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Synthesis and photochemistry of 3-(*o*-stilbeneyl)-4-H/Me/Ph-sydnones; intramolecular cyclization to 1,2-benzodiazepines and/or quinolines

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ABSTRACT

Stilbeneylsydnone derivatives were synthesized by a sequence of reactions in good yields. Irradiation of 3-stilbeneyl-4-methylsydnone **4** gives 1*H*-1,2-benzodiazepine derivative **7** as the main product along with 2-methylquinoline derivative **20**. Irradiation of 3-stilbeneyl-4-phenylsydnone **5** afforded only 1*H*-1,2-benzodiazepine derivative **8** whereas on irradiation of 4-unsubstituted 3-stilbeneylsydnone **3** no benzodiazepine derivative was detected. An efficient novel photochemical approach to 1*H*-1,2-benzodiazepines has been found from the new 3-(*o*-stilbeneyl)-4-substituted-sydnones via intramolecular 1,7-electrocyclization reaction of the photogenerated nitrile imines.

1. Introduction

In continuation of our work on photochemical intramolecular reactions of *o*-substituted stilbenes with pyrrole ring (**1**)[1,2] we extended our research to new heteroaromatic derivatives, sydnone derivatives **2**,[3] and **3**[4] (Fig. 1) as substrates for photochemical transformations to heteropolycyclic structures. Our basic idea was to introduce the general synthetic method to 1*H*-1,2-benzodiazepine derivatives (**6**–**8**) by intramolecular trapping of photochemically generated nitrile imines starting from 4-unsubstituted (**3**), 4-alkyl- (**4**), and 4-aryl-3-stilbeneylsydnone (**5**) (Fig. 1).

Benzodiazepines are a class of compounds belonging to psychoactive drugs with versatile sedative, hypnotic, anxiolytic, anticonvulsant, muscle relaxant, and amnesic properties.[5] They are seven-membered anelated hetarenes with two nitrogens in the seven-membered ring, which could be in [1,2], [1,3], [1,4], and [1,5] mutual position and they are synthesized on diverse methods.[6] So far the only photochemical pathway to 1*H*-1,2-benzodiazepine derivatives[6a,7] was photoinduced ring expansion reaction of *N*-iminoquinolinium ylide dimers. To the best of our knowledge there are no examples of their synthesis from sydnones. Sydnones[8] are the five-membered heterocycles. They belong to a class of dipolar compounds known as 'mesoionic' and can be represented as hybrids of a number of mesomeric/ionic forms. Since their early discovery by Earl and Mackney in 1935, sydnones have been widely studied,[9] not only because of their structure, physical properties, and reactivity, but also because of various biological properties.

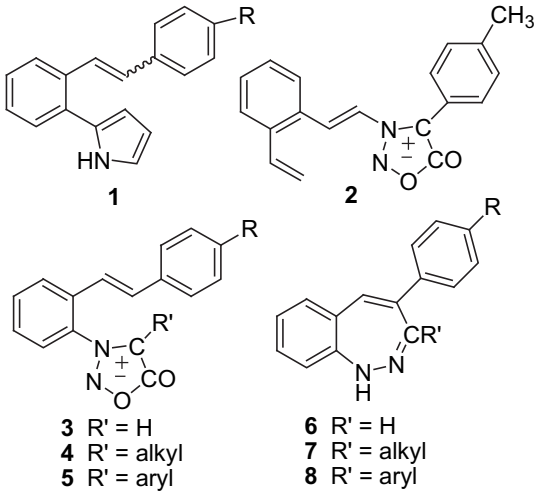

Fig. 1.

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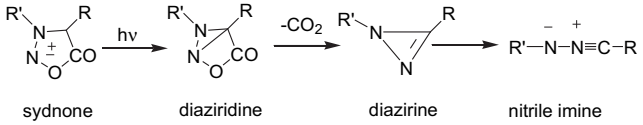
Numerous sydnones have been synthesized and their photochemical behavior studied.[10] All investigators have essentially substantiated the salient features of the mechanistic suggestions advanced by Krauch et al.[11] for the transformations of sydnones (Scheme 1).



Scheme 1.

