3(5)-(2-Hydroxyphenyl)-5(3)-styrylpyrazoles: Synthesis and Diels−Alder Transformations

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Reactions between cinnamoyl(2-hydroxybenzoyl)methanes and hydrazine hydrate in acetic acid gave 3-(2-hydroxyphenyl)-5-styrylpyrazoles, while the corresponding reactions with phenylhydrazine yielded 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles as the major products and 3-(2-hydroxyphenyl)-1-phenyl-5-styrylpyrazoles as by-products. The reaction mechanism of this transformation is discussed. The first cycloaddition reactions between *ortho*-benzoquinodimethane and either 3-(2-hydroxyphenyl)-5-styrylpyrazoles or 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles afforded 5-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]-3-(2-hydroxyphenyl)-pyrazoles or 3-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]-1-phenyl-5-(2-hydroxyphenyl)pyrazoles, respectively. These cycloadducts were converted into the corresponding naphthylpyrazoles by oxidation with DDQ in dry 1,4-dioxane. The structures of all new derivatives have been established by NMR spectroscopy.

Introduction

Pyrazoles are well known five-membered heterocyclic compounds possessing interesting biological properties. Because of their numerous applications in industry, agriculture and medicine, pyrazoles have long been attracting considerable attention, and various procedures for their syntheses have been developed.[1−5] As a result, a wide variety of pyrazole derivatives have been described in the literature. In the last decade, for instance, *C*- and/or *N*-(2-hydroxyphenyl)pyrazoles have been used as ultraviolet stabilisers,[6] as analytical reagents in the complexation of transition metal ions[7] and also as analgesic agents and as platelet aggregation inhibitors,[8] while other *N*-substituted pyrazoles are being used as nonsteroidal anti-inflammatory agents (lonazolac) and in the treatment of rheumatoid arthritis (pirazolac). Some well known drugs such as sildenafil (Viagra) and celecoxib (Celebrex) are also pyrazole derivatives.[4]

Knowledge of these useful applications of pyrazoles has shown that (2-hydroxyphenyl)pyrazoles and their *N*-substituted derivatives are important targets for preparation. Following our interest in the synthesis and molecular structure determination of some types of pyrazoles,[9] we have now devoted our attention to the synthesis of new 3(5)-(2-hydroxyphenyl)pyrazoles and some *N*-substituted derivatives. Some of these compounds were synthesised by treatment of cinnamoyl-(2-hydroxybenzoyl)methanes (or their enolic forms) with hydrazines, while others were obtained from Diels−Alder reactions of the former compounds with the highly reactive diene *ortho*-benzoquinodimethane. These reactions also allowed study of the reaction behaviour both of *N*-substituted or unsubstituted (2-hydroxyphenyl)styrylpyrazoles with these dienes and also of the oxidation of the obtained cycloadducts.

Results and Discussion

Chemistry

Our first approach to the synthesis of 3-(2-hydroxyphenyl)-5-styrylpyrazole (**3a**) involved treatment of cinnamoyl(2-hydroxybenzoyl)methane (**1a**, existing in equilibrium with its enolic form **2a**) with an excess of hydrazine (formed in situ by treatment of hydrazinium sulfate with potassium carbonate), which was added dropwise to the reaction mixture. After some preliminary attempts, the optimal experimental conditions (1:1 mixture of dichloromethane/methanol as solvent; at room temperature for 3 days) allowed the formation of **3a** in 37% yield. As the obtained result was not satisfactory it was decided to investigate treatment of **1a** with hydrazine hydrate, in methanol at

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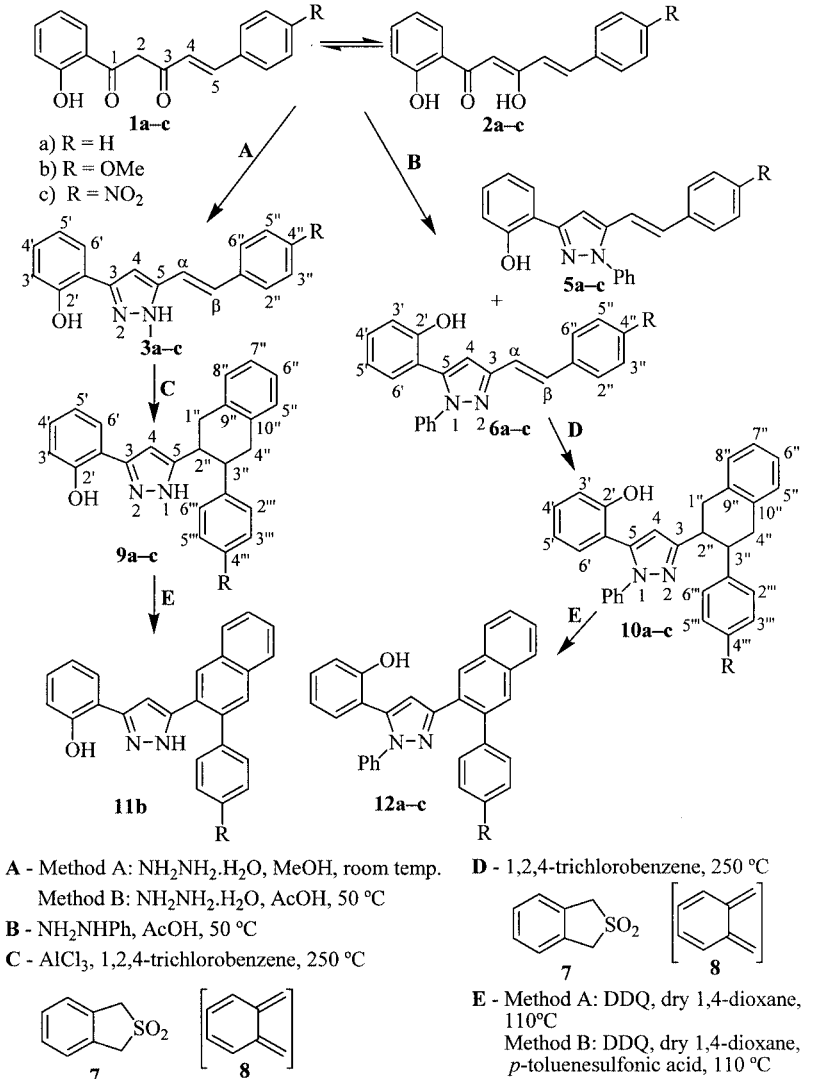
room temperature, until the disappearance of the starting material (Scheme 1). 3-(2-Hydroxyphenyl)-5-styrylpyrazole (**3a**) was obtained in 42% yield. With diketones **1b** and **1c** (in equilibrium with **2b** and **2c**) under the same conditions, the corresponding 3-(2-hydroxyphenyl)pyrazoles **3b** and **3c** were obtained in 28 and 36% yields. Since the obtained results weren′t as good as we had expected, treatment of diketones **1a−c/2a−c** with hydrazine hydrate in acetic acid (at 50 °C for 24 h) was also examined. The 3-(2-hydroxyphenyl)-5-styrylpyrazoles **3a** and **3c** were obtained in better yields (52% and 58%, respectively) than before, but **3b** was obtained only in 34% yield. In this case 4′-methoxy-2-styrylchromone (**4b**)[10] was obtained as a by-product (19% yield), formed by acid-catalysed cyclodehydration of the diketone **1b/2b**.[11]

In the first attempt to synthesise 1-phenyl-3(5)-(2-hydroxyphenyl)-5(3)-styrylpyrazoles (**5a** or **6a**), we also examined the treatment of cinnamoyl(2-hydroxybenzoyl)methanes **1a−c/2a−c** with excess phenylhydrazine (added in 3 batches, over 4 days) in methanol at room temperature (Scheme 1). The reaction mixture was analysed by thin layer chromatography (TLC), and the 3-(2-hydroxyphenyl)-1-phenyl-5-styrylpyrazoles **5a−c** were isolated in 13, 38 and 12% yields, respectively. As each obtained yield was unsatisfactory, some changes in the experimental procedure (quantity of phenylhydrazine, reaction time and temperature) were made, but the yields of pyrazoles **5a−c** did not increase. This prompted us to attempt the reaction in acid medium (similarly to the treatment of **1a−c/2a−c** with hydrazine hydrate, vide supra). Treatment of acetic acid solutions of cinnamoyl(2-hydroxybenzoyl)methanes **1a−c/2a−c** with excess phenylhydrazine for 24 h at 50°C resulted in the formation of mixtures of the two pyrazole isomers **5a−c** and **6a−c**, with the 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles **6a−c** being the more abundant (62−86%), and the 3-(2-hydroxyphenyl)-1-phenyl-5-styrylpyrazoles **5a−c** being obtained as by-products (1−2%) (Scheme 1). Treatment of a monosubstituted hydrazine with an unsymmetrical β-diketone resulted in the formation of a mixture of pyrazole isomers, in a regioselective manner, since the 3-(2-hydroxy-



Scheme 1

phenyl)-1-phenyl-5-styrylpyrazole isomers **5a−c** were obtained in very small quantities.

