, respectively. The ir spectra of **7a-c** and **8b,c** display bands near 3350 cm^{-1} due to an amino group and in the range of 1660~1760 cm^{-1} due to carbonyl groups. The ^1H nmr spectrum of **7a** exhibits four three-proton singlets near δ 3.80 attributable to methoxy-

Scheme 1

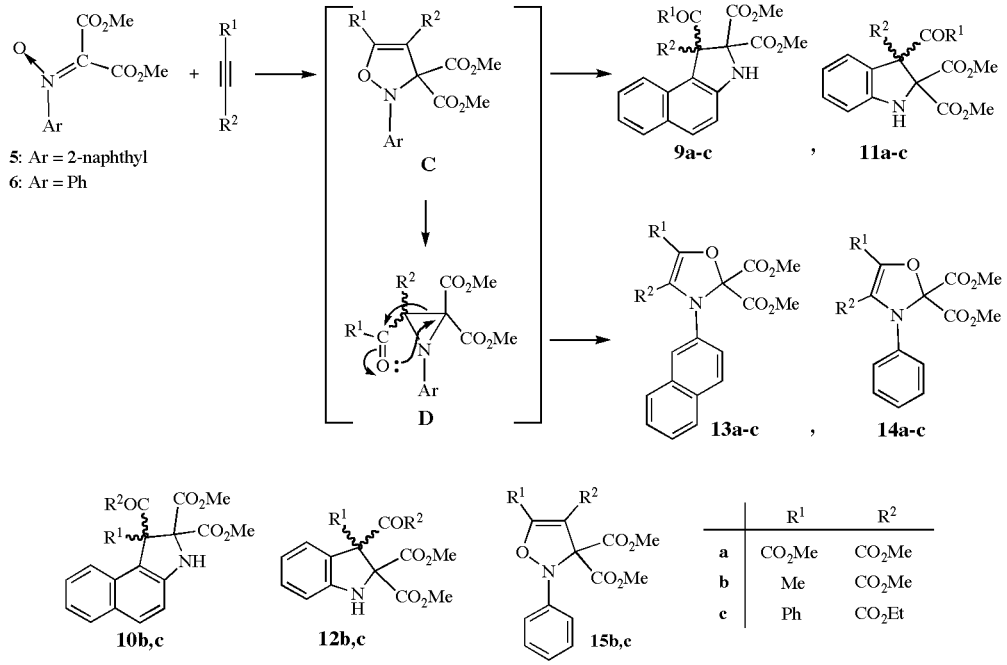


carbonyl groups and a broad one-proton singlet at δ 5.63 assignable to a secondary amino group. The ^{1}H nmr spectrum of **7b** shows three singlets near δ 3.80 for methoxycarbonyl groups and a singlet at δ 2.31 for an acetyl group, whereas **8b** appears as three singlets near δ 3.80 for methoxycarbonyl groups and a singlet at δ 1.76 for a methyl group. Elemental analyses and spectral data of **7a-c** and **8b,c** are consistent with the proposed structures. These findings suggest the possibility that this reaction occurs *via* 1,3-dipolar cycloaddition of **4** and acetylene compounds to form the intermediate 2,3-dihydroisoxazole **A** (path a) rather than **B** (path b), which undergoes ring transformation to give **7a-c** (Scheme 1). These observations indicate that the structure of the intermediate is susceptible to electronic influence of the methoxy(or ethoxy)carbonyl group of dipolarophiles as electron-withdrawing.

Subsequently, the reactions of **5** and **6** with acetylene compounds under the same conditions gave the corresponding indolines **9a-c** (**9a**: 43%, **9b**: 48%, **9c**: 58%) and **11a-c** (**11a**: 69%, **11b**: 56%, **11c**: 59%) together with **10b,c** (**10b**: 3%, **10c**: 2%) and **12b,c** (**12b**: 6%, **12c**: 3%) as by-products. In the case of this reaction, 4-oxazolines **13a-c** (**13a**: 25%, **13b**: 15%, **13c**: 16%) and **14a-c** (**14a**: 17%, **14b**: 15%, **14c**: 29%) were also obtained as rearrangement products (Scheme 2). Furthermore, we found the reaction condition under which the key intermediate 2,3-dihydroisoxazoles **15b,c** could be isolated. Treatment of **6** with methyl 2-butynoate or ethyl phenylpropiolate at room temperature gave the corresponding **15b,c** in 65 and 59% yield, respectively. However, in the case of the reaction of **4** and/or **5** with acetylene compounds, the intermediate **C** such as the 2,3-dihydroisoxazoles **15b,c** could not be isolated at room temperature or another conditions. These results make us believe that the key intermediate 2,3-dihydroisoxazoles **15b,c** are more stable than those of the reactions of **4** and/or **5** with acetylene compounds. Compounds **15b,c** were easily converted to **11b,c** (**11b**: 76%, **11c**: 63%) and **14b,c** (**14b**: 22%, **14c**: 35%) in refluxing benzene. The formation of **9**, **11**, **13** and **14** can be explained in terms of Scheme 2. A 1,3-dipolar cycloaddition of nitrones **5** and **6** to acetylene compounds gives the intermediate 2,3-dihydroisoxazole **C**, which undergoes ring transformation to afford the indolines **9** and **11**. On the other hand, a ring contraction of the intermediate **C** to the aziridine **D** easily occurs, which could then undergo ring expansion to give 4-oxazolines **13** and **14**. The structures of **9a-c**, **10b,c**, **11a-c**, **12b,c**, **13a-c**, **14a-c** and **15b,c** were confirmed by elemental analyses and spectral data.