In this work we describe for the first time the photochemical behavior of stilbeneylsydnones **3**–**5**, a system in which the sydnone ring at the position 3 is directly coupled to the *ortho*-position of the stilbene moiety. If the excitations of **3**–**5** would give the nitrile imine intermediates they should undergo intramolecular 1,7-electrocyclization to the target benzodiazepine derivatives **6**–**8** (Fig. 1). Namely, nitrile imines, generated thermally from *o*-alkenyl substituted arylhydrazonoyl halogenides,[12] gave benzodiazepine derivatives by 1,7-electrocyclization process.

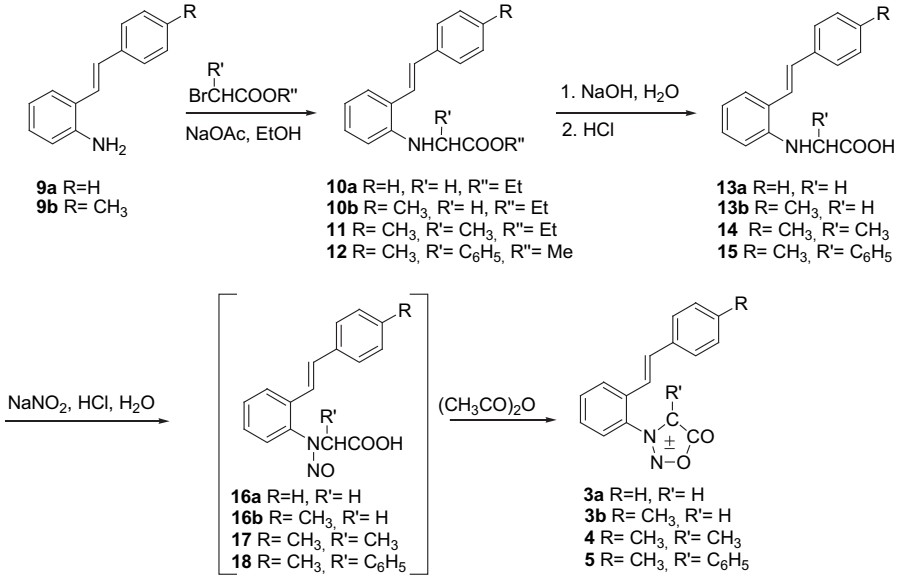
2. Results and discussion

Investigating compounds, 3-{2-[2-(phenyl/4-tolyl)ethenyl]phenyl}sydnones (**3a**,**b**) and 4-methyl/phenyl-3-{2-[2-(4-tolyl)ethenyl]phenyl}sydnones (**4**,**5**) were prepared by a sequence of reactions starting from *o*-aminostilbene **9a**/**9b** (Scheme 2). By substitution reaction with the esters of α-bromoacetic acid, α-bromopropionic acid or α-bromophenyl acetic acid, respectively, the esters of amino acids **10a**,**b**–**12** were obtained and hydrolyzed to amino acid derivatives **13a**,**b**–**15**. The obtained acids were transformed to *N*-nitroso glycines **16a**,**b**–**18** and without isolation, and further purification submitted to ring closure by dehydratation with acetic anhydride to sydnones **3**–**5**. All new compounds are spectroscopically characterized and identified.