The reaction between a β-diketone and phenylhydrazine is apparently a simple reaction, but it conceals a complex mechanistic problem.[12] In this case, the diketones have two tautomeric forms − **1a−c** and **2a−c** − and phenylhydrazine can react initially through the NH or NH_2. When the reactions between diketones **1a−c/2a−c** and phenylhydrazine were carried out in methanol, there was a nucleophilic attack of NH_2 at the more electrophilic centre of the diketone C-1, and only the **5a−c** isomers were obtained, although in low yields. Under acidic conditions, the more basic (NH_2) amine group in the phenylhydrazine was protonated and consequently the nucleophilic attack at the more electrophilic centres in the diketones **1a−c/2a−c** was performed by the NH, 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles **6a−c** therefore being the main reaction products (62−86%).

In development of our previous work,[9a] we tried to prepare 3-(2-hydroxyphenyl)pyrazoles **5a−c** in better yields through reactions between the appropriate 2-styrylchromones and phenylhydrazine. However, we found that the styrylchromones were much less reactive than diketones and we did not obtain the expected isomers, either from the reaction in acidic medium or from that in methanol.

With continuing interest in heterocyclic structures and also in Diels−Alder cycloaddition reactions of styryl compounds,[10,13] we studied reactions between some of the synthesised styrylpyrazoles **3a−c** and **6a−c** and the highly reactive *ortho*-benzoquinodimethane (**8**; Scheme 1). *N*-Substituted pyrazoles **6a−c** reacted with *ortho*-benzoquinodimethane (**8**), formed in situ by thermal extrusion of sulfur dioxide from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (**7**),[14] at reflux in 1,2,4-trichlorobenzene over 24 h, to give cycloadducts **10a−c** in good yields (69−91%). The styryl double bond was less reactive when there was an electron-donating substituent on the *para* position of the styryl moiety and more reactive if there was an electron-withdrawing substituent at the same position.

Pyrazoles **3a−c** are less reactive than *N*-phenylpyrazoles, since the reactions between **3a−c** and excess *ortho*-benzoquinodimethane (**8**) took longer (50−65 h) and gave the expected cycloadducts **9a−c** in lower yields (48, 24 and 48%, respectively), without recovery of any starting material. An alternative approach to improve the efficiency of these Diels−Alder reactions was the addition of aluminium chloride,[15] which probably forms a chelate with the hydroxy oxygen and the free nitrogen of the pyrazole nucleus. This complex makes the styryl double bond of pyrazoles **3a−c** more reactive, and cycloadducts **9a** and **9b** were indeed obtained in better yields (56 and 53%). In the case of pyrazole **3c** there was extensive decomposition in the reaction medium and the cycloadduct **9c** was obtained only in 25% yield.

In order to prepare new pyrazoles with complete and extended aromatic structures, we studied the oxidation of cycloadducts **10a−c**. In initial investigations, dehydrogenation of compounds **10a−c** with five molar equivalent of DDQ at reflux in dry 1,4-dioxane over several days resulted in the formation of 5-(2-hydroxyphenyl)-3-naphthylpyrazole derivatives **12a−c** (Scheme 1, **E,** Method A). The dehydrogenation of compound **10b**, bearing an electron-donating substituent at the *para* position of the phenyl group linked to the hydroaromatic ring, was faster and gave the expected compound **12b** in better yields than in the other two cases (Table 1). This can be explained by taking the reaction mechanism of these oxidation reactions into account. In this case it involves a (benzylic) hydride transfer from compounds **10a−c** to DDQ, and the presence of an electron-donating substituent in the phenyl ring should stabilise the formed carbocation (C-3′′). In an attempt to optimise the experimental procedure we found that the presence of a small amount (20% molar equivalent) of *p*-toluenesulfonic acid[16] resulted in faster formation of the expected 5-(2-hydroxyphenyl)-3-naphthylpyrazoles **12a−c** with slightly improved reaction yields (Table 1, Scheme 1, **E,** Method B).

Other oxidative systems such as MnO_2/chlorobenzene, NBS followed by NEt_3, I_2/DMSO and chloranil were used, but were not as efficient as DDQ. It was also found that a strong oxidant such as DDQ is the most suitable oxidative agent to perform the dehydrogenation reaction of compounds **10a−c** into **12a−c**.

We also attempted the oxidation of cycloadducts **9a−c** by all the methods described, but only unknown (decomposition) products were obtained. Only in the oxidation of 3-(2-hydroxyphenyl)-5-{2-[3-(4-methoxyphenyl)]-1,2,3,4-tetrahydronaphthyl}pyrazole (**9b**) with five molar equivalents of DDQ at reflux in dry 1,4-dioxane in the presence of a small amount (20% molar equivalent) of *p*-toluenesulfonic acid[16] did we succeed in isolating and characterising

Table 1. Yields obtained in the oxidation of cycloadducts **10a−c** with DDQ in dry 1,4-dioxane

Starting compounds	**E**, Method A R	Reaction time (days)	Yield of 12 (%)	**E**, Method B R	Reaction time (hours)	Yield of 12 (%)
10a	H	5	**12a** (25)	H	3	**12a** (29)
10b	OCH_3	2	**12b** (59)	OCH_3	2	**12b** (57)
10c	NO_2	6	**12c** (17)	NO_2	7	**12c** (36)

the corresponding pyrazole **11b** in low yield (13%) (Scheme 1, **E,** Method B).

Nuclear Magnetic Resonance

The ^{1}H NMR spectra of the 3-(2-hydroxyphenyl)-5-styrylpyrazoles **3a**−**c** presented two deshielded broad singlets, due to the N*H* and 2′-O*H* resonances, at δ = 10.04−10.79 and 10.78−12.81 ppm. The high-frequency value of the hydroxy proton is due to the intramolecular hydrogen bond with N2. These intramolecular hydrogen bonds prevent the prototropy of N*H*-pyrazoles **3a**−**c**.

The main criteria by which to distinguish between the two isomers of 3(5)-(2-hydroxyphenyl)-1-phenyl-5(3)-styrylpyrazoles **5a**−**c** and **6a**−**c** was the resonance of 2′-O*H*. In the case of pyrazoles **5a**−**c** this appears as a singlet at δ 10.68−10.90 ppm, due to the intramolecular hydrogen bond between the hydroxy proton and N2 of the pyrazole nucleus, while in the case of pyrazoles **6a**−**c** this intramolecular hydrogen bond is not observed and the resonance of 2′-O*H* appears at lower frequencies (δ = 5.30−5.48 ppm).

Other important features of the NMR spectra of pyrazoles **3a-c**, **5a-c** and **6a**−**c** are the presence in each of a singlet due to the resonance of 4-H (δ ≈ 6−7 ppm) and doublets due to the resonances of H-α and H-β (δ ≈ 7 ppm). The coupling constant values, of $^3J_{H\alpha,H\beta}$ ≈ 16−16.5 Hz, indicate the *trans* configuration in the vinylic moieties. The connectivities found in the HMBC spectra of these pyrazoles **3a-c**, **5a-c** and **6a**−**c** allowed the unequivocal assignments of their C-3 and C-5 carbon resonances (4-H, H-α, H-β → C-5 and 4-H and 6′-H → C-3).

The main feature in each of the ^{1}H NMR spectra of cycloadducts **9a**−**c** and **10a**−**c** is the presence of a multiplet in the aliphatic region of the spectra due to the proton resonances of the tetrahydroaromatic ring and the absence of H-α and H-β resonances. Dehydrogenation of the tetrahydroaromatic rings in cycloadducts **9b** and **10a**−**c** induces some changes in the ^{1}H NMR spectra of the new compounds **11b** and **12a**−**c**. Instead of a multiplet in the aliphatic region, we observed two singlets at δ = 7.86−7.89 and 8.14−8.48 ppm, due to the resonances of 4′′-H and 1′′-H, respectively. The connectivities between 1′′-H and C-5 found in the HMBC spectra of **11b** and **12a**−**c** allowed the unequivocal assignment of this carbon resonance. The O*H* and N*H* resonances of the compounds **9a**−**c**, **10a**−**c**, **11b** and **12a**−**c** show behaviour similar to that of the starting pyrazoles **3a-c**, **5a-c** and **6a**−**c**.

Conclusion

Reactions between cinamoyl(2-hydroxybenzoyl)methanes **1a**−**c/2a**−**c** and hydrazine hydrate or phenylhydrazine in acetic acid have been studied, and a new synthesis of 3-(2-hydroxyphenyl)-5-styrylpyrazoles **3a**−**c** and 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles **6a**−**c** has been established. Treatment of **1a**−**c/2a**−**c** with phenylhydrazine also gave 3-(2-hydroxyphenyl)-1-phenyl-5-styrylpyrazoles **5a**−**c** as by-products. Diels−Alder reactions between *ortho*-benzoquinodimethane (**8**) and both the 3-(2-hydroxyphenyl)-5-styrylpyrazoles **3a**−**c** and the 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazoles **6a**−**c** were also studied and afforded the corresponding cycloadducts 5-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]-3-(2-hydroxyphenyl)pyrazoles **9a**−**c** and 3-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]-1-phenyl-5-(2-hydroxyphenyl)pyrazoles **10a**−**c**, respectively. The oxidation of these cycloadducts with DDQ in dry 1,4-dioxane was performed and the new naphthylpyrazoles **11b** and **12a**−**c** were obtained. All these reactions allowed us to establish new synthetic methods for novel (2-hydroxyphenyl)pyrazoles.

