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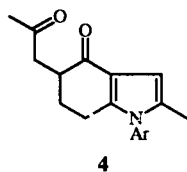
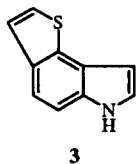
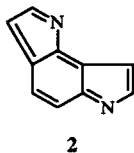
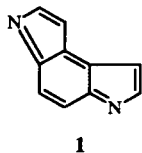
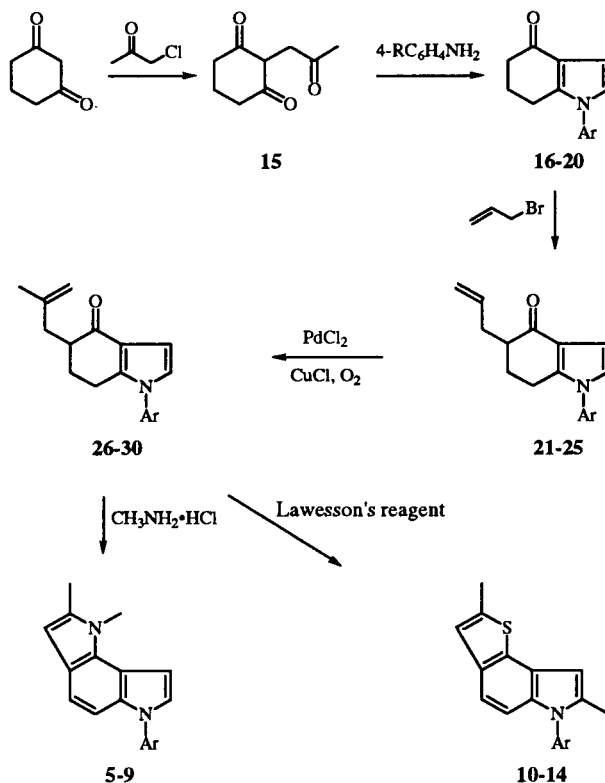
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A novel synthesis of substituted pyrrolo[2,3-*e*]indoles and thieno[2,3-*e*]indoles is described. This new approach uses 1,3-cyclohexanedione as the starting material. Diketone intermediates are obtained in four steps from the aforementioned ketone. Using these intermediates, the title compounds are synthesized efficiently.

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The benzo[1,2-*b*: 4,3-*b'*]dipyrrole nucleus **1** occurs in the phosphodiesterase inhibitors PDI and PDII [3]. It is also found, with the same substitution pattern, in the potent antitumor antibiotic CC-1065 [4]. Their novel structures and biological activities have stimulated considerable synthetic efforts [5]. Despite the fact that pyrrolo[2,3-*e*]indole ring **2** is the closest analog of nucleus **1**, this class of compounds remains practically uninvestigated and there are only two synthetic procedures reported in the literature for the preparation of this tricyclic system [6]; significantly the two procedures affords only the free N-H pyrrolo[2,3-*e*]indole ring. On the other hand, after an exhaustive review of literature we found only one report [7] reporting the synthesis of the thieno[2,3-*e*]indole ring **3**. As a part of a program directed toward the synthesis of heterocyclic compounds from 1,3-cyclohexanediones [8] we felt therefore that construction of one intermediate such as **4** offers an attractive route to heterocycles as **2** and **3**. We now report a novel approach to 1,2,6,7-tetrasubstituted pyrrolo[2,3-*e*]indoles **5-9** and 1,6,7-trisubstituted thieno[2,3-*e*]indoles **10-14** from 1,3-cyclohexanedione.

The alkylation of 1,3-cyclohexanedione with chloro-2-propanone, in presence of sodium ethoxide in ethanol [9],



furnishes the corresponding tricarbonyl compound **15** [10]. This compound was refluxed, in glacial acetic acid, with 4-substituted anilines to provide 4-tetrahydroindolones **16-20** (**16**, X = OCH₃; **17**, X = CH₃; **18**, X = H; **19**, X = Br; **20**, X = Cl) in moderate yields [11]. Numerous attempts to alkylate **16-20** at C5, with chloro-2-propanone under different conditions were unsuccessful; these include modification in base, solvent and temperature. We always observed decomposition of starting material by tlc. Palladium catalyzed oxidation reactions of terminal olefins to produce ketones was then examined. The procedure is based on the