Finally, we have examined the aromatization of **7a** and **11a** with triethylamine, hydrogen chloride and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in order to confirm their structures (Scheme 3). The reactions of **7a** and **11a** with triethylamine gave the corresponding trimethyl indoline-2,2,3-tricarboxylates **16a,b** (**16a**: 90%, **16b**: 99%). Treatment of **16a,b** with hydrogen chloride caused demethoxycarbonylation to afford dimethyl *cis*- and *trans*-indoline-2,3-dicarboxylates **17a,b** (*cis*-**17a**: 11%, *trans*-**17a**: 50%, *cis*-**17b**: 13%, *trans*-**17b**: 29%). These diastereomers of **17a,b** could be separated by silica gel chromatography (see experimental section). Compounds *cis*- and *trans*-**17a,b** reacted with DDQ to yield the corresponding dimethyl indole-2,3-dicarboxy-

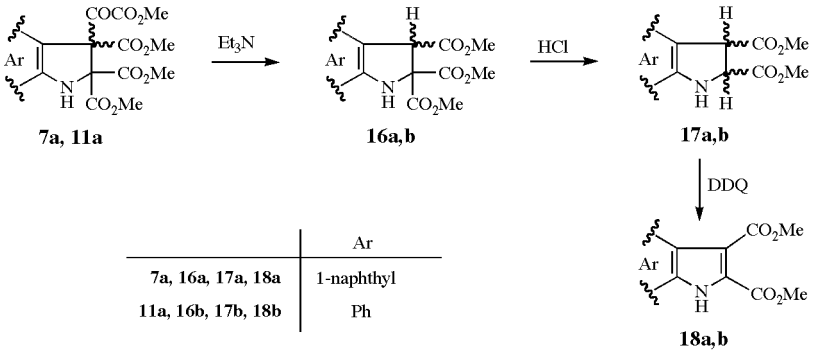
Scheme 2



	R^1	R^2
a	CO_2Me	CO_2Me
b	Me	CO_2Me
c	Ph	CO_2Et

lates **18a,b** (**18a**: 85% from *cis*-**17a**, 81% from *trans*-**17a**; **18b**: 77% from *cis*-**17b**, 85% from *trans*-**17b**), which were identical with authentic samples prepared according to the method of Mitchell *et al.* [23] or prepared according to the method of Diels *et al.* [24].

Scheme 3



EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a JASCO A-302 spectrometer or a JASCO FT/IR-230 spectrometer. The ^{1}H nmr spectra were recorded on a HITACHI R-90 H spectrometer (90 MHz) or a JEOL JNM-MH-100 (100 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. Mass (70 eV, electron impact ionization) spectra were obtained on a JEOL JMS-D 300 spectrometer. Elemental analyses were performed on a HERAUS CHNO-RAPID analyzer or a YANACO MT-6 CHN analyzer. Nitrosobenzene was obtained from Aldrich Chemical Company, Inc. 1- and 2-Nitrosonaphthalene were prepared according to the method of Earl Brill [22].

General Procedure for the Preparation of *N*-Aryl-*C,C*-dimethoxycarbonylnitrones **4-6**.

To an ice-cooled and stirred solution of arylnitroso compounds **1-3** (30 mmoles) in tetrahydrofuran (30 ml) were added dimethyl bromomalonate (6.96 g, 33 mmoles) and a solution of sodium hydroxide (1.32 g, 33 mmoles) in water (3 ml). After the mixture was stirred for 3 hours with ice-cooling, cold water was added to the reaction mixture. The precipitate was collected by filtration, washed with water, dried and recrystallized from diethyl ether to yield **4-6**.

C,C-Dimethoxycarbonyl-*N*-(1-naphthyl)nitrone (**4**).