Experimental Section

General Remarks: Melting points were measured in a Reichert Thermovar apparatus fitted with a microscope and are uncorrected. NMR spectra were recorded with Bruker AMX and DRX 300 spectrometers (300.13 for ^{1}H and 75.47 MHz for ^{13}C), in $CDCl_3$ as solvent, if not stated otherwise. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz; internal standard was TMS. Unequivocal ^{13}C assignments were made with the aid of 2D *g*HSQC (or HETCOR) and *g*HMBC (delays for one-bond and long-range *J* C/H couplings were optimised for 145 and 7 Hz, respectively) experiments. Electron impact (EI, 70 eV) MS were recorded with VG Autospec Q and M spectrometers. Elemental analyses were obtained with Carlo Erba 1108 and LECO 932 CHNS analysers. Preparative thin-layer chromatography was performed with Merck silica gel (60 DGF_{254}). Column chromatography was performed with Merck silica gel 60 (70−230 mesh). All other chemicals and solvents used were obtained from commercial sources and were either used as received or dried by standard procedures.

1-(2-Hydroxyphenyl)-5-phenyl-4-pentene-1,3-diones 1a−**c** (which exist in equilibrium with their enolic forms **2a-c**) were obtained as previously described in the literature.[10]

Synthesis of 3-(2-Hydroxyphenyl)-5-styrylpyrazoles 3a−**c. Method A:** Hydrazine hydrate (4.72 mL, 97.2 mmol) was added to a solution of the appropriate diketone **1a** or **1b/2a** or **2b** (12.2 mmol) in methanol (300 mL). The mixture was stirred at room temperature under nitrogen for 2:30 h. After that, the reaction mixture was poured into chloroform (250 mL) and washed with an acidic aqueous solution (pH 5; 2 × 250 mL). The organic layer was collected and the solvent was partially removed. The concentrated organic layer was purified by column chromatography with dichloromethane as eluent. The solvent was evaporated to dryness and the residue was recrystallised from a mixture of dichloromethane/cyclohexane, giving the expected 3-(2-hydroxyphenyl)-5-styrylpyrazoles (**3a** and **3b**) as white needles: **3a**, 1.34 g (42%) and **3b**, 999 mg (28%).

Compound **3c** was prepared by the same procedure, but with use of only 5 molar equivalents of hydrazine hydrate instead of 8 equivalents, and the reaction mixture was stirred at room temperature under nitrogen for 24 h. The organic layer was purified by column chromatography with a mixture of dichloromethane/ethyl acetate (8:2) as eluent. 3-(2-Hydroxyphenyl)-5-(4-methoxystyryl)pyrazole (**3c**) was obtained as white needles (1.35 g, 36%).

Method B: Hydrazine hydrate (0.82 mL, 16.9 mmol) was added to a solution of the appropriate diketones **1a** or **1b/2a** or **2b** (1.69 mmol) in acetic acid (50 mL). The mixture was heated to 50°C

under nitrogen for 24 h. After that period the reaction mixture was poured into a mixture of ice and water (100 mL). The obtained solid was removed by filtration, taken up in chloroform (100 mL) and washed with water (2 × 100 mL). The concentrated organic layer was purified by column chromatography with dichloromethane as eluent. The solvent was evaporated to dryness, and the residue was recrystallised from a mixture of dichloromethane/cyclohexane, giving the expected 3-(2-hydroxyphenyl)-5-styrylpyrazole (**3a** and **3c**) as white needles: **3a**, 231 mg (52%) and **3c**, 301 mg (58%). In the reaction between **1b/2b** and hydrazine hydrate, the reaction mixture was purified by preparative TLC, with dichloromethane as eluent. After several elutions, three spots were collected; the first one was identified as 4′-methoxy-2-styrylchromone (**4b**; 19.0%), the second was the expected 3-(2-hydroxyphenyl)-5-(4-methoxystyryl)-pyrazole (**3b**; 168 mg, 34%) and the third was the starting material **1b/2b** (7%).

3-(2-Hydroxyphenyl)-5-styrylpyrazole (3a): M.p. 120−121°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 6.78 (s, 1 H, 4-H), 6.94 (dt, *J* = 7.6, 1.2 Hz, 1 H, 5′-H), 6.98 (d, *J* = 16.5 Hz, 1 H, H-α), 7.04 (dd, *J* = 8.0, 1.2 Hz, 1 H, 3′-H), 7.12 (d, *J* = 16.5 Hz, 1 H, H-β), 7.24 (ddd, *J* = 7.6, 8.0, 1.6 Hz, 1 H, 4′-H), 7.32 (tt, *J* = 7.1, 1.3 Hz, 1 H, 4′′-H), 7.40 (dd, *J* = 8.4, 7.1 Hz, 2 H, 3′′,5′′-H), 7.51 (dd, *J* = 8.4, 1.3 Hz, 2 H, 2′′,6′′-H); 7.61 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 10.10 (br. s, 1 H, N*H*), 10.78 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 99.7 (C−4), 114.3 (C-α), 116.4 (C-1′), 117.1 (C-3′), 119.4 (C-5′), 126.5 (C-6′), 126.7 (C-2′′,6′′), 128.7 (C-4′′), 128.9 (C-3′′,5′′), 129.4 (C-4′), 132.2 (C-β), 135.8 (C-1′′), 142.0 (C-5), 152.9 (C-3), 155.9 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 262 (22) [M$^{+\cdot}$], 261 (9) [M − H]$^+$, 236 (100), 207 (18), 178 (9), 131 (6), 118 (5), 104 (15), 7 (12), 63 (5). $C_{17}H_{14}N_2O$ (262.1): calcd. C 77.84, H 5.38, N 10.68; found C 77.84, H 5.20, N 10.69.

3-(2-Hydroxyphenyl)-5-(4-methoxystyryl)pyrazole (3b): M.p. 117−119°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.84 (s, 3 H, 4′′-OC*H*$_3$), 6.76 (s, 1 H, 4-H), 6.83 (d, *J* = 16.6 Hz, 1 H, H-α), 6.92 (d, *J* = 8.8 Hz, 2 H, 3′′,5′′-H), 6.93 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1 H, 5′-H), 7.04 (dd, *J* = 8.4, 1.2 Hz, 1 H, 3′-H), 7.05 (d, *J* = 16.6 Hz, 1 H, H-β), 7.24 (dt, *J* = 8.2, 1.6 Hz, 1 H, 4′-H), 7.44 (d, *J* = 8.8 Hz, 2 H, 2′′,6′′-H), 7.60 (dd, *J* = 7.3, 1.6 Hz, 1 H, 6′-H), 10.04 (br. s, 1 H, N*H*), 10.83 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 55.4 (4′′-O*C*H$_3$), 99.2 (C-4), 112.1 (C-α), 114.3 (C-3′′,5′′), 116.5 (C-1′), 117.1 (C-3′), 119.3 (C-5′), 126.5 (C-6′), 128.0 (C-2′′,6′′), 128.6 (C-1′′), 129.4 (C-4′), 131.8 (C-β), 142.3 (C-5), 152.9 (C-3), 160.1 (C-4′′), 156.0 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 292 (100) [M$^{+\cdot}$], 291 (51) [M − H]$^+$, 277 (11), 261 (7) [M − OCH$_3$)$^+$, 248 (10), 146 (11), 131 (7), 121 (8), 115 (10), 102 (9), 89 (8), 77 (11), 63 (10). $C_{18}H_{16}N_2O_2$ (292.1): calcd. C 73.95, H 5.52, N 9.58; found C 74.09, H 5.58, N 9.62.

3-(2-Hydroxyphenyl)-5-(4-nitrostyryl)pyrazole (3c): M.p. 218−220°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 6.93 (ddd, *J* = 7.8, 7.6, 1.0 Hz, 1 H, 5′-H), 6.95 (dd, *J* = 8.0, 1.0 Hz, 1 H, 3′-H), 7.19 (s, 1 H, 4-H), 7.22 (ddd, *J* = 8.0, 7.6, 1.6 Hz, 1 H, 4′-H), 7.52 (s, 2 H, H-α and H-β), 7.74 (dd, *J* = 7.8, 1.6 Hz, 1 H, 6′-H), 7.89 (d, *J* = 7.0 Hz, 2 H, 2′′,6′′-H), 8.28 (d, *J* = 7.0 Hz, 2 H, 3′′,5′′-H), 10.79 (br. s, 1 H, N*H*), 12.81 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 101.4 (C-4), 117.4 (C-1′), 117.5 (C-3′), 120.1 (C-5′), 124.9 (C-3′′,5′′), 127.5 (C-6′), 128.2 (C-2′′,6′′), 130.0 (C-4′), 130.5 (C-α and C-β), 142.0 (C-1′′), 143.1 (C-5), 146.6 (C-4′′), 148.1 (C-3), 156.9 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 307 (100) [M$^{+\cdot}$], 306 (20) [M − H]$^+$, 292 (11), 277 (21) [M − NO$_2$]$^+$, 260 (10), 231 (4), 202 (4), 173 (13), 121 (7), 106 (11), 91 (7), 77 (8), 72 (6), 58 (10). $C_{17}H_{13}N_3O_3$ (307.1): calcd. C 66.44, H 4.26, N 13.67; found C 65.84, H 4.19, N 13.47.