allylation of ketones followed by the palladium catalyzed oxidation of the terminal olefin to the methylketone [12]. Reactions of **16-20** with propenyl bromide, in the presence of lithium diisopropylamide in tetrahydrofuran at -75° , furnished α -allyl ketones **21-25** in good yields. These α -allyl ketones were subjected to oxidation with palladium chloride-cuprous chloride system in dimethylformamide under an oxygen atmosphere to give the desired dicarbonyl compounds **26-30** in good yields. Reaction of compounds **26-30** with methylamine hydrochloride, in glacial acetic acid, afforded the pyrrolo[2,3-*e*]indoles **5-9** in moderate yields. Treatment of dicarbonyl compounds **26-30** with Lawesson's reagent in refluxing toluene [13] furnished thieno[2,3-*e*]indoles **10-14** in moderate yields. The methodology described in this paper allows access to the pyrrolo[2,3-*e*]indole and thieno[2,3-*e*]indole nuclei from readily available starting materials. We are continuing to examine the chemistry of intermediate **4** to synthesize different heterocyclic compounds.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nicolet FT-55X spectrophotometer. The ^1H nmr spectra were determined on a Varian FT-200 and on a Varian FT-300 instrument. All nmr spectra were obtained with the pulse sequence as part of the spectrometer's software and was determined in deuteriochloroform solution containing tetramethylsilane as the internal standard with chemical shifts (δ) expressed downfield from tetramethylsilane. Mass spectra were obtained with a Jeol SX-100 mass spectrometer. Column chromatography was carried out on Merck Kieselgel 60 F₂₅₄. Thin layer chromatography was carried out on Merck Kieselgel 60 PF₂₅₄. All of the solvents used were dried over the appropriate drying agent. Compound **15** has been prepared following a reported procedure and its structure was supported by spectral data [10].

Synthesis of 2-Methyl-1-(4-*R*-phenyl)-4,5,6,7-tetrahydro-1*H*-4-indolones **16-20**. 2-Methyl-1-(4-methoxyphenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **16**.

General Procedure (*R* = OMe).

4-Methoxyaniline 0.72 g, (6.0 mmole) was added to a solution of 1.0 g of **15** (6.0 mmole) in 5 ml of acetic acid. The mixture was refluxed for 18 hours and then ice water was added. The resulting precipitate was filtered and column chromatographed (silica gel). Elution with hexane/ethyl acetate, 90/10, afforded **16** as a colourless solid (hexane) (1.07 g, 72%), mp $120-121^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ 2.02 (d, 3H, *J* = 0.90 Hz, CH_3C_2), 2.07 (m, 2H, H₆), 2.48 (m, 4H, H₅, H₇), 3.87 (s, 3H, OCH₃), 6.34 (q, 1H, *J* = 0.90 Hz, H₃), 7.01-7.14 (m, 4H, ArH); ms: *m/z* 255 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.30; H, 6.70; N, 5.51.

2-Methyl-1-(4-methylphenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **17**.

This compound was obtained as a colorless solid (hexane) (42%), mp $138-139^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr

(deuteriochloroform): δ 2.05 (d, 3H, *J* = 0.90, CH_3C_2), 2.10 (m, 2H, H₆), 2.50 (m, 4H, H₅, H₇), 2.45 (s, 3H, $\text{CH}_3\text{-Ar}$), 6.37 (q, 1H, *J* = 0.90 Hz, H₃), 7.20-7.10 (m, 4H, ArH); ms: *m/z*: 239 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.32; H, 7.15; N, 5.86.

2-Methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-4-indolone **18**.

This compound was obtained as a colorless solid (hexane) (59%), mp $150-151^{\circ}$ ir (chloroform): δ 1656 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ 2.02 (d, 3H, *J* = 0.90, CH_3C_2), 2.05 (m, 2H, H₆), 2.48 (m, 4H, H₅, H₇), 6.35 (q, 1H, *J* = 0.90 Hz, H₃), 7.45-7.20 (m, 4H, ArH); ms: *m/z*: 225 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.01; H, 6.70; N, 6.21.

2-Methyl-1-(4-bromophenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **19**.

