NEW SYNTHETIC APPLICATIONS OF
PHENYLACETYLPHENYLACETIC ACIDS: A DIVERGENT
SYNTHESIS OF BENZO[a]CARBAZoles AND
INDOLO[2,1-α]ISOQUINOLINES

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Abstract - Here we describe a common access to benzo[a]carbazoles and
indolo[2,1-α]isoquinolines from 2-(2’-nitrophenylacetyl)phenylacetic acids.

The antineoplastic activity of a number of isoquinolines, including ellipticines,1 benzophenanthridines2
and berberines,3 is attributed to their ring systems containing an embedded planar 2-phenylnaphthalene-
like structure. Indoles that are related to these isoquinolines and retain their embedded planar
2-phenylnaphthalene-like structure likewise have antineoplastic potential or known antineoplastic
activity. Indolonaphthoquinones are related in this way to ellipticines, benzo[a]carbazoles (1)4 to
benzophenanthridines,2 and dibenzopyrrocolines (2)5 to berberines.3 Benzo[a]carbazoles in particular,
besides having industrial applications as colorants,6 are known carcinogens with anti-arrhythmic,
antimicrobial and antitumoral activity,7 and are also related to indolo[2,3-α]quinolizine alkaloids.8
Dibenzopyrrocolines have hitherto been studied mainly in the context of theories of the biogenesis of
isoquinoline alkaloids.9

In previous work,10 we developed an easy, efficient total synthesis of indolonaphthoquinones from
phenylacetylphenylacetic acids. Phenylacetylphenylacetic acids have in fact proved to be of great value
for the synthesis of a variety of isoquinolines and related compounds11: they have been used in our
laboratory for the first total syntheses of 4,5-dioxoaporphines,11a 5-oxoaporphines,11b
dibenzochromanones,11c dibenzocoumaranones11d and naphthoisouquinolines11e, and in novel total
syntheses of aporphines,11b phenanthrene alkaloids11c and aristolactams11d as well as
indolonaphthoquinones;10 and by other research groups to prepare pavines,12
dibenzopyrrocolines,13
berberines14 and benzophenanthridines.15

As a continuation of our work on the preparation of indoles from phenylacetylphenylacetic acids we have
developed an easy, efficient common route to benzo[a]carbazoles and dibenzopyrrocolines.

Retrosynthetic analysis (Scheme 1) suggested that both benzo[a]carbazoles and dibenzopyrrocolines
might be obtainable from indoles (3) (by linking the two-carbon chain to indole-ring positions 3 and 1
respectively), and that indoles (3) should be readily derivable from nitrophenylacetylphenylacetic acids (4).

Nitro keto acid (4a)\(^{16}\) was indeed easily converted into indole (3a) in two steps (Scheme 2): treatment with methanol containing a few drops of concentrated sulfuric acid afforded nitro keto ester (5a) and catalytic hydrogenation of 5a gave 3a directly in 71% yield, probably by condensation of the carbonyl and amino groups of the intermediate (6a). The identity of 3a was deduced from spectroscopic and analytical data, \(^1\)H NMR spectrum showing singlets for five aromatic protons at 6.46, 6.83, 6.95, 7.04 and 7.08 ppm, and a low field singlet for N-H at 9.89 ppm.