This compound was obtained as yellow prisms (4.19 g, 49%), mp 187-188°; ir (potassium bromide): ν 1730 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 3.54 (s, 3H, CO_2Me), 3.99 (s, 3H, CO_2Me), 7.58-7.73 (m, 5H, aromatic H), 8.02-8.18 ppm (m, 2H, aromatic H); ms: m/z 287 (M^+).

Anal. Calcd. for $C_{15}H_{13}NO_5$: C, 62.72; H, 4.56; N, 4.88. Found: C, 63.01; H, 4.58; N, 5.06.

C,C-Dimethoxycarbonyl-*N*-(2-naphthyl)nitrone (**5**).

This compound was obtained as yellow prisms (6.97 g, 81%), mp 101-103°; ir (potassium bromide): ν 1735 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.64 (s, 3H, CO_2Me), 3.97 (s, 3H, CO_2Me), 7.37-7.56 (m, 3H, aromatic H), 7.79-7.91 ppm (m, 4H, aromatic H); ms: m/z 287 (M^+).

Anal. Calcd. for $C_{15}H_{13}NO_5$: C, 62.72; H, 4.56; N, 4.88. Found: C, 62.78; H, 4.50; N, 4.88.

C,C-Dimethoxycarbonyl-*N*-phenylnitrone (**6**).

This compound was obtained as yellow prisms (5.83 g, 82%), mp 74-75°; ir (potassium bromide): ν 1738 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.67 (s, 3H, CO_2Me), 3.96 (s, 3H, CO_2Me), 7.30-7.52 ppm (m, 5H, aromatic H); ms: m/z 237 (M^+).

Anal. Calcd. for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.91. Found: C, 55.56; H, 4.68; N, 5.64.

General Procedure for the Preparation of **7a-c**, **8b,c**, **9a-c**, **10b,c**, **11a-c**, **12b,c**, **13a-c** and **14a-c** from **4-6** and Acetylene Compounds.

A mixture of **4-6** (5 mmoles) and dimethyl acetylenedicarboxylate (0.71 g, 5 mmoles), methyl 2-butynoate (0.49 g, 5 mmoles) or ethyl phenylpropiolate (0.87 g, 5 mmoles) in benzene (5 ml) was refluxed for 2 hours (in the case of dimethyl acetylenedicarboxylate) or 8 hours (methyl 2-butynoate and ethyl phenylpropiolate). After removal of the solvent *in vacuo*, the residue was recrystallized from an appropriate solvent (a fractional recrystallization) to give **7a-c**, **9a-c**, **11a-c**, **13a-c** and **14a-c**. The mother solvent was purified by silica gel chromatography using an ethyl acetate-hexane (1:4) as the eluent to give **8b,c**, **10b,c** and **12b,c**.

Trimethyl 3-Methoxalyl-1*H*-benz[*g*]indoline-2,2,3-tricarboxylate (**7a**).

This compound was obtained as orange prisms (1.91 g, 89%), mp 149-150° (acetone-diethyl ether); ir (potassium bromide): ν 3380 (NH), 1760, 1725 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.75 (s, 3H, CO_2Me), 3.82 (s, 6H, 2xCO_2Me), 3.83 (s, 3H, CO_2Me), 5.63 (br s, 1H, NH), 7.35-7.47 (m, 4H, aromatic H), 7.70-7.83 ppm (m, 2H, aromatic H); ms: m/z 429 (M^+).

Anal. Calcd. for $C_{21}H_{19}NO_9$: C, 58.74; H, 4.46; N, 3.26. Found: C, 58.72; H, 4.44; N, 2.96.

Trimethyl 3-Acetyl-1*H*-benz[*g*]indoline-2,2,3-tricarboxylate (**7b**).

This compound was obtained as colorless prisms (1.56 g, 81%), mp 174-177° (acetone-diethyl ether); ir (potassium bromide): ν 3385 (NH), 1745, 1715 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.31 (s, 3H, COMe), 3.76 (s, 3H, CO_2Me), 3.80

(s, 3H, CO_2Me), 3.81 (s, 3H, CO_2Me), 5.50 (br s, 1H, NH), 7.33-7.56 (m, 4H, aromatic H), 7.72-7.85 ppm (m, 2H, aromatic H); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.17; H, 4.92; N, 3.49.

Dimethyl 3-Benzoyl-3-ethoxycarbonyl-1*H*-benz[*g*]indoline-2,2-dicarboxylate (**7c**).

This compound was obtained as yellow prisms (2.12 g, 92%), mp 182-183° (acetone); ir (potassium bromide): ν 3320 (NH), 1757, 1742, 1660 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.22 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 3.64 (s, 3H, CO_2Me), 3.76 (s, 3H, CO_2Me), 4.24 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 5.61 (br s, 1H, NH), 7.22-7.87 ppm (m, 11H, aromatic H); ms: m/z 461 (M^+).