This compound was obtained as colorless solid (hexane) (67%), mp $200-202^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ 2.02 (d, 3H, *J* = 0.90, CH_3C_2), 2.06 (m, 2H, H₆), 2.49 (m, 4H, H₅, H₇), 6.35 (q, 1H, *J* = 0.90 Hz, H₃), 7.60-7.05 (m, 4H, ArH); ms: *m/z*: 303 (M^+ , 100%);

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{NOBr}$: C, 59.23; H, 4.64; N, 4.60. Found: C, 59.25; H, 4.65; N, 4.58.

2-Methyl-1-(4-chlorophenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **20**.

This compound was obtained as a colorless solid (hexane) (32%), mp $165-166^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ 2.02 (d, 3H, *J* = 0.90, CH_3C_2), 2.06 (m, 2H, H₆), 2.4 (m, 4H, H₅, H₇), 6.35 (q, 1H, *J* = 0.90 Hz, H₃), 7.48-7.15 (m, 4H, ArH); ms: *m/z*: 259 (M^+ , 100%);

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{NOCl}$: C, 69.36; H, 5.43; N, 5.39. Found: C, 69.38; H, 5.42; N, 5.42.

Synthesis of 5-Allyl-2-methyl-1-(4-*R*-phenyl)-4,5,6,7-tetrahydro-1*H*-4-indolones **21-25**. 5-Allyl-2-methyl-1-(4-methoxyphenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **21**.

General Method (*R* = -OMe).

A solution of 0.088 g of diisopropylamine (0.88 mmole) in 5 ml tetrahydrofuran, at -78° , was treated with 0.056 g of 1.6 *M* *n*-butyllithium (0.88 mmole). After 10 minutes 0.15 g of **16** (0.06 mmole) in tetrahydrofuran was added dropwise. After 20 minutes was added 0.01 g (0.06 mmole) of allyl bromide in 3 ml of tetrahydrofuran. After 1 hour stirring the mixture was warmed at -20° , poured into a saturated ammonium chloride solution, extracted with methylene chloride, dried over anhydrous sulphate and the solvent evaporated. The resulting oil was column chromatographed (silica gel). Elution with hexane/ethyl acetate, 3/1, afforded **21** as a colorless solid (hexane) (0.14 g, 81%), mp $80-81^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ 1.84 (m, 2H, H_{1'}), 2.0 (d, 3H, *J* = 1.0 Hz, CH_3C_2), 2.17 (m, 2H, H₆), 2.48 (m, 1H, H₅), 2.65 (m, 2H, H₇), 3.84 (s, 3H, OCH₃), 5.04 (m, 2H, H_{3'}), 5.80 (m, 1H, H_{2'}), 6.32 (q, 1H, *J* = 1.0 Hz, H₃), 6.98-7.13 (m, 4H, ArH); ms: *m/z*: 295 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{19}\text{H}_{21}\text{NO}_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.28; H, 7.16; N, 4.78.

5-Allyl-2-methyl-1-(4-methylphenyl)-4,5,6,7-tetrahydro-1*H*-4-indolone **22**.

This compound was obtained as a colorless solid (hexane) (58%), mp $90-91^{\circ}$; ir (chloroform): ν 1656 cm^{-1} (CO); ^1H nmr

(deuteriochloroform): δ 1.99 (m, 2H, H1'), 2.15 (d, 3H, J = 1.0 Hz, CH₃C2), 2.30 (m, 2H, H6), 2.55 (s, 3H, CH₃-Ar), 2.60 (m, 1H, H5), 2.85 (m, 2H, H7), 5.16 (m, 2H, H3'), 5.95 (m, 1H, H2'), 6.47 (q, 1H, J = 1.0 Hz, H3), 7.20-7.30 (m, 4H, ArH); ms: m/z: 279 (M⁺, 100%).

Anal. Calcd. for C₁₉H₂₁NO: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.72; H, 7.59; N, 5.03.

5-Allyl-2-methyl-1-phenyl-4,5,6,7-tetrahydro-1H-4-indolone 23.

This compound was obtained as a colorless solid (hexane) (68%), mp 116-117°; ir (chloroform): ν 1656 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 2.0 (m, 2H, H1'), 2.18 (d, 3H, J = 1.0 Hz, CH₃C2), 2.35 (m, 2H, H6), 2.65 (m, 1H, H5), 2.85 (m, 2H, H7), 5.19 (m, 2H, H3'), 5.85 (m, 1H, H2'), 6.5 (q, 1H, J = 1.0 Hz, H3), 7.60-7.35 (m, 4H, ArH); ms: m/z: 265 (M⁺, 100%).