Stirring of a solution of 3a in dichloromethane with traces of \(p\)-toluenesulfonic acid at room temperature afforded the new dibenzopyrrocoline derivative (7a) in 78% yield; the structure of 7a was established.
from its spectroscopic and analytical data, its IR spectrum showing the amide carbonyl at 1640 cm$^{-1}$ and its $^1$H NMR spectrum singlets for five aromatic protons at 6.43, 6.50, 6.78, 6.95 and 7.96 ppm. Reduction of $3\text{a}$ with NaBH$_4$ in methanol$^{17}$ gave the unstable alcohol ($8\text{a}$), which was directly transformed into the tetracyclic indole ($1\text{a}$) by acidification of a solution of $8\text{a}$ in dichloromethane with $p$-toluenesulfonic acid and further stirring at room temperature for 12 hours [yield 60%; mp 192-194 °C (methanol)]. The structure of $1\text{a}$ was firmly established from its spectroscopic and analytical data, its $^1$H NMR spectrum showing five singlets at 6.92, 6.99, 7.20, 7.25 and 7.47 ppm from its uncoupled aromatic protons and the N-H, and doublets at 6.62 and 7.92 ppm ($J=7.3$ Hz) for the two coupled aromatic protons. It seems like that transformation of $8\text{a}$ into $1\text{a}$ involved intramolecular elimination of water followed by oxidation of the resulting dehydrobenzo[a]carbazole ($9\text{a}$).

Compounds ($7\text{b}$) and ($1\text{b}$) were obtained similarly from nitro keto ester ($5\text{b}$), which was prepared by Friedel-Crafts acylation of methyl-3,4-dimethoxyphenylacetate with 2-nitrophenylacetyl chloride.

Compounds ($7\text{a}$) and ($7\text{b}$) were easily transformed into the corresponding dibenzopyrrocolines ($11\text{a}$) and ($11\text{b}$), respectively, so completing a new total synthesis of the latter. Refluxing enamide ($7\text{a}$) with zinc powder and acetic acid for 1 hour afforded the unstable dibenzopyrrocoline ($2\text{a}$) quantitatively via the tetracyclic lactam ($10\text{a}$) (the involvement of $10\text{a}$ is proved by the fact that gave a mixture of compounds ($10\text{a}$) and ($2\text{a}$), and further reaction of isolated $10\text{a}$ with zinc powder as above afforded $2\text{a}$ quantitatively); and methyl iodide treatment of $2\text{a}$, (which because of its instability was not isolated) gave O-methylcryptaustoline iodide ($11\text{a}$).$^{13a}$ Compound ($11\text{b}$) was similarly obtained from $7\text{b}$ via $10\text{b}$ and $2\text{b}$.

![Scheme 3](image)

**Scheme 3**: i) Zn, HCl, AcOH/H$_2$O. ii) MeI, MeOH.

To sum up, we have developed new total syntheses of benzo[a]carbazoles and dibenzopyrrocolines that share the steps leading from phenylacetylphenylacetic acids ($4$) to the key indole intermediates ($3$). The new route to benzo[a]carbazoles, which is more convenient than previous ones,$^{18,19}$ is now being applied to the synthesis of indolo[2,3-$a$]quinolizine alkaloids,$^{20}$ and we believe that it will no prove difficult to
extend it to another class of biologically interesting compounds, indeneindoles (indeneindoles have recently been named as possible inhibitors of pathogenic radical chain reactions, some of the member of the family being among the most potent antioxidants known).21

EXPERIMENTAL

Melting points were determined on a Kofler Thermogerate apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 1420 spectrophotometer; NMR spectra were acquired in a Bruker WM-250 apparatus using deuterochloroform as solvent and tetramethylsilane as internal standard (except where indicated), and MS were obtained on a Kratos MS 50 TC mass spectrometer. TLC was performed on Merck GF-254 Type 60 silica gel plates using dichloromethane-methanol mixtures as eluent and ultraviolet light or iodine vapour to visualize the TLC spots. Column chromatography was carried out using Merck type 9385 silica gel. Solvents were purified as per ref. 22 and dried with anhydrous sodium sulfate. Compound (5a) was prepared as per ref. 16.