Anal. Calcd. for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.47; H, 5.19; N, 2.80.

Dimethyl 3-Methoxalyl-3-methyl-1*H*-benz[*g*]indoline-2,2-dicarboxylate (**8b**).

This compound was obtained as orange prisms (58 mg, 3%), mp 129-130° (acetone); ir (potassium bromide): ν 3390 (NH), 1753, 1730, 1712 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.76 (s, 3H, 3-Me), 3.52 (s, 3H, CO_2Me), 3.76 (s, 3H, CO_2Me), 3.84 (s, 3H, CO_2Me), 5.60 (br s, 1H, NH), 7.06 (d, J = 8 Hz, 1H, 4-H), 7.33 (d, J = 8 Hz, 1H, 5-H), 7.40-7.88 ppm (m, 4H, aromatic H); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.23; H, 4.97; N, 3.66.

Dimethyl 3-Ethoxalyl-3-phenyl-1*H*-benz[*g*]indoline-2,2-dicarboxylate (**8c**).

This compound was obtained as orange prisms (46 mg, 2%), mp 181-182° (acetone-diethyl ether); ir (potassium bromide): ν 3360 (NH), 1738 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.03 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 3.05 (s, 3H, CO_2Me), 3.93 (s, 3H, CO_2Me), 4.03 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 5.46 (br s, 1H, NH), 7.30-7.93 ppm (m, 11H, aromatic H); ms: m/z 461 (M^+).

Anal. Calcd. for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.62; H, 5.05; N, 3.12.

Trimethyl 1-Methoxalyl-3*H*-benz[*e*]indoline-1,2,2-tricarboxylate (**9a**).

This compound was obtained as red prisms (0.92 g, 43%), mp 162-164° (acetone-petroleum ether); ir (potassium bromide): ν 3370 (NH), 1755, 1741, 1726 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.70 (s, 3H, CO_2Me), 3.76 (s, 6H, 2xCO_2Me), 3.81 (s, 3H, CO_2Me), 5.40 (s, 1H, NH), 7.02-7.39 (m, 4H, aromatic H), 7.68-7.77 ppm (m, 2H, aromatic H); ms: m/z 429 (M^+).

Anal. Calcd. for $C_{21}H_{19}NO_9$: C, 58.74; H, 4.46; N, 3.26. Found: C, 58.71; H, 4.46; N, 3.07.

Trimethyl 1-Acetyl-3*H*-benz[*e*]indoline-1,2,2-tricarboxylate (**9b**).

This compound was obtained as colorless prisms (0.92 g, 48%), mp 148-151° (acetone-petroleum ether); ir (potassium bromide): ν 3340 (NH), 1758, 1745, 1730, 1703 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.51 (s, 3H, COMe), 3.69 (s, 3H, CO_2Me), 3.75 (s, 3H, CO_2Me), 3.82 (s, 3H, CO_2Me), 5.20 (s, 1H, NH), 7.09 (d, J = 8.5 Hz, 1H, 4-H), 7.17-7.41 (m, 3H, aromatic H), 7.74 (d, J = 8.5 Hz, 1H, 5-H), 7.69-7.79 ppm (m, 1H, aromatic H); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.36; H, 5.13; N, 3.85.

Dimethyl 1-Benzoyl-1-ethoxycarbonyl-3*H*-benz[*e*]indoline-2,2-dicarboxylate (**9c**).

This compound was obtained as pale yellow prisms (1.34 g, 58%), mp 160-161° (acetone-petroleum ether); ir (potassium bromide): ν 3330 (NH), 1745, 1670 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.06 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 3.34 (s, 3H, CO_2Me), 3.82 (s, 3H, CO_2Me), 4.10 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 5.37 (s, 1H, NH), 7.06-7.76 ppm (m, 11H, aromatic H); ms: m/z 461 (M^+).

Anal. Calcd. for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.55; H, 4.83; N, 2.82.

Dimethyl 1-Methoxalyl-1-methyl-3*H*-benz[*e*]indoline-2,2-dicarboxylate (**10b**).

This compound was obtained as yellow prisms (58 mg, 3%), mp 147-148° (ethyl acetate-hexane); ir (potassium bromide): ν 3345 (NH), 1739, 1711 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.90 (s, 3H, 1-Me), 3.42 (s, 3H, CO_2Me), 3.79 (s, 3H, CO_2Me), 3.81 (s, 3H, CO_2Me), 5.22 (s, 1H, NH), 7.05-7.52 (m, 4H, aromatic H), 7.66-7.75 ppm (m, 2H, aromatic H); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.16; H, 5.03; N, 3.89.

Dimethyl 1-Ethoxalyl-1-phenyl-3*H*-benz[*e*]indoline-2,2-dicarboxylate (**10c**).

