Pergamon

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Tetrahedron Letters 44 (2003) 7337–7340

TETRAHEDRON LETTERS

Photochemistry of stilbenyl-pyrroles: a new approach to indole and isoindole derivatives

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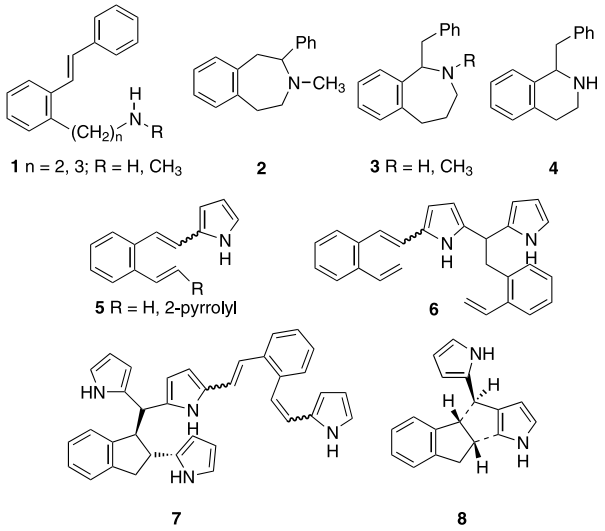
Received 16 May 2003; revised 20 July 2003; accepted 31 July 2003

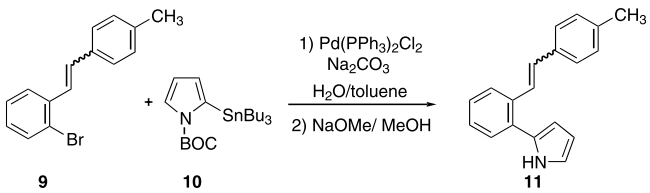
Abstract—A new 2-{2-[2-(4-methylphenyl)ethenyl]phenyl}pyrrole (**11**) was prepared and transformed by a photochemical reaction furnishing two cyclised products 4,5-dihydro-4-(*p*-methylphenyl)benzo[*g*]indole (**12**) and 4*H*-4-(*p*-methylbenzyl)pyrrolo[2,1-*a*]isoindole (**13**), and a reduction product, 2-{2-[2-(4-methylphenyl)ethyl]phenyl}pyrrole (**14**).

Lewis and co-workers have reported an efficient photochemical ring closure of primary and secondary *o*-alkylaminostilbenes (**1**).[1] By irradiation of a secondary amine, after an electron transfer and a proton transfer, two biradicals are formed depending on the alkyl chain length. Radical recombination furnished benzazepine derivatives (**2**, or **3** R = CH_3, respectively). Primary amines cannot react under direct irradiation due to their higher oxidation potential. Therefore, their photochemical conversion was achieved by irradiation in the presence of an external oxidising agent, dicyanobenzene. Photochemical reaction gave the benzazepine derivative **3** (R = H) or the tetrahydroisoquinoline derivative **4**.



In our previous papers we reported the photochemical behaviour of styrylpyrroles **5**.[2] By irradiation of the styrylpyrrole **5**, (R = H), a regiospecific intermolecular addition of the pyrrole moiety to the double bond gave a mixture of dimers **6**. By introduction of the second pyrrolyl ring to the hexatriene system **5**, (R = 2-pyrrolyl) the photochemical reaction gave an indane intermediate that was further attacked intermolecularly by the pyrrole moiety giving adducts **7** (40%) or intramolecularly giving traces of pentalene product **8**.

In this paper we demonstrate the synthesis and photochemical transformation of a new pyrrole derivative, the stilbenylpyrrole **11**.[3] The stilbenylpyrrole **11** was prepared using a Stille reaction (Scheme 1) from 2-bromo-4′-methylstilbene (**9**)[4] and *N*-Boc pyrrolylstannane **10** according to a modified[5] procedure. The new *N*-Boc pyrrolyl stannane **10** was prepared from *N*-Boc



Scheme 1.

Keywords: indoles; photochemistry; pyrroles; stilbenes.