Synthesis of 3(5)-(2-Hydroxyphenyl)-1-phenyl-5(3)-styrylpyrazoles 5a−c and 6a−c: Phenylhydrazine (0.74 mL, 7.51 mmol) was added to a solution of the appropriate diketone **1a** or **1b/2a** or **2b** (0.75 mmol) in acetic acid (50 mL). The mixture was heated (50°C) under nitrogen for 21 h. After that period the reaction mixture was poured into ice and water (100 mL). The obtained solid was removed by filtration, taken up in chloroform (100 mL), washed with water (2 × 100 mL) and dried (anhydrous sodium sulfate). After partial concentration in vacuo, the obtained solution was purified by silica gel thin layer chromatography with a mixture of light petroleum/ethyl acetate (9:1). After several elutions, two fractions were collected; the higher R_f fraction was in each case identified as the 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazole **6a−c**, followed by the 3-(2-hydroxyphenyl)-1-phenyl-5-styrylpyrazole **5a−c**. The solvent was evaporated to dryness and the residue in each case was recrystallised from methanol.

5-(2-Hydroxyphenyl)-1-phenyl-3-styrylpyrazole (6a): Yield 86% (218 mg). M.p. 151−153°C (recrystallised from methanol). ^{1}H NMR: δ = 5.48 (s, 1 H, 2′-O*H*), 6.79 (s, 1 H, 4-H), 6.86 (ddd, *J* = 7.6, 7.4, 1.0 Hz, 1 H, 5′-H), 6.95 (dd, *J* = 8.4, 1.0 Hz, 1 H, 3′-H), 7.00 (dd, *J* = 7.6, 1.7 Hz, 1 H, 6′-H), 7.20 (d, *J* = 16.5 Hz, 1 H, H-α), 7.24−7.32 (m, 7 H, 4′,4′′,2′′′,3′′′, 4′′′,5′′′,6′′′-H), 7.26 (d, *J* = 16.5 Hz, 1 H, H-β), 7.34 (dd, *J* = 8.4, 7.2 Hz, 2 H, 3′′,5′′-H), 7.54 (dd, *J* = 8.4, 1.2 Hz, 2 H, 2′′,6′′-H) ppm. ^{13}C NMR: δ = 105.8 (C-4), 116.1 (C-3′), 117.0 (C-1′), 120.0 (C-α), 120.6 (C-5′), 124.1 (C-2′′′,6′′′), 126.2 (C-2′′,6′′), 127.4 (C-4′′′), 127.9 (C-4′′), 128.7 (C-3′′,5′′), 128.9 (C-3′′′,5′′′), 130.8 (C-4′), 130.85 (C-6′), 131.2 (C-β), 136.9 (C-1′′), 138.6 (C-5), 139.6 (C-1′′′), 151.5 (C-3), 153.2 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 338 (100) [M$^{+\cdot}$], 337 (94) [M − H]$^+$, 321 (2), 310 (2), 261 (3), 246 (4), 234 (7), 217 (4), 196 (13), 180 (4), 169 (4), 128 (3), 115 (5), 91 (5), 77 (18). $C_{23}H_{18}N_2O$ (338.1): calcd. C 81.63, H 5.36, N 8.28; found C 81.34, H 5.34, N 8.12.

3-(2-Hydroxyphenyl)-1-phenyl-5-styrylpyrazole (5a): Yield 1.3% (3.3 mg). M.p. 182−184°C (recrystallised from methanol). ^{1}H NMR: δ = 6.92 (d, *J* = 16.3 Hz, 1 H, H-α), 6.96 (dt, *J* = 7.6, 1.0 Hz, 1 H, 5′-H), 7.04 (dd, *J* = 8.0, 1.0 Hz, 1 H, 3′-H), 7.04 (s, 1 H, 4-H), 7.22 (d, *J* = 16.3 Hz, 1 H, H-β), 7.25 (ddd, *J* = 8.0, 7.6, 1.5 Hz, 1 H, 4′-H), 7.20−7.28 (m, 1 H, 4′′′-H), 7.28−7.39 (m, 3 H, 3′′,4′′,5′′-H), 7.44 (dd, *J* = 7.6, 2.0 Hz, 2 H, 2′′,6′′-H), 7.52−7.55 (m, 4 H, 2′′′,3′′′,5′′′,6′′′-H), 7.66 (dd, *J* = 7.6, 1.5 Hz, 1 H, 6′-H), 10.82 (s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 100.5 (C-4), 115.0 (C-α), 116.2 (C-1′), 117.2 (C-3′), 119.3 (C-5′), 125.2 (C-2′′′,6′′′), 126.5 (C-6′), 126.8 (C-2′′,6′′), 128.3 (C-4′′′), 128.7 (C-4′′), 128.9 (C-3′′,5′′), 129.4 (C-3′′′,5′′′), 129.5 (C-4′), 133.6 (C-β), 136.1 (C-1′′), 138.8 (C-1′′′), 142.0 (C-5), 151.9 (C-3), 156.1 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 338 (100) [M$^{+\cdot}$], 337 (30) [M − H]$^+$, 261 (7), 247 (3), 234 (2), 217 (5), 206 (7), 191 (2), 178 (2), 169 (4), 142 (2), 128 (3), 115 (6), 102 (2), 91 (6), 77 (15), 65 (3). EI-HRMS ($C_{23}H_{18}N_2O$): calcd. 338.1419; found 338.1419.

5-(2-Hydroxyphenyl)-3-(4-methoxystyryl)-1-phenylpyrazole (6b): Yield 84% (232 mg). M.p. 137−139°C (recrystallised from methanol). ^{1}H NMR: δ = 3.84 (s, 3 H, 4′′-OC*H*$_3$), 5.48 (s, 1 H, 2′-O*H*), 6.76 (s, 1 H, 4-H), 6.85 (dt, *J* = 7.6, 1.0 Hz, 1 H, 5′-H), 6.92 (d, *J* = 8.7 Hz, 2 H, 3′′,5′′-H), 6.95 (d, *J* = 8.2 Hz, 1 H, 3′-H), 7.00 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 7.10 (d, *J* = 16.5 Hz, 1 H, H-α), 7.16 (d, *J* = 16.5 Hz, 1 H, H-β), 7.25−7.31 (m, 7 H, 4′,4′′,2′′′,3′′′,4′′′,5′′′,6′′′-H), 7.48 (d, *J* = 8.7 Hz, 2 H, 2′′,6′′-H) ppm. ^{13}C NMR: δ = 55.3 (4′′-O*C*H$_3$), 105.6 (C-4), 114.2 (C-3′′,5′′), 116.1 (C-3′), 117.0 (C-1′), 117.9 (C-α), 120.6 (C-5′), 124.1

(C-2′′′,6′′′), 127.3 (C-4′′′), 127.8 (C-2′′,6′′), 128.9 (C-3′′′,5′′′), 129.7 (C-1′′), 130.7 (C-4′), 130.80 (C-β), 130.84 (C-6′), 138.4 (C-5), 139.6 (C-1′′′), 151.9 (C-3), 153.3 (C-2′), 159.5 (C-4′′) ppm. EI-MS: *m*/*z* (rel. int., %) = 369 (33) [M + H]$^+$, 368 (100) [M$^{+\cdot}$], 367 (60) [M − H]$^+$, 353 (6), 324 (2), 276 (2), 264 (6), 247 (2), 233 (3), 218 (2), 208 (3), 196 (13), 184 (6), 165 (3), 152 (3), 139 (2), 121 (2), 115 (3), 102 (3), 89 (5), 77 (22), 63 (5). $C_{24}H_{20}N_2O_2$ (368.2): calcd. C 78.24, H 5.47, N 7.60; found C 78.16, H 5.46, N 7.59.