Methyl 2-(2'-nitro-4',5'-dimethoxyphenylacetyl)-4,5-dimethoxyphenylacetate (5a)

A solution of 4a16 (3 g, 7.16 mmol) in methanol (100 mL) was refluxed for 2 h after addition of three drops of concentrated sulfuric acid. The methanol was then evaporated in vacuo and the residue suspended in water (200 mL) and extracted with dichloromethane (3x50 mL). The organic extract was dried, filtered and concentrated to dryness in vacuo to give nitro keto ester (5a) quantitatively. mp 118-120 °C (methanol). IR (NaCl, ν/cm⁻¹): 1730 (C=O) and 1680 (C=O). ¹H NMR (δ, ppm): 3.64 (s, 3H, -OCH₃), 3.87 (s, 2H, -CH₂-), 3.95 (s, 3H, -OCH₃), 3.97 (s, 9H, 3x-OCH₃), 4.64 (s, 2H, -CH₂-), 6.74 (s, 1H, Ar-H), 6.76 (s, 1H, Ar-H), 7.49 (s, 1H, Ar-H) and 7.77 (s, 1H, Ar-H). MS (EI, m/z, %): 433 (M +, 2), 237 (32), 209 (100) and 179 (12).

2-[2'-Methylcarboxyethyl-4',5'-dimethoxyphenyl]-5,6-dimethoxyindole (3a)

A mixture of keto ester (5a) (0.4 g, 0.92 mmol), methanol (240 mL), isopropanol (40 mL) and 10% Pd/C (40 mg) was vigorously stirred under hydrogen (P=1.2 atm) for 1 h. The suspension was then filtered through celite and the filtrate was condensed to give an oil which on purification by column chromatography (99:1 dichloromethane/methanol) yielded 0.25 g of indole (3a) (71%). mp 124-126 °C (methanol). IR (NaCl, ν/cm⁻¹): 3320 (-NH) and 1740 (C=O). ¹H NMR (δ, ppm): 3.69 (s, 2H, -CH₂-), 3.81 (s, 3H, -OCH₃), 3.90 (s, 3H, -OCH₃), 3.92 (s, 3H, -OCH₃), 3.93 (s, 3H, -OCH₃), 3.94 (s, 3H, -OCH₃), 6.46 (s, 1H, Ar-H), 6.83 (s, 1H, Ar-H), 6.95 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.08 (s, 1H,
Ar-H) and 9.89 (s, 1H, -N-H). $^{13}$C NMR (δ, ppm): 38.45 (-CH$_2$-), 52.21 (-OCH$_3$), 55.66 (-OCH$_3$), 55.80 (-OCH$_3$), 55.91 (-OCH$_3$), 56.15 (-OCH$_3$), 94.62 (Ar-H), 101.41 (Ar-H), 102.13 (Ar-H), 113.30 (Ar-H), 113.48 (Ar-H), 121.51 (C), 123.64 (C), 126.66 (C), 130.92 (C), 136.08 (C), 145.14 (C), 146.94 (C), 148.18 (C), 148.60 (C), 174.08 (C=O). MS (EI, m/z, %): 385 (M+, 100), 370 (26), 338 (10), 282 (10) and 266 (9). HRMS calculated for C$_{21}$H$_{23}$NO$_6$, 285.15254; found, 285.15271.

2,3,8,9-Tetramethoxy-11H-benzo[a]carbazole (1a)