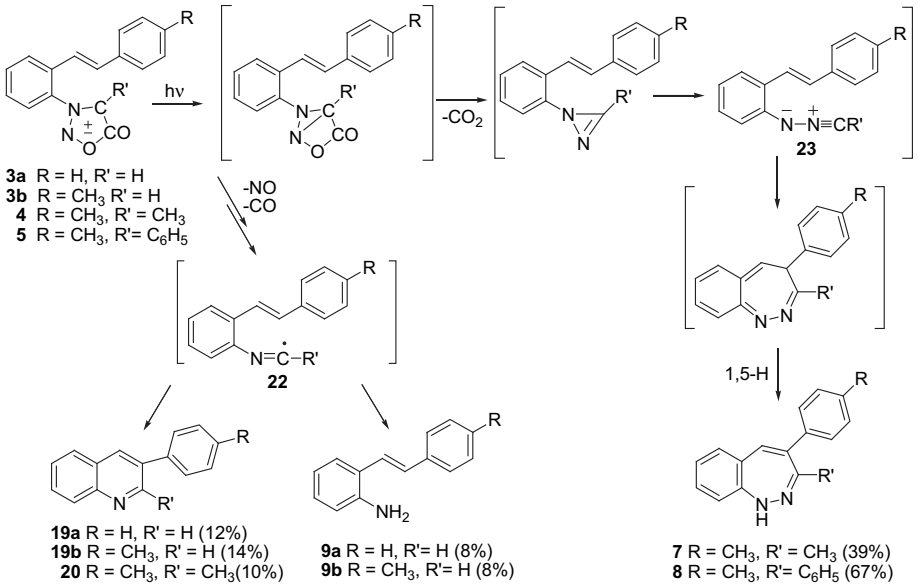
The irradiation experiments on **3**–**5** were performed in 10^{-3} M solutions of benzene and/or acetonitrile in a Rayonet reactor at 300 nm (**3**, **4**) and 350 nm (**5**) until the full conversion (based on ^{1}H NMR 60 min for **3** and **4**, 20 min for **5**) under anaerobic conditions. The photomixture of 3-substituted sydnones **3a**/**3b** contained a complex mixture of many products in small quantities. On separation by column chromatography it was possible to isolate only quinolines **19a**/**19b** and *trans*-*o*-aminostilbenes **9a**/**9b** (Scheme 3). No 1,2-benzodiazepine structure **6**, unsubstituted at the 3-position, was detected. Contrary to these results, the irradiation of 4-phenyl substituted 3-stilbeneylsydnone **5** gave only benzodiazepine derivative **8** in good yield whereas the irradiation of 4-methyl-3-stilbeneylsydnone **4** afforded a mixture of benzodiazepine **7** and quinoline **20** in 4:1 ratio, and moderate yield. The obtained new photoproducts are identified by MS and NMR using 2D techniques. The structure of quinoline **20** was obvious from its MS spectrum, where the *m*/*z* 233 indicated on loss of CO and NO, in addition to its ^{1}H and ^{13}C NMR spectra. Finally, its structure is irrevocably confirmed by its independent synthesis using the described method for some other derivatives.[13] The structures of known compounds **19a**,**b** were confirmed by comparison of their spectroscopic data in literature.[14] The compounds **7** and **8** showed in MS spectrum *m*/*z* 248 and *m*/*z* 310, respectively, which indicated on loss of CO_2 and benzodiazepine structure. Combining the data from IR, ^{1}H, and ^{13}C NMR using the additional COSY and NOESY techniques the benzodiazepines **7** and **8** are completely analyzed.

On irradiation of 4-phenyl derivative **5** possible formation of the side product, 2-phenylquinoline derivative was ruled out by comparison the NMR spectra of photomixture with the ^{1}H NMR spectrum of, for this purpose, prepared 2,3-diphenylquinoline (**21**, Experimental section).

It is obvious from the experiments that in our fully conjugated system several competitive processes are operating. The main pathway of the reaction depends on the substituent in the position 4 of the starting sydnone. The desired benzodiazepine derivatives **7** and **8** (Scheme 3) are formed in good yields from 3,4-disubstituted sydnones by 1,7-electrocyclization of nitrile imines **23**, formed by initial CO_2 elimination, followed by 1,5-H shift and formation of fully unsaturated seven-membered ring. As depicted in Scheme 3 the plausible formation mechanism of the quinolines **19** and **20** might be best explained via imine radical **22**, formed by NO and/or



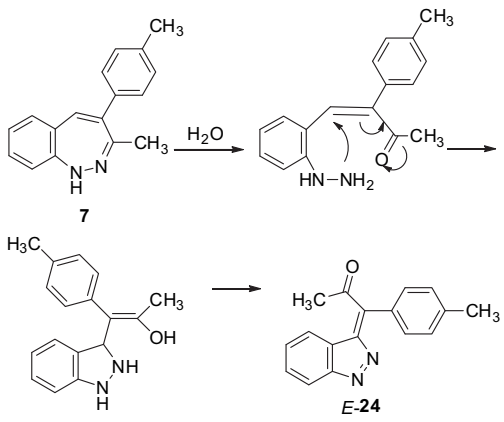
Scheme 2.