Anal. Calcd. for C₁₈H₁₉NO: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.49; H, 7.21; N, 5.30.

5-Allyl-2-methyl-1-(4-bromophenyl)-4,5,6,7-tetrahydro-1H-4-indolone 24.

This compound was obtained as colorless solid (hexane) (54%), mp 118-119°; ir (chloroform): ν 1656 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.95 (m, 2H, H1'), 2.13 (d, 3H, J = 1.0 Hz, CH₃C2), 2.30 (m, 2H, H6), 2.62 (m, 1H, H5), 2.82 (m, 2H, H7), 5.13 (m, 2H, H3'), 5.95 (m, 1H, H2'), 6.46 (q, 1H, J = 1.0 Hz, H3), 7.74-7.21 (m, 4H, ArH); ms: m/z: 343 (M⁺, 100%).

Anal. Calcd. for C₁₈H₁₈NOBr: C, 62.80; H, 5.27; N, 4.07. Found: C, 62.82; H, 5.27; N, 4.10.

5-Allyl-2-methyl-1-(4-chlorophenyl)-4,5,6,7-tetrahydro-1H-4-indolone 25.

This compound was obtained as a colorless solid (hexane) (72%), mp 110-111°; ir (chloroform): ν 1656 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 2.05 (m, 2H, H1'), 2.15 (d, 3H, J = 1.0 Hz, CH₃C2), 2.35 (m, 2H, H6), 2.55 (m, 1H, H5), 2.73 (m, 2H, H7), 5.06 (m, 2H, H3'), 5.95 (m, 1H, H2'), 6.38 (q, 1H, J = 1.0 Hz, H3), 7.49-7.20 (m, 4H, ArH); ms: m/z: 299 (M⁺, 100%).

Anal. Calcd. for C₁₈H₁₈NOCl: C, 72.11; H, 6.05; N, 4.67. Found: C, 72.13; H, 6.06; N, 4.68.

Synthesis of 2-Methyl-1-(4-*R*-phenyl)-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolones **26-30**. 2-Methyl-1-(4-methoxyphenyl)-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolone **26**.

General Method (R = OMe).

Cuprous chloride (0.4 g, 4.0 mmoles) and palladium chloride (0.2 g, 1.4 mmoles) were suspended in dimethylformamide (10 ml) and water (1.2 ml). The mixture was shaken under oxygen atmosphere until absorption of oxygen ceased. Then 0.8 g of **21** (2.7 mmoles) was added and the mixture was shaken under oxygen at room temperature for 22 hours. The reaction mixture was poured into 3N hydrochloric acid and the product was extracted with dichloromethane. The crude product was purified by column chromatography (silica gel). Elution with hexane/ethyl acetate, 4/1, afforded **26** as a colorless solid (hexane) (0.63 g, 76%), mp 141-142°; ir (chloroform): ν 1714, 1650 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.80 (m, 2H, H1'), 1.98 (d, 3H, J = 1.0 Hz, CH₃C2), 2.21 (s, 3H, CH₃CO), 2.46 (m, 2H, H6), 2.75 (m, 1H, H5), 2.80 (m, 2H, H7), 3.84 (s, 3H, OCH₃), 6.29 (q, 1H, J = 1.0 Hz, H3), 7.11-6.96 (m, 4H, ArH); ms: m/z: 311 (M⁺, 75%).

Anal. Calcd. for C₁₉H₂₁NO₃: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.31; H, 6.79; N, 4.52.

2-Methyl-1-(4-methylphenyl)-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolone 27.

This compound was obtained as a colorless solid (hexane) (68%), mp 130-131°; ir (chloroform): ν 1714, 1650 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.82 (m, 2H, H1'), 2.0 (d, 3H, J = 1.0, CH₃C2), 2.21 (s, 3H, CH₃CO), 2.45 (m, 2H, H6), 2.76 (m, 1H, H5), 2.79 (m, 2H, H7), 2.40 (s, 3H, CH₃-Ar), 6.30 (q, 1H, J = 1.0 Hz, H3), 7.06-7.11 (m, 4H, ArH); ms: m/z: 295 (M⁺, 97%).