This compound was obtained as orange prisms (46 mg, 2%), mp 212-213° (ethyl acetate-hexane); ir (potassium bromide): ν 3360 (NH), 1750, 1732, 1721 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.69 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 2.99 (s, 3H, CO_2Me), 3.67-3.96 (m, 2H, $CO_2CH_2CH_3$), 3.90 (s, 3H, CO_2Me), 5.34 (s, 1H, NH), 6.87-7.87 ppm (m, 11H, aromatic H); ms: m/z 461 (M^+).

Anal. Calcd. for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.48; H, 5.17; N, 3.05.

Trimethyl 3-Methoxalylindoline-2,2,3-tricarboxylate (**11a**).

This compound was obtained as yellow prisms (1.31 g, 69%), mp 129-130° (methylene chloride-diethyl ether); ir (potassium bromide): ν 3380 (NH), 1767, 1750, 1730 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.75 (s, 3H, CO_2Me), 3.82 (s, 6H, 2xCO_2Me), 3.83 (s, 3H, CO_2Me), 5.15 (br s, 1H, NH), 6.72-7.36 ppm (m, 4H, aromatic H); ms: m/z 379 (M^+).

Anal. Calcd. for $C_{17}H_{17}NO_9$: C, 53.83; H, 4.52; N, 3.69. Found: C, 53.75; H, 4.52; N, 3.40.

Trimethyl 3-Acetylindoline-2,2,3-tricarboxylate (**11b**).

This compound was obtained as colorless prisms (0.94 g, 56%), mp 148-149° (acetone); ir (potassium bromide): ν 3345 (NH), 1742, 1729, 1714 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.28 (s, 3H, COMe), 3.75 (s, 3H, CO_2Me), 3.79 (s, 6H, 2xCO_2Me), 5.04 (br s, 1H, NH), 6.73 (d, J = 8 Hz, 1H, 4-H), 6.85 (dd, J = 1, 8 Hz, 1H, 5 or 6-H), 7.12 (dd, J = 1, 8 Hz, 1H, 5 or 6-H), 7.35 ppm (d, J = 8 Hz, 1H, 7-H); ms: m/z 335 (M^+).

Anal. Calcd. for $C_{16}H_{17}NO_7$: C, 57.31; H, 5.11; N, 4.18. Found: C, 57.41; H, 5.15; N, 4.16.

Dimethyl 3-Benzoyl-3-ethoxycarbonylindoline-2,2-dicarboxylate (**11c**).

This compound was obtained as pale yellow prisms (1.21 g, 59%), mp 115-116° (acetone-diethyl ether); ir (potassium bromide): ν 3345 (NH), 1752, 1739, 1663 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.22 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 3.63 (s, 3H, CO_2Me), 3.73 (s, 3H, CO_2Me), 4.23 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 4.60 (br s, 1H, NH), 6.64-6.83 (m, 2H, aromatic H), 7.05-7.65 ppm (m, 7H, aromatic H); ms: m/z 411 (M^+).

Anal. Calcd. for $C_{22}H_{21}NO_7$: C, 64.23; H, 5.15; N, 3.41. Found: C, 63.96; H, 5.10; N, 3.31.

Dimethyl 3-Methoxalyl-3-methylindoline-2,2-dicarboxylate (**12b**).

This compound was obtained as yellow prisms (0.10 g, 6%), mp 110-111° (diethyl ether); ir (potassium bromide): ν 3350 (NH), 1743, 1710 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.68 (s, 3H, 3-Me), 3.61 (s, 3H, CO_2Me), 3.76 (s, 3H, CO_2Me), 3.80 (s, 3H, CO_2Me), 4.96 (br s, 1H, NH), 6.68-7.25 ppm (m, 4H, aromatic H); ms: m/z 335 (M^+).

Anal. Calcd. for $C_{16}H_{17}NO_7$: C, 57.31; H, 5.11; N, 4.18. Found: C, 57.25; H, 5.10; N, 4.29.

Dimethyl 3-Ethoxalyl-3-phenylindoline-2,2-dicarboxylate (**12c**).

This compound was obtained as orange oil (62 mg, 3%); ir (neat): ν 3370 (NH), 1740 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.12 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 3.07 (s, 3H, CO_2Me), 3.89 (s, 3H, CO_2Me), 4.10 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 5.04 (br s, 1H, NH), 6.76-6.91 (m, 2H, aromatic H), 7.16-7.55 ppm (m, 7H, aromatic H); high-resolution ms: Calcd. for $C_{22}H_{21}NO_7$ 411.1318, found 411.1334.

Tetramethyl 3-(2-Naphthyl)-4-oxazoline-2,2,4,5-tetracarboxylate (**13a**).