Sodium borohydride (150 mg, 3.96 mmol) was added in small portions over 15 min to a stirred solution of indole (3a) (50 mg, 0.13 mmol) in 10 mL of methanol. Then 50 mL of water were added and the mixture was extracted with chloroform (2x25 mL); saturated sodium bicarbonate solution (10 mL) was added to prevent emulsion. The organic extract was then acidified with p-toluenesulfonic acid (50 mg, 0.26 mmol) and stirred at rt for 3.5 h and added to water (50 mL) before extraction with chloroform (2x10 mL). The chloroform extract was dried and condensed to dryness in vacuo, and the residue was purified by flash column chromatography (dichloromethane) to give compound (1a) (26.3 mg, 60%). mp 192-194 °C (methanol). IR (NaCl, $\nu$/cm$^{-1}$): 3367 (-NH). $^1$H NMR (δ, ppm): 3.99 (s, 6H, 2x-OCH$_3$), 4.02 (s, 3H, -OCH$_3$), 4.05 (s, 3H, -OCH$_3$), 6.62 (d, J=7.3 Hz, 1H, Ar-H), 6.92, 6.99, 7.20, 7.25, 7.47 (5x s, 5H, 4xAr-H and N-H), 7.92 (d, J=7.3 Hz, 1H, Ar-H). $^{13}$C NMR (δ, ppm, CDCl$_3$/CD$_3$OD): 55.92 (-OCH$_3$), 56.05 (-OCH$_3$), 56.24 (-OCH$_3$), 56.48 (-OCH$_3$), 93.37 (Ar-H), 101.63 (Ar-H), 104.79 (Ar-H), 107.94 (Ar-H), 108.37 (Ar-H), 120.22 (C), 120.52 (C), 120.56 (Ar-H), 122.33 (C), 122.52 (C), 125.74 (C), 133.81 (C), 146.10 (C), 147.21 (C), 149.23 (2xC). MS (EI, m/z, %): 337 (M+, 100). Anal. Calcd for C$_{20}$H$_{19}$NO$_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.25; H, 5.82; N, 4.02.

Methyl 2-(2’-nitrophenylacetyl)-4,5-dimethoxyphenylacetate (5b)

A mixture of commercial 2-nitrophenylacetic acid (3.36 g, 18.56 mmol) and thionyl chloride (10 mL, 127 mmol) was refluxed in a dry atmosphere (calcium chloride tube) for 1 h. The excess thionyl chloride was evaporated off in vacuo and the residue dissolved in dry nitrobenzene (2 mL). This solution was added dropwise to a stirred suspension of aluminium trichloride (3.8 g, 28.5 mmol) in dry nitrobenzene (1.5 mL), and to this mixture, cooled to 4 °C in an ice/water bath, a solution of methyl 3,4-dimethoxyphenylacetate (3 g, 14.29 mmol) in dry nitrobenzene (1.5 mL) was added dropwise over 15 min. The mixture was stirred for 2.5 h at rt and then added to 100 mL of a 1:1 (w/w) mixture of ice and concentrated hydrochloric acid. The nitrobenzene was removed by steam distillation, and the residue extracted with dichloromethane (3x50 mL). The organic extract was washed with saturated sodium bicarbonate solution followed by water, dried and concentrated in vacuo to give an oil which on crystallization from methanol afforded 2.7 g (51%) of 5b as white crystals. mp 118-119 °C. IR (KBr, $\nu$/cm$^{-1}$): 1733 (C=O), 1677 (C=O). $^1$H NMR (δ, ppm): 3.62 (s, 3H, -OCH$_3$), 3.84 (s, 2H, -CH$_2$-), 3.94 (s, 3H, -OCH$_3$), 3.96 (s, 3H, -OCH$_3$), 4.66 (s, 2H, -CH$_2$-), 6.75 (s, 1H, Ar-H), 7.33-7.63 (m, 4H, 4xAr-H), 8.12 (dd, J=8.19 and 1.16 Hz, 1H, Ar-H). $^{13}$C NMR (δ, ppm): 39.70 (-CH$_2$-), 45.80 (-CH$_2$-), 51.82
(-OCH₃), 56.00 (-OCH₃), 56.30 (-OCH₃), 112.86 (Ar-H), 115.45 (Ar-H), 125.27 (Ar-H), 128.34 (Ar-H), 129.02 (C), 129.45 (C), 130.93 (C), 133.50 (Ar-H), 133.80 (Ar-H), 147.67 (C), 152.06 (C), 172.14 (C=O), 196.78 (C=O). MS (EI, m/z, %): 373 (M⁺, 5), 237 (22), 209 (100).