Anal. Calcd. for C₁₉H₂₁NO₂: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.29; H, 7.18; N, 4.72.

2-Methyl-1-phenyl-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolone 28.

This compound was obtained as a colorless solid (hexane) (80%), mp 122-124°; ir (chloroform): ν 1716, 1652 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.82 (m, 2H, H1'), 2.07 (d, 3H, J = 1.0, CH₃C2), 2.21 (s, 3H, CH₃CO), 2.46 (m, 2H, H6), 2.78 (m, 1H, H5), 2.81 (m, 2H, H7), 6.32 (q, 1H, J = 1.0 Hz, H3), 7.2-7.4 (m, 4H, ArH); ms: m/z: 281 (M⁺, 92%).

Anal. Calcd. for C₁₈H₁₉NO₂: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.88; H, 6.80; N, 5.00.

2-Methyl-1-(4-bromophenyl)-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolone 29.

This compound was obtained as a colorless solid (hexane) (67%), mp 128-129°; ir (chloroform): ν 1716, 1653 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.84 (m, 2H, H1'), 2.04 (d, 3H, J = 1.0, CH₃C2), 2.23 (s, 3H, CH₃CO), 2.48 (m, 2H, H6), 2.78 (m, 1H, H5), 2.81 (m, 2H, H7), 6.31 (q, 1H, J = 1.0 Hz, H3), 7.20-7.32 (m, 4H, ArH); ms: m/z: 359 (M⁺, 57%).

Anal. Calcd. for C₁₈H₁₈NO₂Br: C, 60.01; H, 5.04; N, 3.89. Found: C, 60.05; H, 5.01; N, 3.86.

2-Methyl-1-(4-chlorophenyl)-5-(2-oxopropyl)-4,5,6,7-tetrahydro-1H-4-indolone 30.

This compound was obtained as a colorless solid (hexane) (89%), mp 120-121°; ir (chloroform): ν 1716, 1653 cm⁻¹ (CO); ¹H nmr (deuteriochloroform): δ 1.89 (m, 2H, H1'), 2.05 (d, 3H, J = 1.0, CH₃C2), 2.25 (s, 3H, CH₃CO), 2.50 (m, 2H, H6), 2.79 (m, 1H, H5), 2.81 (m, 2H, H7), 6.35 (q, 1H, J = 1.0 Hz, H3), 7.18-7.49 (m, 4H, ArH); ms: m/z: 315 (M⁺, 80%).

Anal. Calcd. for C₁₈H₁₈NO₂Cl: C, 68.46; H, 5.74; N, 4.36. Found: C, 68.49; H, 5.73; N, 4.38.

Synthesis of 1,2,7-Trimethyl-6-(4-*R*-phenyl)-1,6-dihydropyrrolo[2,3-*e*]indoles **5-9**. 1,2,7-Trimethyl-6-(4-methoxyphenyl)-1,6-dihydropyrrolo[2,3-*e*]indole **5**.

General Method (R = OMe).

Methylamine hydrochloride (0.025 g, 0.37 x mmole) was added to a solution of 0.1 g of **26** (0.34 mmole) in 5 ml of acetic acid. The mixture was refluxed for 16 hours and then ice-water was added. The resulting precipitate was filtered and column chromatographed (silica gel). Elution with hexane/dichloromethane, 80/20, afforded **5** as a colorless solid (hexane) (0.080 g, 782%), mp 164-166°; ¹H nmr (deuteriochloroform): δ 2.31 (d, 3H, J = 0.98 Hz, CH₃C7), 2.44 (d, 3H, J = 0.88 Hz, CH₃C2), 3.89 (s, 3H, OCH₃), 3.98 (s, 3H, NCH₃), 6.26 (q, 1H, J = 0.98 Hz, H8), 6.68 (q, 1H, J = 0.88 Hz, H3), 6.76 (d, 1H, J = 9.0 Hz, H4), 7.19 (d, 1H, J = 9.0 Hz, H5), 7.04-7.29 (m, 4H, ArH); ms: m/z: 304 (M⁺, 100%).