This compound was obtained as colorless prisms (0.54 g, 25%), mp 154-156° (diethyl ether); ir (potassium bromide): ν 1777, 1753, 1740, 1720 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.64 (s, 3H, CO_2Me), 3.67 (s, 6H, 2xCO_2Me), 3.87 (s, 3H, CO_2Me), 7.33-7.52 (m, 3H, aromatic H), 7.70-7.79 ppm (m, 4H, aromatic H); ms: m/z 429 (M^+).

Anal. Calcd. for $C_{21}H_{19}NO_9$: C, 58.74; H, 4.46; N, 3.26. Found: C, 58.82; H, 4.52; N, 3.49.

Trimethyl 5-Methyl-3-(2-naphthyl)-4-oxazoline-2,2,4-tricarboxylate (**13b**).

This compound was obtained as colorless prisms (0.29 g, 15%), mp 127-130° (diethyl ether-petroleum ether); ir (potassium bromide): ν 1760, 1710 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.44 (s, 3H, 5-Me), 3.57 (s, 3H, CO_2Me), 3.59 (s, 6H, 2xCO_2Me), 7.36-7.46 (m, 3H, aromatic H), 7.60-7.77 ppm (m, 4H, aromatic H); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.13; H, 5.03; N, 3.41.

Dimethyl 4-Ethoxycarbonyl-3-(2-naphthyl)-5-phenyl-4-oxazoline-2,2-dicarboxylate (**13c**).

This compound was obtained as pale yellow prisms (0.37 g, 16%), mp 123-125° (diethyl ether-petroleum ether); ir (potassium bromide): ν 1757, 1713 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.84 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 3.63 (s, 6H, 2xCO_2Me), 4.00 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 7.36-8.13 ppm (m, 12H, aromatic H); ms: m/z 461 (M^+).

Anal. Calcd. for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.75; H, 4.93; N, 3.03.

Tetramethyl 3-Phenyl-4-oxazoline-2,2,4,5-tetracarboxylate (**14a**).

This compound was obtained as colorless prisms (0.32 g, 17%), mp 95-97° (diethyl ether-petroleum ether); ir (potassium bromide): ν 1758, 1744, 1720 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.68 (s, 3H, CO_2Me), 3.69 (s, 6H, 2xCO_2Me), 3.86 (s, 3H, CO_2Me), 7.30 ppm (s, 5H, aromatic H); ms: m/z 379 (M^+).

Anal. Calcd. for $C_{17}H_{17}NO_9$: C, 53.83; H, 4.52; N, 3.69. Found: C, 53.80; H, 4.39; N, 3.77.

Trimethyl 5-Methyl-3-phenyl-4-oxazoline-2,2,4-tricarboxylate (**14b**).

This compound was obtained as colorless plates (0.25 g, 15%), mp 100° (diethyl ether-petroleum ether); ir (potassium bromide): ν 1770, 1746, 1706 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.41 (s, 3H, 5-Me), 3.60 (s, 3H, CO_2Me), 3.63 (s, 6H, 2xCO_2Me), 7.06-7.26 ppm (m, 5H, aromatic H); ms: m/z 335 (M^+).

Anal. Calcd. for $C_{16}H_{17}NO_7$: C, 57.31; H, 5.11; N, 4.18. Found: C, 57.20; H, 5.16; N, 4.15.

Dimethyl 4-Ethoxycarbonyl-3,5-diphenyl-4-oxazoline-2,2-dicarboxylate (**14c**).

This compound was obtained as pale yellow prisms (0.60 g, 29%), mp 92-93° (diethyl ether-petroleum ether); ir (potassium bromide): ν 1760, 1740, 1710 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.91 (t, J = 7.5 Hz, 3H, $CO_2CH_2CH_3$), 3.66 (s, 6H, 2xCO_2Me), 4.02 (q, J = 7.5 Hz, 2H, $CO_2CH_2CH_3$), 7.08-7.46 (m, 8H, aromatic H), 7.94-8.05 ppm (m, 2H, aromatic H); ms: m/z 411 (M^+).

Anal. Calcd. for $C_{22}H_{21}NO_7$: C, 64.23; H, 5.15; N, 3.41. Found: C, 63.99; H, 5.06; N, 3.13.

General Procedure for the Preparation of **15b,c** from **6** and Methyl 2-Butynoate or Ethyl Phenylpropiolate.