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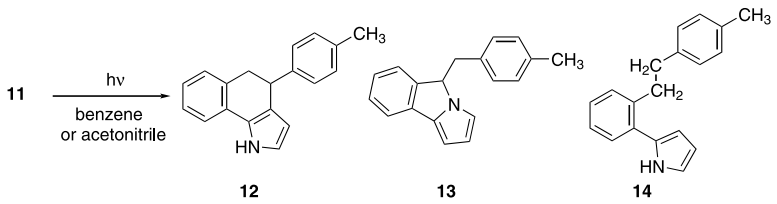
0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01869-0



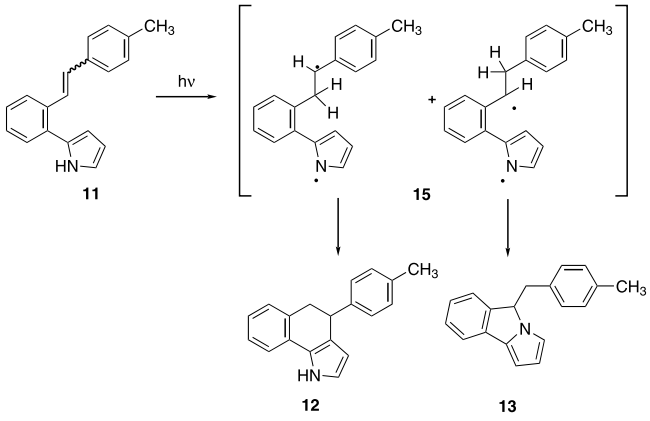
Scheme 2.

pyrrole[6] that was lithiated[7] with *n*-BuLi and 2,2,6,6-tetramethylpiperidine and subsequently quenched by Bu_3SnCl. The reaction mixture of **9** and **10** (Scheme 1) was refluxed for 3 days in a water/toluene solvent system in the presence of sodium carbonate and palladium as a catalyst. *N*-Boc stilbenylpyrrole was obtained in 98% yield and further treatment with sodium methoxide in methanol under reflux for one hour gave deprotected **11** in an 82% yield.

Irradiation of the stilbenylpyrrole **11** was performed in benzene or acetonitrile. A 1.5×10^{-3} M solution of **11** was purged with argon and irradiated for 30 minutes at 300 nm. Chromatographic separation on silica gel using dichloromethane–petroleum ether as solvent furnished three products besides traces of unidentified compounds and a high-weight-material that remained on the column (Scheme 2). The dihydrobenzo[*g*]indole **12**[8] was isolated in 33% yield. In the aliphatic region of the ^{1}H NMR spectrum of **12** a typical ABX system with doublets of doublets at 4.10, 3.05 and 3.01 ppm undoubtedly signified addition to the stilbene double bond. In the aromatic region of the ^{1}H NMR spectrum, chemical shifts of the pyrrole protons were present at δ 7.21 (NH), 6.29 and 6.04 ppm. In the ^{13}C NMR spectrum, two pyrrole doublets were seen at 117.98 and 107.62 ppm, while in the aliphatic region a doublet at 39.75 and a triplet at 39.52 ppm were present. The six-membered ring closure was obvious from the MS data. Besides the basic M^+ signal at m/z 259, an additional signal at m/z 168 (80%) corresponding to cleavage of the tolyl group undoubtedly indicated formation of a dihydroindole structure.

The pyrrolo[2,1-*a*]isoindole (**13**),[8] isolated in a 5% yield showed three doublets of doublets in the aliphatic region of the ^{1}H NMR spectrum at δ 4.86, 2.96 and 2.79 ppm, while three pyrrole protons appeared as a very narrow multiplet at 6.53–6.57 ppm. In the ^{13}C NMR spectrum pyrrole doublets were seen at 115.59, 112.16 and 98.04 ppm. In the aliphatic region a doublet at 61.52 and a triplet at 40.71 indicated addition to the stilbene double bond. The five-membered ring closure was evident from the MS spectrum where besides M^+ at m/z 259, a base signal at m/z 154 was present, corresponding to the *p*-methylbenzyl cleavage.

The structure of the reduction product **14**[8] isolated in 10% yield, was assigned according to the appearance of two multiplets in the ^{1}H NMR spectrum at 2.93–3.05 and 2.70–2.78 ppm, two triplets in the ^{13}C NMR at 36.78 and 35.40 ppm and M^+ at m/z 261 in the MS spectrum, clearly indicating the addition of two hydrogens.



Scheme 3.

The intramolecular photoproducts were presumably obtained via photoinduced intramolecular electron transfer followed by an intramolecular pyrrole N–H proton transfer. Biradicals **15** (Scheme 3) formed in such a way, recombine giving compounds **12** or **13**, respectively.

Although there are many reports for the preparation of pyrrolo[2,1-*a*]isoindoles[9] and benzo[*g*]indoles[10] we have demonstrated here a new convenient photochemical method for the preparation of pyrrolo-fused heterocycles. This is also the first example of an intramolecular pyrrole addition to a stilbene double bond.[11]

Acknowledgements

This work was supported by grants from the Ministry of Science and Technology of the Republic of Croatia (Grant Nos. 0125004 and 0098059).