Anal. Calcd. for C₂₀H₂₀N₂O: C, 78.91; H, 6.62; N, 9.21. Found: C, 78.92; H, 6.60; N, 9.23.

1,2,7-Trimethyl-6-(4-methylphenyl)-1,6-dihydropyrrolo[2,3-*e*]-indole 6.

This compound was obtained as a colorless solid (hexane) (42%), mp 138-139°; ¹H nmr (deuteriochloroform): δ 2.31 (d, 3H, J = 0.98 Hz, CH₃C7), 2.42 (d, 3H, J = 0.88 Hz, CH₃C2), 2.44 (s, 3H, CH₃-Ar), 3.96 (s, 3H, NCH₃), 6.24 (q, 1H, J = 0.98 Hz, H8), 6.68 (q, 1H, J = 0.88 Hz, H3), 6.78 (d, 1H, J = 9.0 Hz, H4), 7.21 (d, 1H, J = 9.0 Hz, H5), 7.17-6.78 (m, 4H, ArH); ms: m/z: 288 (M⁺, 100%).

Anal. Calcd. for C₂₀H₂₀N₂: C, 83.29; H, 6.99; N, 9.72. Found: C, 83.31; H, 7.01; N, 9.71.

1,2,7-Trimethyl-6-phenyl-1,6-dihydropyrrolo[2,3-*e*]indole 7.

This compound was obtained as colorless solid hexane) (28%), mp 135-137°; ¹H nmr (deuteriochloroform): δ 2.34 (d, 3H, J = 0.98 Hz, CH₃C7), 2.44 (d, 3H, J = 0.88 Hz, CH₃C2), 3.98 (s, 3H, NCH₃), 6.26 (q, 1H, J = 0.98 Hz, H8), 6.71 (q, 1H, J = 0.88 Hz, H3), 6.81 (d, 1H, J = 9.0 Hz, H4), 7.38 (d, 1H, J = 9.0 Hz, H5), 7.38-6.81 (m, 4H, ArH); ms: m/z: 274 (M⁺, 100%).

Anal. Calcd. for C₁₉H₁₈N₂: C, 83.17; H, 6.61; N, 10.21. Found: C, 83.19; H, 6.60; N, 10.20.

1,2,7-Trimethyl-6-(4-bromophenyl)-1,6-dihydropyrrolo[2,3-*e*]indole 8.

This compound was obtained as a colorless solid (hexane) (28%), mp 140-141°; ¹H nmr (deuteriochloroform): δ 2.32 (d, 3H, J = 0.98 Hz, CH₃C7), 2.44 (d, 3H, J = 0.88 Hz, CH₃C2), 3.97 (s, 3H, NCH₃), 6.25 (q, 1H, J = 0.98 Hz, H8), 6.70 (q, 1H, J = 0.88 Hz, H3), 6.78 (d, 1H, J = 9.0 Hz, H4), 7.21 (d, 1H, J = 9.0 Hz, H5), 7.48-7.34 (m, 4H, ArH); ms: m/z: 352 (M⁺, 100%).

Anal. Calcd. for 91 C₁₉H₁₇N₂Br: C, 64.60; H, 4.85; N, 7.93. Found: C, 64.63; H, 4.87; N, 7.00.

1,2,7-Trimethyl-6-(4-chlorophenyl)-1,6-dihydropyrrolo[2,3-*e*]indole 9.

This compound was obtained as a colorless solid (hexane) (27%), mp 130-131°; ¹H nmr (deuteriochloroform): δ 2.33 (d, 3H, J = 0.98 Hz, CH₃C7), 2.44 (d, 3H, J = 0.88 Hz, CH₃C2), 3.97 (s, 3H, NCH₃), 6.27 (q, 1H, J = 0.98 Hz, H8), 6.71 (q, 1H, J = 0.88 Hz, H3), 6.78 (d, 1H, J = 9.0 Hz, H4), 7.21 (d, 1H, J = 9.0 Hz, H5), 7.50-7.32 (m, 4H, ArH); ms: m/z: 308 (M⁺, 100%).

Anal. Calcd. for C₁₉H₁₇N₂Cl: C, 73.90; H, 5.55; N, 9.07. Found: C, 73.93; H, 5.53; N, 9.10.