3-(2-Hydroxyphenyl)-5-(4-methoxystyryl)-1-phenylpyrazole (5b): Yield 1.7% (4.69 mg). M.p. 165−167°C (recrystallised from methanol). ^{1}H NMR: δ = 3.83 (s, 3 H, 4′′-OC*H*$_3$), 6.77 (d, *J* = 16.3 Hz, 1 H, H-α), 6.89 (d, *J* = 8.8 Hz, 2 H, 3′′,5′′-H), 6.95 (dt, *J* = 7.5, 1.2 Hz, 1 H, 5′-H), 7.00 (s, 1 H, 4-H), 7.04 (dd, *J* = 8.2, 1.2 Hz, 1 H, 3′-H), 7.17 (d, *J* = 16.3 Hz,1 H, H-β), 7.25 (ddd, *J* = 8.2, 7.5, 1.6 Hz, 1 H, 4′-H), 7.38 (d, *J* = 8.8 Hz, 2 H, 2′′,6′′-H), 7.53−7.55 (m, 5 H, 2′′′,3′′′,5′′′,4′′′,6′′′-H), 7.66 (dd, *J* = 7.5, 1.6 Hz, 1 H, 6′-H), 10.90 (s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 55.3 (4′′-O*C*H$_3$), 100.0 (C-4), 112.7 (C-α), 114.2 (C-3′′,5′′), 116.2 (C-1′), 117.2 (C-3′), 119.3 (C-5′), 125.2 (C-2′′′,6′′′), 126.4 (C-6′), 128.2 (C-2′′,6′′), 128.8 (C-1′′), 129.3 (C-3′′′,5′′′), 129.4 (C-4′′′ and C-4′), 133.1 (C-β), 128.8 (C-1′′), 142.3 (C-5), 151.8 (C-3), 156.1 (C-2′), 160.0 (C-4′′) ppm. EI-MS: *m*/*z* (rel. int., %) = 369 (39) [M + H]$^+$, 368 (100) [M$^{+\cdot}$], 367 (28) [M − H]$^+$, 353 (5), 337 (14) [M − OCH$_3$]$^+$, 325 (2), 324 (3), 277 (2), 261 (8), 247 (4), 236 (7), 217 (2), 204 (4), 191 (2), 184 (7), 165 (2), 131 (2), 121 (4), 115 (3), 102 (2), 91 (5), 77(11), 65 (2). EI-HRMS $C_{24}H_{20}N_2O_2$: calcd. 368.1525; found 368.1516.

5-(2-Hydroxyphenyl)-3-(4-nitrostyryl)-1-phenylpyrazole (6c): Yield 62% (178 g). M.p. 211−213°C (recrystallised from methanol). ^{1}H NMR: δ = 5.30 (s, 1 H, 2′-O*H*), 6.82 (s, 1 H, 4-H), 6.88 (dt, *J* = 7.6, 1.4 Hz, 1 H, 5′-H), 6.94 (dd, *J* = 8.2, 1.4 Hz, 1 H, 3′-H), 7.03 (dd, *J* = 7.6, 1.7 Hz, 1 H, 6′-H), 7.23−7.33 (m, 7 H, 4′,4′′,2′′′,3′′′,4′′′,5′′′,6′′′-H), 7.25 (d, *J* = 16.5 Hz, 1 H, H-β), 7.39 (d, *J* = 16.5 Hz, 1 H, H-α), 7.65 (d, *J* = 8.8 Hz, 2 H, 2′′,6′′-H), 8.24 (d, *J* = 8.8 Hz, 2 H, 3′′,5′′-H) ppm. ^{13}C NMR: δ = 106.4 (C-4), 116.2 (C-3′), 116.8 (C-1′), 120.8 (C-5′), 124.2 (C-2′′′,6′′′ and C-4′), 124.1 (C-3′′,5′′), 124.7 (C-α), 126.9 (C-2′′,6′′), 127.6 (C-4′′′), 128.4 (C-β), 129.0 (C-3′′′,5′′′), 130.9 (C-4′,6′), 139.1 (C-5), 139.5 (C-1′′′), 143.4 (C-1′′), 146.9 (C-4′′), 150.4 (C-3), 153.1 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 384 (25) [M + H]$^+$, 383 (100) [M$^{+\cdot}$], 382 (78) [M − H]$^+$, 366 (2), 353 (13) [M − NO]$^+$, 336 (18), 319 (2), 307 (2), 290 (5), 279 (3), 261 (2), 247 (3), 233 (4), 217 (3), 202 (3), 196 (16), 180 (4), 168 (3), 135 (2), 115 (2), 102 (2), 91 (4), 77 (20), 65 (2), 58 (30). $C_{23}H_{17}N_3O_3$ (383.1): calcd. C 72.05, H 4.47, N 10.96; found C 71.50, H 4.37, N 10.85.

3-(2-Hydroxyphenyl)-5-(4-nitrostyryl)-1-phenylpyrazole (5c): Yield 0.5% (1.44 mg). M.p. 236−237°C (recrystallised from methanol). ^{1}H NMR: δ = 6.97 (dt, *J* = 7.6, 1.1 Hz, 1 H, 5′-H), 7.04 (s, 1 H, 4-H), 7.07 (d, *J* = 16.4 Hz, 1 H, H-α), 7.08 (dd, *J* = 8.3, 1.1 Hz, 1 H, 3′-H), 7.36 (d, *J* = 16.4 Hz, 1 H, H-β), 7.51−7.61 (m, 6 H, 4′,2′′′,3′′′,4′′′,5′′′,6′′′-H), 7.57 (d, *J* = 8.8 Hz, 2 H, 2′′,6′′-H), 7.66 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 8.22 (d, *J* = 8.8 Hz, 2 H, 3′′,5′′-H), 10.68 (s, 1 H, 2′-O*H*) ppm. EI-MS: *m*/*z* (rel. int., %) = 383 (100) [M$^{+\cdot}$], 353 (5) [M − NO]$^+$, 336 (6), 279 (3), 261 (6), 251 (3), 231 (2), 217 (5), 204 (4), 167 (4), 149 (8), 115 (3), 91 (4), 77 (10), 57 (3). EI-HRMS ($C_{23}H_{17}N_3O_3$): calcd. 383.1270; found 383.1269.

1,3-Dihydrobenzo[*c*]thiophene 2,2-Dioxide (7): Prepared according to literature procedures.[14]

Synthesis of 5-[2-(3-Aryl-1,2,3,4-tetrahydronaphthyl)]-3-(2-hydroxyphenyl)pyrazoles 9a−c: 1,3-Dihydrobenzo[*c*]thiophene 2,2-dioxide (**7**; 0.19 g, 1.14 mmol) was added to a solution of the 3-(2-hydroxyphenyl)-5-styrylpyrazole **3a** or **3b** (7.62 × 10^{-1} mmol) in 1,2,4-trichlorobenzene (50 mL) in the presence of aluminium chloride (0.10 g, 7.62 × 10^{-1} mmol). The mixture was heated at reflux under nitrogen for 24 h. After cooling to room temperature, the reaction mixture was poured into water (100 mL) and ice and extracted with chloroform (2 × 100 mL). The organic layer was dried (sodium sulfate) and concentrated to dryness. The obtained residue was taken up in light petroleum and purified by column chromatography; 1,2,4-trichlorobenzene was eluted with light petroleum and the reaction products were then eluted with chloroform. The expected compounds {5-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]-3-(2-hydroxyphenyl)pyrazoles **9a** and **9b**} were obtained as white crystals and recrystallised in each case from a dichloromethane/light petroleum mixture.

3-(2-Hydroxyphenyl)-5-{2-[3-(4-nitrophenyl)]-1,2,3,4-tetrahydronaphthyl}pyrazole (**6c**) was obtained by the same procedure, but in the absence of aluminium chloride.

3-(2-Hydroxyphenyl)-5-[2-(3-phenyl-1,2,3,4-tetrahydronaphthyl)]-pyrazole (9a): Yield 56% (156 mg). M.p. 170−172°C (recrystallised from a dichloromethane/light petroleum mixture). ^{1}H NMR: δ = 3.16−3.19 (m, 3 H, 2 × 1′′-H, 3′′-H), 3.23−3.30 (m, 2 H, 2 × 4′′-H), 3.38−3.46 (m, 1 H, 2′′-H), 6.45 (s, 1 H, 4-H), 6.88 (dt, *J* = 7.6, 1.0 Hz, 1 H, 5′-H), 6.96 (dd, *J* = 8.2, 1.0 Hz, 1 H, 3′-H), 7.15−7.24 (m, 4 H, 2′′′,6′′′,3′′′,5′′′-H), 7.26−7.33 (m, 6 H, 5′′,6′′,7′′,8′′,4′,4′′′-H), 7.50 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 9.09 (br. s, 1 H, N*H*), 10.68 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 35.8 (C-4′′), 37.5 (C-1′′), 38.3 (C-2′′), 46.8 (C-3′′), 99.4 (C-4), 116.6 (C-1′), 116.9 (C-3′), 119.1 (C-5′), 126.26 (C-6′), 126.30 (C-8′′), 126.4 (C-5′′), 127.21 (C-4′′′), 127.24 (C-2′′′,6′′′), 128.6 (C-3′′′,5′′′), 129.0 (C-6′′,7′′ and C-4′), 134.5 (C-10′′), 135.6 (C-9′′), 143.7 (C-1′′′), 146.9 (C-5), 151.8 (C-3), 155.8 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 366 (100) [M$^{+\cdot}$], 365 (5) [M − H]$^+$, 351 (2), 275 (54), 262 (15), 250 (8), 202 (4), 193 (13), 178 (13), 165 (5), 142 (4), 128 (7), 115 (29), 104 (14), 91 (22), 78 (7), 65 (3). EI-HRMS ($C_{25}H_{22}N_2O$): calcd. 366.1732, found 366.1721.