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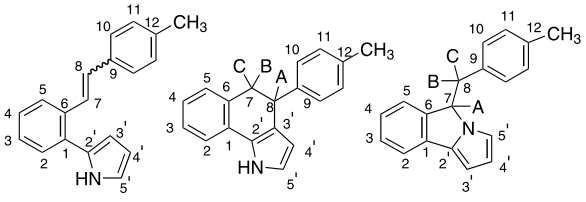
8. **Spectroscopic and analytical data**:



***cis*-2-{2-[2-(4-Methylphenyl)ethenyl]phenyl}pyrrole** (*cis*-**11**): colourless crystals; mp 72°C; UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 280.8 (17456), 297.1 (17955); IR (oil) ν_{max}/cm^{-1}: 3435 (NH); ^{1}H NMR (C_6D_6) δ/ppm (300 MHz): 8.04 (broad s, 1H, NH), 7.40 (d, 1H, J=7.2 Hz, H_5), 7.37 (d, 1H, J=7.5 Hz, H_2), 7.25 (d, 2H, J=8.1 Hz, H_{10}), 7.12 (dd, 1H, J=7.5 and J=7.8 Hz, H_4), 6.91 (dd, 1H, J=7.8 and J=7.2 Hz, H_3), 6.87 (d, 2H, J=8.1 Hz, H_{11}), 6.81 (m, 1H, $H_{5'}$), 6.67 (d, 1H, J=12.0 Hz, H_7), 6.51 (m, 1H, $H_{3'}$), 6.50 (d, 1H, J=12.0 Hz, H_8), 6.44 (dd, 1H, J=2.7 and J=3.3 Hz, $H_{4'}$), 2.07 (s, 3H, CH_3); ^{13}C NMR (C_6D_6) δ/ppm (75 MHz): 137.52 (s), 134.96 (s), 134.64 (s), 132.89 (s), 131.61 (s), 131.34 (d), 131.22 (d), 130.90 (d), 129.72 (d, 2C), 129.67 (d, 2C), 128.18 (d), 127.96 (d), 126.65 (d), 119.48 (d), 110.37 (d), 110.25 (d), 21.51 (q); Elemental analysis of the isomer mixture calcd for $C_{19}H_{17}N$ (M_r=259.34): C, 87.99; H, 6.61; N, 5.40. Found: C, 87.71; H, 6.86; N, 5.13%.

***trans* - 2 - {2 - [2 - (4 - Methylphenyl)ethenyl]phenyl}pyrrole** (*trans*-**11**): colourless crystals; mp 98°C; UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 276.9 (27693), 300.0 (sh, 21978); IR (KBr) ν_{max}/cm^{-1}: 3344 (NH); ^{1}H NMR (C_6D_6) δ/ppm (300 MHz): 7.58–7.62 (m, 1H, H_2–H_5), 7.57 (d, 1H, J=16.2 Hz, H_{et}), 7.44 (broad s, 1H, NH), 7.30 (d, 2H, J=8.1 Hz, H_{10}), 7.22–7.29 (m, 1H, H_2–H_5), 7.12–7.18 (m, 2H, H_2–H_5), 7.02 (d, J=16.2 Hz, 1H), 7.01 (d, 2H, J=8.1 Hz, H_{11}), 6.57 (m, 1H, $H_{3'}$), 6.45 (m, 1H, $H_{5'}$), 6.41 (dd, 1H, J=2.7 and J=3.0 Hz, $H_{4'}$), 2.15 (s, 3H, CH_3); ^{13}C NMR (C_6D_6) δ/ppm (75 MHz): 137.81 (s), 136.18 (s), 135.72 (s), 133.28 (s), 131.31 (s), 130.80 (d), 130.10 (d, 2C), 129.32 (d), 128.03 (d), 127.96 (d), 127.53 (d), 127.46 (d), 127.31 (d, 2C), 119.29 (d), 110.71 (d), 110.27 (d), 21.56 (q); MS m/z (%, fragment): 259 (100, M^+), 258 (80), 168 (92).