Synthesis of 2,7-Dimethyl-6-(4-*R*-phenyl)-6*H*-thieno[2,3-*e*]indoles 10-14. 2,7-Dimethyl-6-(4-methoxyphenyl)-6*H*-thieno[2,3-*e*]indole 10.

General Method (R = OMe).

A solution of 0.1 g of **26** (0.34 mmole) and 0.134 g of Lawesson's reagent (0.33 mmole) in benzene-dimethoxyethane (5-2.5 ml) was heated under reflux for 2 hours. After removal of the solvent *in vacuo*, the residual oil was chromatographed on silica gel column (flash chromatography). Elution with hexane/dichloromethane, 80/20, afforded **10** as a colorless solid (hexane) (0.069 g, 71%), mp 162-163°; ¹H nmr (deuteriochloroform): δ 2.29 (d, 3H, J = 0.96 Hz, CH₃C7), 2.59 (d, 3H, J = 1.0 Hz, CH₃C2), 3.87 (s, 3H, OCH₃), 6.47 (q, 1H, J = 0.96 Hz, H8), 6.95 (1H, q, J = 1.0 Hz, H3), 6.98 (d, 1H, J = 8.8 Hz, H4), 7.23-7.04 (m, 4H, ArH), 7.29 (d, 1H, J = 8.8 Hz, H5); ms: m/z: 307 (M⁺, 100%).

Anal. Calcd. for C₁₉H₁₇NOS: C, 74.23; H, 5.58; N, 4.56. Found: C, 74.31; H, 5.61; N, 4.70.

2,7-Dimethyl-6-(4-methylphenyl)-6*H*-thieno[2,3-*e*]indole 11.

This compound was obtained as a colorless solid (hexane) (31%), mp 145-147°; ¹H nmr (deuteriochloroform): δ 2.31 (d, 3H, J = 0.96 Hz, CH₃C7), 2.60 (d, 3H, J = 1.0 Hz, CH₃C2), 2.46 (s, 3H, CH₃-Ar), 6.49 (q, 1H, J = 0.96 Hz, H8), 6.99 (q, 1H, J = 1.0 Hz, H3), 7.03 (d, 1H, J = 8.8 Hz, H4), 7.23-7.32 (m, 4H, ArH), 7.25 (d, 1H, J = 8.8 Hz, H5); ms: m/z: 291 (M⁺, 100%).

Anal. Calcd. for C₁₉H₁₇NS: C, 78.31; H, 5.88; N, 4.81. Found: C, 78.40; H, 5.90; N, 4.85.

2,7-Dimethyl-6-phenyl-6*H*-thieno[2,3-*e*]indole 12.

This compound was obtained as a colorless solid (hexane) (76%), mp 150-151°; ¹H nmr (deuteriochloroform): δ 2.33 (d, 3H, J = 0.96 Hz, CH₃C7), 2.60 (d, 3H, J = 1.0 Hz, CH₃C2), 6.51 (q, 1H, J = 0.96 Hz, H8), 7.0 (q, 1H, J = 1.0 Hz, H3), 6.99 (d, 1H, J = 8.8 Hz, H4), 7.52-7.37 (m, 4H, ArH), 7.30 (d, 1H, J = 8.8 Hz, H5); ms: m/z: 277 (M⁺, 100%).

Anal. Calcd. for C₁₈H₁₅NS: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.99; H, 5.45; N, 4.98.

2,7-Dimethyl-6-(4-bromophenyl)-6*H*-thieno[2,3-*e*]indole 13.

This compound was obtained as a colorless solid (hexane) (37%), mp 138-140°; ¹H nmr (deuteriochloroform): δ 2.31 (d, 3H, J = 0.96 Hz, CH₃C7), 2.60 (d, 3H, J = 1.0 Hz, CH₃C2), 6.51 (q, 1H, J = 0.96 Hz, H8), 7.0 (q, 1H, J = 1.0 Hz, H3), 7.25 (d, 1H, J = 8.8 Hz, H4), 7.30-7.54 (m, 4H, ArH), 7.36 (d, 1H, J = 8.8 Hz, H5); ms: m/z: 355 (M⁺, 14%).

Anal. Calcd. for C₁₈H₁₄NSBr: C, 60.68; H, 3.96; N, 3.93. Found: C, 60.70; H, 3.97; N, 3.90.