3-(2-Hydroxyphenyl)-5-{2-[3-(4-methoxyphenyl)]-1,2,3,4-tetrahydronaphthyl}pyrazole (9b): Yield 53% (160 mg). M.p. 156−157°C (recrystallised from a dichloromethane/light petroleum mixture). ^{1}H NMR: δ = 3.09−3.19 (m, 3 H, 2 × 1′′-H and 3′′-H), 3.26−3.49 (m, 3 H, 2′′-H and 2 × 4′′-H), 3.78 (s, 3 H, 4′′′-OC*H*$_3$), 6.46 (s, 1 H, 4-H), 6.83 (d, *J* = 8.3 Hz, 2 H, 3′′′,5′′′-H), 6.88 (ddd, *J* = 8.3, 7.6, 0.7 Hz, 1 H, 5′-H), 6.97 (dd, *J* = 8.3, 0.7 Hz, 1 H, 3′-H), 7.10 (d, *J* = 8.3 Hz, 2 H, 2′′′,6′′′-H), 7.13−7.23 (m, 5 H, 5′′,6′′,7′′,8′′-H and 4′-H), 7.51 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 9.11 (br. s, 1 H, N*H*), 10.72 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 35.8 (C-4′′), 37.8 (C-1′′), 38.5 (C-2′′), 45.9 (C-3′′), 55.2 (4′′′-O*C*H$_3$), 99.4 (C-4), 114.4 (C-3′′′,5′′′), 116.7 (C-1′), 116.9 (C-3′), 119.1 (C-5′), 126.2 (C-8′′), 126.3 (C-5′′), 126.4 (C-6′), 128.2 (C-2′′′,6′′′), 128.6 (C-6′′,7′′), 129.1 (C-4′), 134.6 (C-10′′), 135.65 (C-9′′), 135.7 (C-1′′′), 147.1 (C-5), 151.8 (C-3), 155.9 (C-2′), 158.5 (C-4′′′) ppm. EI-MS: *m*/*z* (rel. int., %) = 396 (100) [M$^{+\cdot}$], 395 (7) [M − H]$^+$, 292 (9), 275 (39), 261 (7), 223 (21), 198 (5), 173 (9), 145 (6), 128 (6), 121 (92), 115 (26), 115 (29), 104 (8), 91 (10), 77 (7), 65 (4). EI-HRMS ($C_{26}H_{24}N_2O_2$): calcd. 396.1838, found 396.1833.

3-(2-Hydroxyphenyl)-5-{2-[3-(4-nitrophenyl)]-1,2,3,4-tetrahydronaphthyl}pyrazole (9c): Yield 48% (150 mg). M.p. 202−204°C (recrystallised from a dichloromethane/light petroleum mixture). ^{1}H NMR: δ = 3.15−3.18 (m, 2 H, 2 × 1′′-H), 3.22−3.26 (m, 2 H, 2 × 4′′-H), 3.35−3.40 (m, 1 H, 3′′-H), 3.42−3.48 (m, 1 H, 2′′-H), 6.39 (s, 1 H, 4-H), 6.87 (dt, *J* = 7.6, 1.1 Hz, 1 H, 5′-H), 6.96 (dd, *J* = 8.2, 1.1 Hz, 1 H, 3′-H), 7.18 (ddd, *J* = 8.2, 7.6, 1.6 Hz, 1 H, 4′-H), 7.20−7.26 (m, 5 H, 5′′,6′′,7′′,8′′-H and 4′′′-H), 7.32 (d, *J* =

8.6 Hz, 2 H, 2‴,6‴-H), 7.45 (dd, J = 7.6, 1.6 Hz, 1 H, 6′-H), 8.09 (d, J = 8.6 Hz, 2 H, 3‴,5‴-H), 9.90 (br. s, 2 H, N*H* and 2′-O*H*) ppm. ^{13}C NMR: δ = 36.1 (C-4″), 37.1 (C-1″), 38.2 (C-2″), 46.6 (C-3″), 99.6 (C-4), 116.3 (C-1′), 117.0 (C-3′), 119.3 (C-5′), 124.1 (C-2‴,6‴), 126.4 (C-6′), 126.7 (C-8″), 126.8 (C-5″), 128.2 (C-3‴,5‴), 128.6 (C-6″), 128.7 (C-7″), 129.4 (C-4′), 134.2 (C-10″), 134.6 (C-9″), 146.4 (C-5), 146.8 (C-1‴), 151.2 (C-4‴), 152.2 (C-3), 155.7 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 411 (100) [M$^{+\cdot}$], 410 (3) [M − H]$^+$, 394 (3), 381 (8) [M − NO]$^+$, 307 (6), 284 (3), 275 (33), 261 (10), 236 (2), 215 (2), 202 (4), 191 (5), 173 (10), 165 (3), 152 (2), 132 (4), 121 (6), 118 (12), 115 (14), 106 (16), 104 (15), 91 (23). $C_{25}H_{21}N_3O_3$ (411.2): calcd. C 72.98, H 5.14, N 10.21; found C 73.08, H 5.07, N 9.67.

Synthesis of 3-[2-(3-Aryl-1,2,3,4-tetrahydronaphthyl)]-1-phenyl-5-(2-hydroxyphenyl)pyrazoles 10a−c: 1,3-Dihydrobenzo[*c*]thiophene 2,2-dioxide (**7**; 0.82 g, 4.90 mmol) was added to a solution of the appropriate 5-(2-hydroxyphenyl)-1-phenyl-3-styrylpyrazole (**6a−c**, 3.27 mmol) in 1,2,4-trichlorobenzene (20 mL). The mixture was heated at reflux under nitrogen for 24 h. After cooling to room temperature, the reaction mixture was purified by column chromatography; 1,2,4-trichlorobenzene was eluted with light petroleum and the reaction products were then eluted with dichloromethane. The expected compounds − 5-(2-hydroxyphenyl)-1-phenyl-3-[2-(3-phenyl-1,2,3,4-tetrahydronaphthyl)]pyrazoles **10a−c** − were obtained as white crystals and in each case recrystallised from a mixture of dichloromethane/cyclohexane.

5-(2-Hydroxyphenyl)-1-phenyl-3-[2-(3-phenyl-1,2,3,4-tetrahydronaphthyl)]pyrazole (10a): Yield 87% (1.26 g). M.p. 169−171°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.23−3.49 (m, 6 H, 2 × 1″,4″-H and 2″,3″-H), 5.22 (s, 1 H, 2′-O*H*), 6.03 (s, 1 H, 4-H), 6.74 (ddd, J = 7.6, 6.8, 1.0 Hz, 1 H, 5′-H), 6.78 (dd, J = 7.6, 2.1 Hz, 1 H, 6′-H), 6.89 (dd, J = 8.0, 1.0 Hz, 1 H, 3′-H), 7.10 (dd, J = 8.0, 1.8 Hz, 2 H, 2⁗,6⁗-H), 7.10−7.31 (m, 13 H, 4′-H, 5″,6″,7″,8″-H and 2‴, 6‴,3‴,5‴,4‴,3⁗,5⁗,4⁗-H) ppm. ^{13}C NMR: δ = 36.4 (C-4″), 37.9 (C-1″), 40.6 (C-2″), 47.0 (C-3″), 107.0 (C-4), 115.8 (C-3′), 116.9 (C-1′), 120.2 (C-5′), 124.2 (C-2⁗,6⁗), 125.83 (C-8″), 125.87 (C-5″), 126.3 (C-4⁗), 127.1 (C-4‴), 128.0 (C-2‴,6‴), 128.2 (C-3‴,5‴), 128.6 (C-6″), 128.7 (C-3⁗,5⁗), 128.75 (C-7″), 130.4 (C-6′), 130.5 (C-4′), 135.9 (C-10″), 136.0 (C-9″), 136.9 (C-5), 139.5 (C-1‴), 144.7 (C-1⁗), 153.3 (C-2′), 156.1 (C-3) ppm. EI-MS: *m*/*z* (rel. int., %) = 442 (100) [M$^{+\cdot}$], 441 (17) [M − H]$^+$, 427 (6), 365 (8), 350 (25), 351 (65), 338 (8), 337 (15), 326 (16), 275 (5), 250 (23), 221 (4), 209 (6), 196 (13), 181 (24), 180 (25), 170 (4), 145 (6), 129 (4), 115 (13), 104 (10), 91 (14), 85 (6), 77 (14), 57 (4). $C_{31}H_{26}N_2O$ (442.2): calcd. C 84.10, H 5.92, N 6.33; found C 83.94, H 5.92, N 6.31.