A mixture of **6** (1.19 g, 5 mmoles) and methyl 2-butynoate (0.49 g, 5 mmoles) or ethyl phenylpropiolate (0.87 g, 5 mmoles) in benzene (5 ml) was stirred at room temperature for 6 days. After removal of the solvent *in vacuo*, the residue was purified by silica gel chromatography using an ethyl acetate-hexane (1:4) as the eluent to afford **15b,c**. The second fraction gave **14b** (34 mg, 2%) and **14c** (12 mg, 3%). The third fraction gave **12b** (0.10 g, 6%) and **12c** (0.16 g, 8%). The last fraction gave **11b** (0.18 g, 11%) and **11c** (0.21 g, 10%). The melting points and ir spectra of **11b,c**, **12b** and **14b,c** coincided with those of authentic samples prepared from **6** and methyl 2-butynoate or ethyl phenylpropiolate. The ir spectrum of **12c** coincided with that of authentic sample prepared from **6** and ethyl phenylpropiolate.

Trimethyl 2,3-Dihydro-5-methyl-2-phenylisoxazole-3,3,4-tricarboxylate (**15b**).

This compound was obtained as colorless needles (1.09 g, 65%), mp 116° (ethyl acetate-hexane); ir (potassium bromide): ν 1753, 1694 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.41 (s, 3H, 5-Me), 3.61 (s, 6H, 2xCO_2Me), 3.73 (s, 3H, CO_2Me), 7.08-7.42 ppm (m, 5H, aromatic H); ms: m/z 335 (M^+).

Anal. Calcd. for $C_{16}H_{17}NO_7$: C, 57.31; H, 5.11; N, 4.18. Found: C, 57.40; H, 5.12; N, 4.40.

Dimethyl 4-Ethoxycarbonyl-2,3-dihydro-2,5-diphenylisoxazole-3,3-dicarboxylate (**15c**).

This compound was obtained as colorless needles (1.21 g, 59%), mp 90-91° (ethyl acetate-hexane); ir (potassium bromide): ν 1757, 1742, 1726 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.15 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 3.64 (s, 6H, 2xCO_2Me), 4.16 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 7.08-7.52 (m, 8H, aromatic H), 7.83-7.94 ppm (m, 2H, aromatic H); ms: m/z 411 (M^+).

Anal. Calcd. for $C_{22}H_{21}NO_7$: C, 64.23; H, 5.15; N, 3.41. Found: C, 64.22; H, 5.23; N, 3.59.

The Preparation of **11b,c** and **14b,c** from **15b,c**.

A mixture of **15b,c** (10 mmoles) in benzene (3 ml) was refluxed for 3 hours. After removal of the solvent *in vacuo*, the residue was purified by silica gel chromatography using an ethyl acetate-hexane (1:4) as the eluent to yield **14b** (0.37 g, 22%) and **14c** (0.72 g, 35%). Further the elution gave **11b** (1.27 g, 76%) and **11c** (1.29 g, 63%), respectively. The melting points and ir spectra of **11b,c** and **14b,c** coincided with those of authentic samples prepared from **6** and methyl 2-butynoate or ethyl phenylpropiolate.

General Procedure for the Preparation of **16a,b** from **7a** and **11a**.

A mixture of **7a** or **11a** (1 mmole) and triethylamine (0.30 g, 3 mmoles) in methanol (5 ml) was refluxed for 2 hours. After removal of the solvent *in vacuo*, cold water was added to the residue. The resulting mixture was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was recrystallized from an appropriate solvent to give **16a,b**.

Trimethyl 1*H*-Benz[*g*]indoline-2,2,3-tricarboxylate (**16a**).

This compound was obtained as colorless prisms (0.31 g, 90%), mp 127-128° (acetone-diethyl ether); ir (potassium bromide): ν 3400 (NH), 1755, 1740 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.69 (s, 3H, CO_2Me), 3.79 (s, 3H, CO_2Me), 3.82 (s, 3H, CO_2Me), 5.18 (s, 1H, 3-H), 5.47 (br s, 1H, NH), 7.33-7.52 (m, 4H, aromatic H), 7.73-7.84 ppm (m, 2H, aromatic H); ms: m/z 343 (M^+).

Anal. Calcd. for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 63.15; H, 5.10; N, 4.15.

Trimethyl Indoline-2,2,3-tricarboxylate (**16b**).

This compound was obtained as colorless prisms (0.29 g, 99%), mp 70-72° (diethyl ether-petroleum ether); ir (potassium bromide): ν 3420 (NH), 1738 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.63 (s, 3H, CO_2Me), 3.76 (s, 3H, CO_2Me), 3.77 (s, 3H, CO_2Me), 4.77 (br s, 1H, NH), 4.96 (s, 1H, 3-H), 6.68-7.16 ppm (m, 4H, aromatic H); ms: m/z 293 (M^+).

Anal. Calcd. for $C_{14}H_{15}NO_6$: C, 57.34; H, 5.16; N, 4.78. Found: C, 57.44; H, 5.21; N, 4.83.

General Procedure for the Preparation of *cis*- and *trans*-**17a,b** from **16a,b**.