Scheme 3.

CO extrusion, followed by an addition to the stilbene double bond. This is in accordance with the literature data for the photolysis of 3-phenylsydnone where the imine radical intermediate, in contrast to 3,4-diphenylsydnone, has been detected by electron spin resonance spectroscopy.[15] However, bearing in mind the experimental conditions and impossibility to give an exact number of radicals generated in the photochemical process, the authors did not rule out also the possibility of nitrile imine intermediates formation. Aminostilbenes **9** are probably by-products formed by hydrolysis of some intermediates.

It should be mentioned that whereas the phenyl derivative **8** is a stable compound the methyl derivative **7** decomposes during the purification in favor of formation of one other compound, indazole derivative *E*-**24** (Scheme 4). The compound was isolated and identified by spectroscopic methods. The *E*-configuration was based on NOESY experiments. The interaction was seen between the methyl protons of the acetyl group at 2.31 ppm and aromatic doublet at 7.15 ppm. A plausible mechanism of its formation is depicted in Scheme 4. It could be assumed that the compound **7** undergoes hydrolysis and ring opening followed by five-membered ring closure and subsequent dehydrogenation.



Scheme 4.

3. Conclusion

We have found a new synthetic route to 3-substituted 1*H*-1,2-benzodiazepines by photolysis of 3-stilbeneyl-4-substituted sydnones and 1,7-electrocyclization of the formed nitrile imines. Although in case of only 3-substituted sydnone derivative **3** expected benzodiazepine structure **6** was not isolated the formation of nitrile imine intermediate **23** could not be completely excluded. If the benzodiazepine derivative **6** had been formed, but in small quantities, it could have been disintegrated during working up procedures.

4. Experimental

4.1. General

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-600 Spectrometer at 300 and 600 MHz. All NMR spectra were measured in CDCl3 or DMSO using tetramethylsilane as reference. UV spectra were measured on a Varian Cary 50 UV/VIS Spectrophotometer. IR spectra were recorded on FTIR-ATR Vertex 70 Bruker or Perkin–Elmer M-297 spectrophotometer. Mass spectra were obtained on Extrel FT MS 2001 DD, Auto Spec Q (VG Analytical Manchester, GB), on Platform LCZ (Micromass, UK) and/or on a Varian Saturn 2200 equipped with Factor Four Capillary Column VF-5ms. Irradiations were performed in a quartz or Pyrex vessel in a Rayonet reactor equipped with RPR 3000 and/or 3500 A° lamps. All irradiation experiments were carried out in deaerated solutions by bubbling a stream of argon for 15 min prior to irradiation. Melting points were obtained using an Original Kofler Mikroheitztisch apparatus (Reichert, Wien) and are uncorrected. Elemental analyses were carried out on Perkin–Elmer, Series II, CHNS Analyzer 2400 at Rudjer Bošković Institute. Silica gel (Merck 0.063–0.2 mm) was used for chromatographic purifications. Thin layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. Solvents were purified by distillation.

Compounds **3a** and **3b** were prepared according to literature procedure for **3b**[3] however no physical and spectral data were given for the intermediates: **10b** and **13b**. All reported yields in this work are isolated yields. Aminostilbenes **9a**,**b** are prepared according to literature.[3,16]

4.2. Synthesis of stilbeneylsidnones 3–5

*4.2.1. Preparation of esters **10**–**12**.*

*4.2.1.1. General procedure for **10a**/**10b** and **11**.* A solution of corresponding amine **10a**/**10b** (0.0174 mol), anhydrous sodium acetate (2.14 g, 0.0261 mol, 1.5 equiv), and ethyl ester of corresponding acid [α-bromoacetic acid (0.0174 mol) for **10a**/**10b** or α-bromopropionic acid (0.0174 mol) for **11**] was heated at reflux for 18 h. Then cold water (70 mL) was added with stirring and cooling in ice bath. The reaction mixture was neutralized with $NaHCO_3$ and then extracted with dichloromethane (3×25 mL). The dichloromethane extracts were dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography on silica gel using dichloromethane/petroleum ether (6/4) mixture as eluent. In first fractions ester was isolated and then unreacted amine.