5-(2-Hydroxyphenyl)-3-{2-[3-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphthyl]}-1-phenylpyrazole (10b): Yield 69% (1.06 g). M.p. 168−170°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.18−3.26 (m, 4 H, 2 × 1″,4″-H), 3.23−3.49 (m, 2 H, 2″,3″-H), 3.79 (s, 3 H, 4‴-OC*H*$_3$), 4.99 (s, 1 H, 2′-O*H*), 6.01 (s, 1 H, 4-H), 6.74 (ddd, J = 8.0, 6.9, 0.6 Hz, 1 H, 5′-H), 6.81 (dd, J = 6.9, 1.0 Hz, 1 H, 6′-H), 6.82 (d, J = 8.6 Hz, 2 H, 3‴,5‴-H), 6.90 (dd, J = 8.4, 0.6 Hz, 1 H, 3′-H), 7.17 (d, J = 8.5 Hz, 2 H, 2⁗,6⁗-H), 7.18 (d, J = 8.5 Hz, 2 H, 3⁗,5⁗-H), 7.16−7.23 (m, 6 H, 4′-H, 4⁗-H and 5″,6″,7″,8″-H), 7.25 (d, J = 8.6 Hz, 2 H, 2‴,6‴-H) ppm. ^{13}C NMR: δ = 36.5 (C-4″), 38.1 (C-1″), 40.9 (C-2″), 46.1 (C-3″), 55.3 (4‴-O*C*H$_3$), 107.0 (C-4), 113.6 (C-3‴,5‴), 115.9 (C-3′), 116.9 (C-1′), 120.2 (C-5′), 124.2 (C-2⁗,6⁗), 125.8 (C-8″), 125.9 (C-5″), 127.1 (C-4⁗), 128.6 (C-6″), 128.78 (C-3⁗,5⁗ and C-7″), 128.8 (C-2‴,6‴), 130.5 (C-6′), 130.52 (C-4′), 135.9 (C-10″), 136.2 (C-9″), 136.7 (C-1‴), 136.8 (C-5), 139.5 (C-1⁗), 153.3 (C-2′), 156.3 (C-3), 158.0 (C-4‴) ppm. EI-MS: *m*/*z* (rel. int., %) = 472 (87) [M$^{+\cdot}$], 471 (7) [M − H]$^+$, 457 (4), 364 (6), 351 (100), 337 (5), 275 (5), 263 (4), 250 (17), 236 (5), 222 (6), 208 (3), 202 (2), 196 (11), 180 (4), 178 (5), 165 (7), 152 (4), 139 (2), 128 (4), 121 (30), 115 (15), 104 (7), 103 (5), 91 (7), 77 (27), 65 (5). $C_{32}H_{28}N_2O_2$ (472.2): calcd. C 81.33, H 5.97, N 5.93; found C 80.65, H 5.91, N 5.84.

5-(2-Hydroxyphenyl)-3-{2-[3-(4-nitrophenyl)-1,2,3,4-tetrahydronaphthyl]}-1-phenylpyrazole (10c): Yield 91% (1.50 g). M.p. 207−209°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.19 (d, J = 7.7 Hz, 2 H, 2 × 1″-H), 3.35 (d, J = 7.5 Hz, 2 H, 2 × 4″-H), 3.45−3.59 (m, 2 H, 2″,3″-H), 5.04 (s, 1 H, 2′-O*H*), 6.14 (s, 1 H, 4-H), 6.76−6.78 (m, 2 H, 5′,6′-H), 6.85 (d, J = 8.2 Hz, 1 H, 3′-H), 7.07 (d, J = 8.1 Hz, 2 H, 2⁗,6⁗-H), 7.16−7.44 (m, 8 H, 3⁗,5⁗,4⁗-H, 5″,6″,7″,8″-H and 4′-H), 7.42 (d, J = 8.7 Hz, 2 H, 2‴,6‴-H), 8.12 (d, J = 8.7 Hz, 2 H, 3‴,5‴-H) ppm. ^{13}C NMR: δ = 36.7 (C-4″), 37.8 (C-1″), 40.2 (C-2″), 46.6 (C-3″), 106.5 (C-4), 115.9 (C-3′), 116.8 (C-1′), 120.5 (C-5′), 124.1 (C-2⁗,6⁗), 126.3 (C-8″), 128.6 (C-7″), 128.8 (C-2‴,6‴), 128.9 (C-3‴,5‴), 130.6 (C-6′ and C-5″), 130.64 (C-4′), 135.1 (C-10″), 135.5 (C-9″), 137.7 (C-5), 139.4 (C-1‴), 146.4 (C-1⁗), 152.7 (C-4‴), 153.0 (C-2′), 155.4 (C-3) ppm. EI-MS: *m*/*z* (rel. int., %) = 487 (100) [M$^{+\cdot}$], 486 (10) [M − H]$^+$, 470 (8), 457 (10) [M − NO]$^+$, 440 (3), 382 (2), 371 (12), 351 (54), 337 (7), 263 (4), 250 (21), 220 (4), 204 (3), 196 (10), 180 (4), 165 (4), 152 (3), 130 (4), 115 (11), 106 (15), 104 (9), 91 (7), 77 (21). $C_{31}H_{25}N_3O_3$ (487.2): calcd. C 76.37, H 5.17, N 8.62; found C 76.48, H 5.14, N 8.66.

Synthesis of 3-[2-(3-Arylnaphthyl)]-5-(2-hydroxyphenyl)-1-phenylpyrazoles 12a−c. Method A: DDQ (0.36 g, 1.57 mmol) was added to a solution of the appropriate 5-(2-hydroxyphenyl)-1-phenyl-3-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]pyrazole (**10a−c**, 3.15 × 10^{-1} mmol) in dry 1,4-dioxane (10 mL). The mixture was heated at reflux under nitrogen for several days (**10a** 5 days, **10b** 2 days and **10c** 6 days). After that period the solvent was evaporated to dryness and the solid residue was dissolved in chloroform and washed with an aqueous solution of potassium hydrogen carbonate. The organic layer was purified by thin layer chromatography with a light petroleum/ethyl acetate mixture as eluent. The 5-(2-hydroxyphenyl)-1-phenyl-3-[2-(3-arylnaphthyl)]pyrazoles **12a−c** were obtained as white crystals and were recrystallised in each case from a dichloromethane/cyclohexane mixture [**12a**, 25% (34.5 mg); **12b**, 59% (87.0 mg); **12c**, 17% (25.9 mg)].

Method B: DDQ (0.19 g, 8.29 × 10^{-1} mmol) and *p*-toluenesulfonic acid (0.026 g, 1.36 × 10^{-1} mmol) were added to a solution of the appropriate 5-(2-hydroxyphenyl)-1-phenyl-3-[2-(3-aryl-1,2,3,4-tetrahydronaphthyl)]pyrazole (**10a−c**, 6.81 × 10^{-1} mmol) in dry 1,4-dioxane (10 mL). The mixture was heated at reflux under nitrogen for several hours (3 h, **10a**; 2 h, **10b** and 7 h, **10c**). After that period the solid residue was filtered off and washed with chloroform. The organic layer was washed with water, the solvent was partially evaporated, and the mixture was purified by column chromatography: some unknown compounds were eluted with hexane and then the 5-(2-hydroxyphenyl)-1-phenyl-3-[2-(3-arylnaphthyl)]-pyrazoles **12a−c** were eluted, with a dichloromethane/hexane mixture (1:1) in each case. Pyrazoles **12a−c** were obtained as white crystals and were recrystallised in each case from a mixture of dichloromethane/cyclohexane [**12a**, 29% (86.5 mg); **12b**, 57% (181.7 mg); **12c**, 36% (11.4 mg)].

5-(2-Hydroxyphenyl)-1-phenyl-3-[2-(3-phenylnaphthyl)]pyrazole (12a): M.p. 160−162°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 5.03 (s, 1 H, 2′-O*H*), 5.81 (s, 1 H, 4-H), 6.75 (ddd, *J* = 7.4, 6.9, 0.8 Hz, 1 H, 5′-H), 6.81 (dd, *J* = 7.4, 1.8 Hz, 1 H, 6′-H), 6.92 (d, *J* = 8.0 Hz, 1 H, 3′-H), 7.16−7.24 (m, 1 H, 4′-H), 7.16−7.34 (m, 10 H, 2′′′,3′′′, 4′′′,5′′′,6′′′-H and 2′′′′,3′′′′,4′′′′,5′′′′,6′′′′-H), 7.50−7.56 (m, 2 H, 5′′,8′′-H), 7.87−7.99 (m, 2 H, 6′′,7′′-H), 7.89 (s, 1 H, 4′′-H), 8.48 (s, 1 H, 1′′-H) ppm. ^{13}C NMR: δ = 109.5 (C-4), 116.0 (C-3′), 116.5 (C-1′), 120.4 (C-5′), 124.4 (C-2′′′′,6′′′′), 128.4 (C-3′′′,5′′′), 126.3 (C-5′′), 126.6 (C-8′′), 127.3 (C-4′′′′), 127.4 (C-6′′,4′′′), 127.7 (C-2′′′,6′′′), 128.0 (C-7′′), 128.2 (C-1′′), 129.1 (C-4′′ and C-3′′′′,5′′′′), 129.9 (C-3′′), 130.5 (C-4′), 130.6 (C-6′), 132.7 (C-10′′), 133.0 (C-9′′), 136.8 (C-5), 138.9 (C-2′′), 139.5 (C-1′′′), 141.9 (C-1′′′′), 152.5 (C-3), 153.2 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 438 (100) [M$^{+\cdot}$], 437 (65) [M − H]$^+$, 421 (2), 361 (2), 351 (6), 331 (4), 317 (3), 302 (2), 250 (2), 243 (16), 228 (5), 215 (8), 196 (31), 180 (4), 167 (2), 152 (3), 118 (2), 104 (3), 91 (4), 77 (26). $C_{31}H_{22}N_2O$ (438.2): calcd. C 84.91, H 5.06, N 6.39; found C 84.54, H 5.05, N 6.26.