Dry hydrogen chloride was bubbled into an ice-cooled and stirred solution of **16a,b** (6 mmoles) in anhydrous methanol (40 ml) for one hour, and then the mixture was refluxed for 8 hours. After removal of the solvent *in vacuo*, the residue was basified with saturated sodium bicarbonate. The resulting mixture was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by silica gel chromatography using a 10% ethyl acetate in hexane as the eluent to yield *cis*-**17a,b**. Further the elution afforded *trans*-**17a,b**.

Dimethyl *cis*-1*H*-Benz[*g*]indoline-2,3-dicarboxylate (*cis*-**17a**).

This compound was obtained as colorless needles (0.19 g, 11%), mp 94-95° (diethyl ether); ir (potassium bromide): ν 3370 (NH), 1752, 1735 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.86 (s, 6H, 2xCO_2Me), 4.71 (d, J = 5 Hz, 1H, 3-H), 4.98 (br s, 1H, NH), 5.15 (d, J = 5 Hz, 1H, 2-H), 7.27-7.50 (m, 4H, aromatic H), 7.72-7.86 ppm (m, 2H, aromatic H); ms: m/z 285 (M^+).

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.65; H, 5.30; N, 5.18.

Dimethyl *trans*-1*H*-Benz[*g*]indoline-2,3-dicarboxylate (*trans*-**17a**).

This compound was obtained as colorless needles (0.85 g, 50%), mp 118-120° (diethyl ether); ir (potassium bromide): ν 3360 (NH), 1738 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.67 (s, 3H, CO_2Me), 3.80 (s, 3H, CO_2Me), 3.92 (br s, 1H, NH), 4.58 (d, J = 10 Hz, 1H, 3-H), 4.86 (d, J = 10 Hz, 1H, 2-H), 7.33-7.47 (m, 4H, aromatic H), 7.69-7.83 ppm (m, 2H, aromatic H); ms: m/z 285 (M^+).

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.38; H, 5.39; N, 4.97.

Dimethyl *cis*-Indoline-2,3-dicarboxylate (*cis*-**17b**).

This compound was obtained as colorless prisms (0.18 g, 13%), mp 74-77° (diethyl ether-petroleum ether); ir (potassium bromide): ν 3410 (NH), 1730, 1713 (C=O) cm^{-1}; ^1H nmr (DMSO-d_6): δ 3.70 (s, 3H, CO_2Me), 3.74 (s, 3H, CO_2Me), 4.37 (d, J = 6.5 Hz, 1H, 3-H), 4.73 (dd, J = 2.5, 6.5 Hz, 1H, 2-H), 6.32 (d, J = 2.5 Hz, 1H, NH), 6.55-6.70 (m, 2H, aromatic H), 6.98-7.19 ppm (m, 2H, aromatic H); ms: m/z 235 (M^+).

Anal. Calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.12; H, 5.60; N, 5.89.

Dimethyl *trans*-Indoline-2,3-dicarboxylate (*trans*-**17b**).

This compound was obtained as colorless prisms (0.41 g, 29%), mp 72-74° (diethyl ether); ir (potassium bromide): ν 3370 (NH), 1735 (C=O) cm^{-1}; ^1H nmr (DMSO-d_6): δ 3.60 (s, 3H, CO_2Me), 3.63 (s, 3H, CO_2Me), 4.50 (d, J = 10 Hz, 1H, 3-H), 4.72 (dd, J = 2.5, 10 Hz, 1H, 2-H), 6.13 (d, J = 2.5 Hz, 1H, NH), 6.52-6.67 (m, 2H, aromatic H), 6.95-7.10 ppm (m, 2H, aromatic H); ms: m/z 235 (M^+).

Anal. Calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 60.90; H, 5.62; N, 5.86.

General Procedure for the Preparation of **18a,b** from *cis*- or *trans*-**17a,b**.

A mixture of *cis*- or *trans*-**17a,b** (1 mmole) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.23 g, 1 mmole) in 1,4-dioxane (2 ml) was refluxed for one hour. After removal of the deposited crystals by filtration, the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform as the eluent to give dimethyl 1*H*-benz[*g*]indole-2,3-dicarboxylate (**18a**) [(0.24 g, 85%, from *cis*-**17a**), (0.23 g, 81%, from *trans*-**17a**)] and dimethyl indole-2,3-dicarboxylate (**18b**) [(0.18 g, 77%, from *cis*-**17b**), (0.20 g, 85%, from *trans*-**17b**)]. The melting points and ir spectra of **18a,b** coincided with

those of authentic samples prepared from dimethyl 1-(1-naphthyl)-1,2,3-triazole-4,5-dicarboxylate [23] or prepared from 1,2-diphenylhydrazine and dimethyl acetylenedicarboxylate [24].

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