*4.2.1.1.1. trans-Ethyl-N-{2-[2-phenylethenyl]phenyl}aminoacetate, **10a**.* Yield 2.05 g (42.0%), yellow solid, mp 52 °C, methanol; TLC R_f=0.42 (6/4 CH_2Cl_2/petroleum ether). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 247 (17,705), 287 (16,882), 346 (10,620). IR (KBr)ν_{max}/cm^{-1}: 3417 (NH), 3059, 3025, 2982, 2930 (CH), 1741 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.56 (d, 2H, *J*=7.5 Hz), 7.46–7.20 (m, 6H), 7.03 (d, 1H, *J*=16.2 Hz), 6.85 (t, 1H, *J*=7.5 Hz), 6.59 (d, 1H, *J*=7.5 Hz), 4.29 (q, 2H, *J*=7.2 Hz), 3.98 (s, 2H), 1.33 (t, 3H, *J*=7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 170.9 (s, C=O), 144.2 (s), 137.3 (s), 130.9 (d), 128.7 (d), 128.5 (d), 127.4 (d), 127.3 (d), 126.3 (d), 124.2 (s), 123.8 (d), 118.2 (d), 111.0 (d), 61.2 (t), 45.8 (t), 14.0 (q). MS *m*/*z*: 281 (M$^+$, 56.9%). Elemental analysis calcd (%) $C_{18}H_{19}NO_2$ (M_r=281.35): C 76.84, H 6.81, N 4.98%; found C 77.10, H 6.81, N 5.08%.

*4.2.1.1.2. trans-Ethyl-N-{2-[2-(4-methylphenyl)ethenyl]phenyl}aminoacetate, **10b**.* Yield 2.84 g (55.4%), yellow oil; TLC R_f=0.42 (6/4 CH_2Cl_2/petroleum ether). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 201 (21,128), 278 (18,270), 294 (18,770). IR (neat) ν_{max}/cm^{-1}: 3415 (NH), 3022, 2981, 2921 (CH), 1740 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.48–7.44 (m, 3H), 7.28–7.20 (m, 4H), 7.01 (d, 1H, *J*=16.2 Hz), 6.86 (t, 1H, *J*=7.8 Hz), 6.59 (d, 1H, *J*=7.8 Hz), 4.30 (q, 2H, *J*=6.9 Hz), 3.98 (s, 2H), 2.41 (s, 3H), 1.34 (t, 3H, *J*=6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 170.9 (s, C=O), 144.1 (s), 137.3 (s), 134.6 (s), 130.9 (d), 129.2 (d), 128.5 (d), 127.2 (d), 126.3 (d), 124.5 (s), 122.7 (d), 118.3 (d), 111.0 (d), 61.2 (t), 45.9 (t), 21.1 (q), 14.0 (q). MS *m*/*z*: 295 (M$^+$, 82.3%).

*4.2.1.1.3. trans-Ethyl-N-{2-[2-(4-methylphenyl)ethenyl]phenyl}amino-(α-methyl)acetate, **11**.* Yield 2.76 g (51.3%), yellow solid, mp 46–47 °C; TLC R_f=0.43 (6/4 CH_2Cl_2/petroleum ether). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 205 (19,953), 216 (19,952), 247 (15,849), 289 (18,621), 349 (11,749). IR(KBr) ν_{max}/cm^{-1}: 3371 (NH), 3011, 2982, 2937, 2871 (CH-ar), 1732 (CO). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.42 (d, 2H, *J*=8.0 Hz), 7.39 (d, 1H, *J*=7.4 Hz), 7.14–7.18 (m, 4H), 6.95 (d, 1H, *J*=16.0 Hz), 6.80 (t, 1H, *J*=7.4 Hz), 6.61 (d, 1H, *J*=7.4 Hz), 4.19 (q, 2H, *J*=7.2 Hz), 4.16 (q, 1H, *J*=6.9 Hz), 2.37 (s, 3H), 1.51 (d, 3H, *J*=6.9 Hz), 1.25 (t, 3H, *J*=7.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 174.6 (s, CO), 144.0 (s), 137.5 (s), 134.9 (s), 131.1 (d), 129.4 (d), 128.7 (d), 127.6 (d), 126.5 (d), 125.0 (s), 123.2 (d), 118.6 (d), 111.8 (d), 61.2 (t), 52.4 (d), 21.3 (q), 19.1 (q), 14.2 (q). MS *m*/*z*: 309 (M$^+$, 100%). Elemental analysis calcd $C_{20}H_{23}NO_2$ (M_r=309): C 77.64, H 7.49, N 4.53%; found C 77.80, H 7.58, N 4.56%.