2,7-Dimethyl-6-(4-chlorophenyl)-6*H*-thieno[2,3-*e*]indole 14.

This compound was obtained as a colorless solid (hexane) (86%), mp 135-137°; ¹H nmr (deuteriochloroform): δ 2.31 (d, 3H, J = 0.96 Hz, CH₃C7), 2.61 (d, 3H, J = 1.0 Hz, CH₃C2), 6.50 (q, 1H, J = 0.96 Hz, H8), 7.01 (q, 1H, J = 1.0 Hz, H3), 7.24 (d, 1H, J = 8.8 Hz, H4), 7.32-7.54 (m, 4H, ArH), 7.38 (d, 1H, J = 8.8 Hz, H5); ms: m/z: 311 (M⁺, 100%).

Anal. Calcd. for C₁₈H₁₄NSCl: C, 69.33; H, 4.53; N, 4.49. Found: C, 69.35; H, 4.54; N, 4.52.

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REFERENCES AND NOTES

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- [2] Contribution No. 1641 from Instituto de Química, UNAM.
- [3] Y. Enomoto, Y. Furutani, H. Naganawa, M. Hamada, T. Takeuchi and H. Umezawa, *Agric. Biol. Chem.*, **42**, 1331, (1978); H. Nakamura, Y. Enomoto, T. Takeuchi, H. Umezawa and Y. Itaka, *Agric. Biol. Chem.*, **43**, 1337 (1978).
- [4] L. J. Hanka, A. Dietz, S. A. Gerpheide, S. L. Kuentzel and D. G. Martin, *J. Antibiot.*, **31**, 1211 (1978); D. G. Martin, C. G. Chidester, D. J. Duchamp and S. A. Miszak, *J. Antibiot.*, **33**, 902 (1980); D. G. Martin, C. Biles, S. A. Gerpheides, L. J. Hanka, W. C. Krueger, J. P. McGovern, S. A. Miszak, G. L. Neil, J. C. Stewart, and J. Visser, *J. Antibiot.*, **34**, 1119 (1981).
- [5] R. J. Sundberg, G. S. Hamilton and J. P. Laurino, *J. Org. Chem.*, **53**, 976 (1988) and references cited therein; J. Ezquerro, C. Pedregal, C. Lamas, J. Barluenga, M. Pérez, M. A. García and J. M. González, *J. Org. Chem.*, **61**, 5804 (1996); J. E. Macor, J. T. Forman,

R. J. Post and K. Ryan, *Tetrahedron Letters*, **38**, 1673 (1997).

[6] Sh. A. Samsoniya, N. L. Targamadze, L. G. Tret'yakova, T. K. Efimova, K. F. Turchin, I. M. Gverdtsiteli and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, 938 (1997); D. O. Kadzhrishvili, S. V. Dolidze, Sh. A. Samsoniya and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, 346 (1990); J. Ezquerro, C. Pedregal, C. Lamas, J. Barluenga, M. Pérez, M.A. García, and J. M. González, *J. Org. Chem.*, **61**, 5804 (1996).

[7] V. I. Shvedov, L. B. Altukhova, A. N. Grinev, A. I. Ermakov and Yu. N. Sheinker, *V sb., Khimiya i Farmakol. Indol'n. Soedinenii*, 57-8 (1975); *Chem. Abstr.*, **84**, 121749u (1976).

[8] R. Martínez, G. López and G. Avila, *J. Heterocyclic Chem.*, **32**, 491 (1995); R. Martínez, G. Avila and E. Reyes, *Synth. Commun.*,

25, 1071 (1995); R. Martínez, G. Espinosa and M. Brito, *J. Chem. Crystallogr.*, **25**, 201 (1995).

[9] H. J. Schaeffer and R. Vince, *J. Org. Chem.*, **27**, 4502 (1962).

[10] H. Stetter and R. Lauterbach, *Liebigs Ann. Chem.*, **652**, 40 (1962).

[11] H. Stetter and R. Lauterbach, *Liebigs Ann. Chem.*, **655**, 20 (1962).

[12] J. Tsuji, I. Shimizu and K. Yamamoto, *Tetrahedron Letters*, 2975 (1976).

[13] T. Nishio, N. Okuda and C. Kashima, *J. Heterocyclic Chem.*, **25**, 1437 (1988).