2-[(2'-Methylcarboxyethyl-4',5'-dimethoxy)phenyl]indole (3b)

Compound (3b) was obtained in 70% yield from 5b using the same procedure as for 3a. mp 148-149 °C (methanol). IR (NaCl, μ/cm⁻¹): 3352 (-NH) and 1733 (C=O). ¹H NMR (δ, ppm): 3.69 (s, 2H, -CH₂-), 3.82 (s, 3H, -OCH₃), 3.91 (s, 3H, -OCH₃), 3.93 (s, 3H, -OCH₃), 6.58 (s, 1H, Ar-H), 6.85 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 7.17 (m, 2H, 2xAr-H), 7.45 (d, J=7.7 Hz, 1H, Ar-H), 7.65 (d, J=7.5 Hz, 1H, Ar-H) and 9.94 (s, 1H, -N-H). ¹³C NMR (δ, ppm): 38.73 (-CH₂-), 52.52 (-OCH₃), 56.03 (-OCH₃), 56.10 (-OCH₃), 101.85 (Ar-H), 111.16 (Ar-H), 113.61 (Ar-H), 113.89 (Ar-H), 119.93 (Ar-H), 120.31 (Ar-H), 121.85 (Ar-H), 124.10 (C), 126.73 (C), 128.80 (C), 136.55 (C), 137.79 (C), 148.53 (C), 149.23 (C), 174.38 (C=O). MS (EI, m/z, %): 325 (M⁺, 100). HRMS calculated for C₁₉H₁₉NO₄, 325.13141; found, 325.13154.

2,3-Dimethoxy-11H-benzo[a]carbazole (1b)

Compound (1b) was prepared in 50% yield from indole (3b) by the same procedure as was used to prepare 1a. mp 180-181 °C (methanol). IR (NaCl, μ/cm⁻¹): 3354 (-NH). ¹H NMR (δ, ppm): 4.00 (s, 3H, -OCH₃), 4.06 (s, 3H, -OCH₃), 6.65 (d, J=7.4 Hz, 1H, Ar-H), 7.01 (s, 1H), 7.03 (s, 1H), 7.28-7.37 (m, 2H), 7.54 (s, 1H), 7.80 (m, 2H), 6xAr-H and N-H), 8.03 (d, J=7.4 Hz, 1H, Ar-H). ¹³C NMR (δ, ppm, Cl₃CD/CD₃OD): 55.99 (-OCH₃), 56.12 (-OCH₃), 90.66 (Ar-H), 105.26 (Ar-H), 107.24 (C), 108.29 (Ar-H), 109.64 (Ar-H), 119.87 (C), 120.16 (Ar-H), 120.34 (Ar-H), 120.85 (Ar-H), 122.27 (Ar-H), 123.53 (C), 129.10 (2xC), 131.24 (C), 149.59 (C), 149.87 (C). MS (EI, m/z, %): 277 (M⁺, 100). Anal. Calcd for C₁₈H₁₅NO₂: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.15; H, 5.27; N, 4.96.

2,3,9,10-Tetramethoxy-5H-indolo[2,1-a]isoquinolin-6-one (7a)

p-Toluenesulfonic acid (50 mg, 0.26 mmol) was added to a solution of indole (3a) (0.48 g, 1.25 mmol) in dichloromethane (50 mL), and the mixture was stirred at rt for 3.5 h. After that the dichloromethane was evaporated in vacuo, the residue was suspended in water (75 mL), and the suspension was extracted with dichloromethane (3x25 mL). The organic extract was washed with aqueous sodium hydroxide solution (10%, 60 mL) followed by water (60 mL), dried, and filtered. Removal of the solvent in vacuo gave a residue that was subjected to flash column chromatography (eluent: 98:2 dichloromethane/methanol) to afford 0.34 g (78%) of 2,3,9,10-tetramethoxy-5H-indolo[2,1-a]isoquinolin-6-one (7a). mp 176-178 °C (methanol). IR (NaCl, μ/cm⁻¹): 1640 (C=O). ¹H NMR (δ, ppm): 3.73 (s, 2H, -CH₂-), 3.81 (s, 3H, -OCH₃), 3.85 (s, 3H, -OCH₃), 3.89 (s, 3H, -OCH₃), 3.92 (s, 3H, -OCH₃), 6.43 (s, 1H, Ar-H), 6.50 (s, 1H, Ar-H), 6.78 (s, 1H, Ar-H), 6.95 (s, 1H, Ar-H) and 7.96 (s, 1H, Ar-H). ¹³C NMR (δ, ppm): 36.98 (-CH₂-),
55.89 (-OCH₃), 55.97 (2x-OCH₃), 56.16 (-OCH₃), 100.08 (Ar-H), 101.44 (Ar-H), 101.66 (Ar-H), 105.35 (Ar-H), 109.69 (Ar-H), 117.94 (C), 121.95 (C), 123.41 (C), 129.07 (C), 135.33 (C), 147.37 (C), 147.83 (C), 148.64 (C), 149.34 (C), 166.98 (C=O). MS (EI, m/z, %): 353 (M⁺, 100).