5-(2-Hydroxyphenyl)-3-{2-[3-(4-methoxyphenyl)naphthyl]}-1-phenylpyrazole (12b): M.p. 156−158°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.86 (s, 3 H, 4′′′-OC*H*$_3$), 5.14 (s, 1 H, 2′-O*H*), 5.84 (s, 1 H, 4-H), 6.76 (dt, *J* = 7.4, 0.6 Hz, 1 H, 5′-H), 6.83 (dd, *J* = 7.4, 1.8 Hz, 1 H, 6′-H), 6.93 (dd, *J* = 7.7, 0.6 Hz, 1 H, 3′-H), 7.23 (ddd, *J* = 7.7, 7.4, 1.8 Hz, 1 H, 4′-H), 6.96 (d, *J* = 8.5 Hz, 2 H, 3′′′,5′′′-H), 7.28−7.38 (m, 8 H, 2′′′,4′′′6′′′-H and 2′′′′,3′′′′,4′′′′,5′′′′,6′′′′-H), 7.49−7.52 (m, 2 H, 5′′,8′′-H), 7.88−7.96 (m, 2 H, 6′′,7′′-H), 7.86 (s, 1 H, 4′′-H), 8.46 (s, 1 H, 1′′-H) ppm. ^{13}C NMR: δ = 55.5 (4′′-O*C*H$_3$), 109.6 (C-4), 113.5 (C-3′′′,5′′′), 116.0 (C-3′), 116.6 (C-1′), 120.4 (C-5′), 124.4 (C-2′′′′,6′′′′), 126.2 (C-5′′), 126.5 (C-8′′), 127.3 (C-4′′′′), 127.6 (C-7′′), 128.2 (C-6′′), 128.5 (C-1′′), 128.9 (C-2′′′,6′′′), 129.0 (C-4′′), 130.2 (C-3′′), 130.6 (C-4′,6′), 138.6 (C-2′′), 131.0 (C-3′′′′,5′′′′), 132.6 (C-10′′), 133.1 (C-9′′), 134.1 (C-1′′′), 136.8 (C-5), 139.6 (C-1′′′′), 152.7 (C-3), 153.3 (C-2′), 159.1 (C-4′′′) ppm. EI-MS: *m*/*z* (rel. int.) = 468 (100) [M$^{+\cdot}$], 467 (57) [M − H]$^+$, 437 (1) [M − OCH$_3$)$^+$], 351 (3), 304 (2), 289 (2), 273 (14), 245 (2), 234 (7), 216 (3), 196 (26), 180 (3), 121 (2), 91 (2), 77 (21). $C_{32}H_{24}N_2O_2$ (468.2): calcd. C 82.03, H 5.16, N 5.98; found C 82.23, H 5.16, N 6.08.

5-(2-Hydroxyphenyl)-3-{2-[3-(4-nitrophenyl)naphthyl]}-1-phenylpyrazole (12c): M.p. 286−287°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 5.46 (s, 1 H, 2′-O*H*), 6.02 (s, 1 H, 4-H), 6.82 (ddd, *J* = 7.7, 7.4, 1.0 Hz, 1 H, 5′-H), 6.88 (dd, *J* = 7.7, 1.8 Hz, 1 H, 6′-H), 6.78 (dd, *J* = 7.6, 1.0 Hz, 1 H, 3′-H), 7.17−7.27 (m, 3 H, 4′-H, 4′′′-H and 4′′′′-H), 7.22 (d, *J* = 9.5 Hz, 2 H, 2′′′′,6′′′′-H), 7.55 (d, *J* = 9.5 Hz, 2 H, 3′′′′,5′′′′-H), 7.54−7.57 (m, 2 H, 5′′,8′′-H), 7.88−7.97 (m, 2 H, 6′′,7′′-H), 7.87 (s, 1 H, 4′′-H), 8.41 (s, 1 H, 1′′-H) ppm. ^{13}C NMR: δ = 109.5 (C-4), 116.1 (C-3′), 116.7 (C-1′), 120.6 (C-5′), 123.2 (C-3′′′,5′′′), 124.1 (C-2′′′′,6′′′′), 127.0 (C-5′′), 127.1 (C-8′′), 127.4 (C-4′′′′), 127.9 (C-7′′), 128.2 (C-6′′), 128.9 (C-3′′′′,5′′′′), 129.3 (C-4′′), 129.5 (C-3′′), 129.6 (C-1′′), 130.76 (C-4′ and C-6′), 130.77 (C-2′′′,6′′′), 132.8 (C-10′′), 133.1 (C-9′′), 138.0 (C-2′′,5), 128.9 (C-3′′′′,5′′′′), 139.5 (C-1′′′′), 146.9 (C-4′′′), 148.9 (C-1′′′), 151.6 (C-3), 153.1 (C-2′) ppm. EI-MS: *m*/*z* (rel. int., %) = 483 (100) [M$^{+\cdot}$], 484 (42) [M − H]$^+$, 466 (2) [M − OH]$^+$, 453 (10) [M − NO]$^+$, 436 (7), 419 (2), 391 (2), 371 (3), 351 (9), 316 (2), 291 (3), 264 (3), 250 (4), 227 (3), 209 (4), 196 (34), 180 (4), 165 (5), 152 (3), 104 (3), 91 (3), 77 (17). $C_{31}H_{21}N_3O_3$ (483.2): calcd. C 76.99, H 4.38, N 8.69; found C 77.16, H 4.69, N 8.39.

Synthesis of 3-(2-Hydroxyphenyl)-5-{2-[3-(4-methoxyphenyl)]-naphthyl}pyrazole (11b): DDQ (0.52 g, 2.30 mmol) and *p*-toluenesulfonic acid (0.017 g, 9.18 × 10^{-2} mmol) were added to a solution of 3-(2-hydroxyphenyl)-5-{2-[3-(4-methoxyphenyl)]-1,2,3,4-tetrahydronaphthyl}pyrazole (**9b**, 0.18 g, 4.59 × 10^{-1} mmol) in dry dioxane (15 mL). The reaction mixture was heated at reflux under nitrogen for 17 h. After that period, the DDQ was filtered off and washed with chloroform. The organic layer was washed with water and dried (sodium sulfate), and the solvent was evaporated to dryness. The obtained residue was purified by thin layer chromatography with hexane for the first elution and then a dichloromethane/hexane mixture (1:1). 3-(2-Hydroxyphenyl)-5-{2-[3-(4-methoxyphenyl)]naphthyl}pyrazole (**11b**) was obtained as a white solid (23.6 mg, 13%) and recrystallised from a dichloromethane/cyclohexane mixture. M.p. 207−209°C (recrystallised from a mixture of dichloromethane/cyclohexane). ^{1}H NMR: δ = 3.87 (s, 3 H, 4′′-OC*H*$_3$), 6.84 (s, 1 H, 4-H), 6.94 (ddd, *J* = 8.1, 7.8, 1.1 Hz, 1 H, 5′-H), 6.96 (dd, *J* = 6.6, 2.1 Hz, 2 H, 2′′′, 6′′′-H), 7.02 (dd, *J* = 8.2, 1.1 Hz, 1 H, 3′-H), 7.23 (dt, *J* = 8.2, 1.6 Hz, 1 H, 4′-H), 7.30 (dd, *J* = 6.6, 2.1 Hz, 2 H, 3′′′,5′′′-H), 7.55−7.58 (m, 2 H, 5′′,8′′-H), 7.60 (dd, *J* = 7.8, 1.6 Hz, 1 H, 6′-H), 7.86 (s, 1 H, 4′′-H), 7.88−7.94 (m, 2 H, 6′′,7′′-H), 8.14 (s, 1 H, 1′′-H), 9.34 (br. s, 1 H, N*H*), 10.71 (br. s, 1 H, 2′-O*H*) ppm. ^{13}C NMR: δ = 55.4 (4′′′-O*C*H$_3$), 101.8 (C-4), 114.3 (C-3′′′,5′′′), 116.5 (C-1′), 117.1 (C-3′), 119.3 (C-5′), 126.5 (C-6′), 126.8 (C-5′′), 127.4 (C-8′′), 127.7 (C-7′′), 127.9 (C-6′′), 129.2 (C-1′′), 129.3 (C-4′), 130.0 (C-4′′), 130.5 (C-2′′′,6′′′), 132.3 (C-9′′), 133.3 (C-10′′), 137.2 (C-1′′′), 143.4 (C-5), 152.1 (C-3), 155.98 (C-2′), 159.4 (C-4′′′) ppm. EI-MS: *m*/*z* (rel. int., %) = 392 (100) [M$^{+\cdot}$], 391 (64) [M − H]$^+$, 361 (3) [M − OCH$_3$]$^+$, 256 (6), 202 (10), 196 (5), 189 (6), 91 (6), 71 (6), 57 (15). EI-HRMS ($C_{26}H_{20}N_2O_2$): calcd. 392.1525, found 392.1525.

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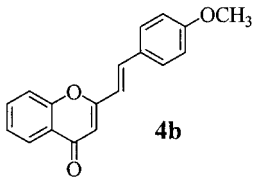

4b

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