4,5-Dihydro-4-(4-methylphenyl)benzo[*g*]indole (**12**): colourless crystals; mp 114°C; ^{1}H NMR (C_6D_6) δ/ppm (500 MHz): 7.21 (broad s, 1H, NH), 7.19 (d, 2H, J=7.9 Hz, H_{10}), 7.14 (dd, 1H, J=7.5 and J=7.6 Hz, H_3 or H_4), 6.95–7.01 (m, 2H, H_3 or H_4 and H_5), 6.97 (d, 2H, J=7.9 Hz, H_{11}), 6.85 (d, 1H, J=7.5 Hz, H_2), 6.29 (dd, 1H, J=2.7 and J=2.5 Hz, $H_{5'}$), 6.04 (dd, 1H, J=2.4 and J=2.5 Hz, $H_{4'}$), 4.10 (dd, 1H, J=7.1 and J=9.9 Hz, H_A), 3.05 (dd, 1H, J=9.9 and J=15.1 Hz, H_B), 3.01 (dd, 1H, J=7.1 and J=15.1 Hz, H_C), 2.11 (s, 3H, CH_3); ^{13}C NMR (C_6D_6) δ/ppm (75 MHz): 142.10 (s, C-9), 134.94 (s, C-12), 133.82 (s, C-1 or 6), 128.91 (s, C-1 or 6), 128.55 (d, 2C-11), 128.04 (d), 127.52 (d, 2C-10), 127.12 (s, C-2′), 125.98 (d), 124.58 (d), 123.36 (s, C-3′), 117.98 (d, C-5′), 117.73 (d, C-2), 107.62 (d, C-4′), 39.75 (d, C-8), 39.52 (t, C-7), 20.22 (q); MS m/z (%, fragment): 259 (100, M^+), 168 (81, M^+–tolyl).

4*H*-4-(4-Methylbenzyl)pyrrolo[2,1-*a*]isoindole (**13**): colourless crystals; mp 78°C; ^{1}H NMR (C_6D_6) δ/ppm (500 MHz): 7.43 (d, 1H, J=7.5 Hz, H_2), 7.19 (dd, 1H, J=7.5 and J=7.5 Hz, H_3), 7.01 (dd, 1H, J=7.5 and J=7.5 Hz, H_4), 7.00 (d, 2H, J=7.8 Hz, H_{11}), 6.91 (d, 1H, J=7.5 Hz, H_5), 6.87 (d, 2H, J=7.8 Hz, H_{10}), 6.53–6.57 (m, 3H, $3H_{pyr}$), 4.86 (dd, 1H, J=5.9 and J=7.7 Hz, H_A), 2.96 (dd, 1H, J=5.9 and J=13.9 Hz, H_B), 2.79 (dd, 1H, J=7.7 and J=13.9 Hz, H_C), 2.18 (s, 3H, CH_3); ^{13}C NMR (C_6D_6) δ/ppm (75 MHz): 143.58 (s), 136.62 (s), 135.51 (s), 133.37 (s), 132.93 (s), 129.00 (d, 2C-10), 128.50 (d, 2C-11), 123.76 (d, C-4), 122.43 (d, C-5), 117.87 (d, C-2), 115.59 (d, C-5′), 112.16 (d, C-3′), 98.04 (d, C-4′), 61.52 (d, C-7), 40.71 (t, C-8), 20.22 (q), C-3 doublet is covered by the solvent; MS m/z (%, fragment): 259 (M^+, 67), 154 (100, M^+–*p*-methylbenzyl).

2-{2-[2-(4-Methylphenyl)ethyl]phenyl}pyrrole (**14**): colourless crystals; mp 38–40°C; ^{1}H NMR (C_6D_6) δ/ppm (300 MHz): 7.00–7.20 (m, 5H, NH, H_2–H_5), 6.96 (d, 2H, J=7.6 Hz, H_{10} or H_{11}), 6.96 (d, 2H, J=7.6 Hz, H_{10} or H_{11}), 6.38–6.43 (m, 2H, $H_{3'}$ and $H_{5'}$), 6.32–6.37 (m, 1H, $H_{4'}$), 2.93–3.05 (m, 2H, H_{et}), 2.70–2.78 (m, 2H, H_{et}), 2.09 (s, 3H, CH_3); ^{13}C NMR (C_6D_6) δ/ppm (75 MHz): 139.23 (s), 138.29 (s), 134.65 (s), 129.38 (d), 129.12 (d), 128.55 (d, 2C), 128.03 (d, 2C), 126.90 (d), 125.49 (d), 117.09 (d), 108.68 (d), 108.03 (d), 36.78 (t), 35.40 (t), 20.19 (q), two singlets are not seen due to small quantities; MS m/z (%, fragment): 261 (M^+, 54), 156 (100).

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