**N-Methyl-2,3,9,10-tetramethoxy-5,6,12,12a-tetrahydroindolo[2,1-a]isoquinolinium iodide (11a)**

To a mixture of compound (7a) (80 mg, 0.23 mmol) in 2:1 acetic acid/water (9 mL) were added concentrated hydrochloric acid (6 mL) and zinc powder (3 g, 45.9 mmol), and the resulting suspension was refluxed for 1.5 h. The mixture was then filtered through celite, basified with commercial 33% NH₃ solution, and extracted with ether (4x20 mL). The organic extract was dried, filtered, and condensed to dryness in vacuo to give a very unstable white solid identified as 2a, which was dissolved in methanol (5 mL) and allowed to react with excess MeI at rt for 48 h. The liquids were removed and the resulting solid (11a) was crystallized from methanol (60 mg, 55%). mp 243-244 °C (ethanol). ¹H NMR (δ, ppm, CDCl₃/CD₃OD): 2.93-3.56 (m, 2H, -CH₂-), 3.58 (m, 2H, -CH₂-), 3.66 (s, 3H, N-CH₃), 3.93 (s, 3H, -OCH₃), 3.95 (s, 3H, -OCH₃), 3.97 (s, 3H, -OCH₃), 4.03 (s, 3H, -OCH₃), 4.41 (m, 1H, -CH₂-), 5.39 (t, J=8.1 Hz, 1H, -CH-), 6.93 (s, 1H, Ar-H), 6.99 (s, 1H, Ar-H), 7.14 (s, 1H, Ar-H), 7.82 (s, 1H, Ar-H). ¹³C NMR (δ, ppm, CDCl₃/CD₃OD): 24.27 (-CH₂-), 37.17 (-CH₂-), 50.81 (N-CH₃), 56.25 (-OCH₃), 56.62 (2x-OCH₃), 58.19 (-OCH₃), 58.94 (-CH₂-), 75.33 (-CH-), 102.02 (Ar-H), 107.90 (Ar-H), 109.48 (Ar-H), 111.30 (Ar-H), 120.91 (2xC), 122.90 (C), 139.06 (C), 149.45 (C), 149.82 (C), 151.06 (C), 151.82 (C). MS (EI, m/z, %): 341 (M⁺-142, 95), 326 (100). Anal. Calcd for C₂₁H₂₆NO₄I: C, 52.18; H, 5.42; N, 2.90. Found: C, 52.02; H, 5.71; N, 2.98.

Shorter reaction times than that reported above for reduction of 7a gave mixtures of compounds (10) and (2a); although both these compounds are unstable, they were separated by flash column chromatography (99:1 dichloromethane/methanol) and the more abundant, more stable 10a was transformed quantitatively into 2a when treated with zinc under the above mentioned conditions for reduction of 7a.

**Compound (10a).** ¹H NMR (δ, ppm): 3.36-3.84 (m, 4H, 2x-CH₂-), 3.87 (s, 3H, -OCH₃), 3.90 (s, 3H, -OCH₃), 3.92 (s, 3H, -OCH₃), 3.93 (s, 3H, -OCH₃), 5.40 (dt, J=11.0 Hz and J=3.0 Hz, 1H, -CH-), 6.73 (s, 1H, Ar-H), 6.75 (s, 1H, Ar-H), 6.82 (s, 1H, Ar-H), 7.96 (s, 1H, Ar-H).

**Compound (2a).** ¹H NMR (δ, ppm): 2.50 (d, J=15.7 Hz, 1H, -CH-), 2.96-3.11 (m, 2H, -CH₂-), 3.34-3.54 (m, 2H, -CH₂-), 3.77 (s, 3H, -OCH₃), 3.81 (s, 3H, -OCH₃), 3.87 (s, 3H, -OCH₃), 3.88 (s, 3H, -OCH₃), 3.91-3.96 (m, 1H, -CH-), 4.86 (d, J=7.4 Hz, 1H, -CH-), 6.37 (s, 1H, Ar-H), 6.49 (s, 1H, Ar-H), 6.66 (s, 1H, Ar-H), 6.72 (s, 1H, Ar-H).

**2,3-Dimethoxy-5H-indolo[2,1-a]isoquinolin-6-one (7b)**

When compound (3b) (61 mg, 0.17 mmol) was subjected to the above procedure for the preparation of 7a, 5H-indolo[2,1-a]isoquinolin-6-one (7b) was obtained in 74% yield. mp 180-181 °C (methanol). IR (NaCl, ν/cm⁻¹): 1701 (C=O). ¹H NMR (δ, ppm): 3.89 (s, 2H, -CH₂-), 3.93 (s, 3H, -OCH₃), 3.95 (s, 3H,
N-Methyl-2,3-dimethoxy-5,6,12,12a-tetrahydroindolo[2,1-a]isoquinolinium iodide (11b)

Compound (11b) was obtained in 30% yield from 7b using the same procedure as for the above preparation of its analogue (11a). mp 215-216 °C (ethanol). \(^1^H\) NMR (δ, ppm): 2.95 (d, J=18.2 Hz, 1H, -CH\(_2\)-), 3.2 (m, 2H, -CH\(_2\)-), 3.62 (s, 3H, N-CH\(_3\)), 3.77 (s, 3H, -OCH\(_3\)), 3.81 (s, 3H, -OCH\(_3\)), 3.97 (dd, J=16.15 and J=7.5 Hz, 1H, -CH\(_2\)-), 4.15 (dt, J=12.76 Hz, and J=4.2 Hz, 1H, -CH\(_2\)-), 5.34 (t, J=8.5 Hz, 1H, -CH\(_2\)-), 6.64 (s, 1H, Ar-H), 6.81 (s, 1H, Ar-H), 7.45 (m, 3H, 3xAr-H), 7.88 (m, 1H, Ar-H). \(^1^3^C\) NMR (δ, ppm): 24.08 (-CH\(_2\)-), 36.82 (-CH\(_2\)-), 49.89 (-CH-), 55.84 (-OCH\(_3\)), 56.22 (-OCH\(_3\)), 58.63 (-CH\(_2\)-), 74.29 (N-CH\(_3\)), 109.37 (Ar-H), 110.38 (Ar-H), 117.86 (Ar-H), 120.29 (C), 120.65 (C), 126.94 (Ar-H), 129.91 (Ar-H), 131.47 (Ar-H), 131.90 (C), 146.47 (C), 149.34 (C), 149.64 (C). MS (EI, m/z, %): 296 (M\(^+\)-127, 0.07), 281 (M\(^+\)-142, 54.9), 280 (M\(^+\)-143, 100). Anal. Calcd for C\(_{19}\)H\(_{22}\)NO\(_2\)I: C, 53.91; H, 5.24; N, 3.31. Found: C, 54.09; H, 5.05; N, 3.63.

ACKNOWLEDGEMENTS

We thank the DGICYT and the Xunta de Galicia for financial support.

REFERENCES