*4.2.1.2. Preparation of trans-methyl-N-{2-[2-(4-methylphenyl)ethenyl]phenyl}amino-(α-phenyl)acetate, **12**.* A solution of amine **9b** (500 mg, 2.4 mmol), anhydrous sodium acetate (300 mg, 3.6 mmol), and methyl ester of α-bromophenyl acetic acid (950 mg, 6.0 mmol) was heated at reflux for 7 h. After cooling, light yellow crystals were precipitated from the solution and collected by filtration. The crude product was purified by column chromatography on silica gel using dichloromethane/petroleum ether (7/3) mixture as eluent. In first fractions was isolated ester **12** and then unreacted amine.

*4.2.1.2.1. trans-Methyl-N-{2-[2-(4-methylphenyl)ethenyl]phenyl}amino-(α-phenyl)acetate, **12**.* Yield 634 mg (74.0%), yellow solid, mp 147 °C. TLC R_f=0.62 (6/4 CH_2Cl_2/petroleum ether). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 249 (8953), 289 (9725), 343 (6433). IR (KBr) ν_{max}/cm^{-1}: 3434 (NH), 2948 (CH), 1737 (CO). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.51 (d, 1H, *J*=7.6 Hz), 7.44 (d, 2H, *J*=7.9 Hz), 7.41–7.31 (m, 5H), 7.24 (d, 1H, *J*=16.0 Hz, H-7/8), 7.18 (d, 2H, *J*=7.9 Hz), 7.03 (t, 1H, *J*=7.6 Hz), 6.99 (d, 1H, *J*=16.0 Hz, H-7/8), 6.75 (t, 1H, *J*=7.6 Hz), 6.41 (d, 1H, *J*=7.6 Hz), 5.13 (s, 1H, CH), 3.74 (s, 3H, CH_3), 2.37 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 172.6 (s, CO), 143.4 (s), 137.8 (s), 137.7 (s), 135.0 (s), 131.4 (d), 129.6 (d), 129.1 (d), 128.8 (d), 128.5 (d), 127.6 (d), 127.4 (d), 126.7 (d), 124.8 (s), 123.1 (d), 118.6 (d), 112.3 (d), 61.1 (q, CH_3-est), 53.1 (d, CH), 21.5 (q, CH_3). MS *m*/*z*: 357 (M$^+$, 100%). Elemental analysis calcd $C_{24}H_{23}NO_2$ (M_r=357): C 80.64, H 6.49, N 3.92%; C 80.36, H 6.69, N 4.02%.

*4.2.2. Preparation of acids **13**–**15**.*

*4.2.2.1. General procedure for **13a**/**13b** and **14**.* Suspension of corresponding ester (0.0115 mol) and NaOH (0.552 g, 0.0138 mol) dissolved in water (30 mL) was heated for 3 h at reflux after which time the reaction mixture was homogeneous. After cooling the reaction mixture was extracted with dichloromethane (3×5 mL). The aqueous layer was acidified to pH 4 with concentrated hydrochloric acid. A white solid precipitated from the solution and collected by filtration.

*4.2.2.1.1. trans-N-{2-[2-Phenylethenyl]phenyl}aminoacetic acid, **13a**.* Yield 2.25 g (77.2%); white solid, mp 138–139 °C. IR (KBr) ν_{max}/cm^{-1}: 3424 (NH), 1725 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.53 (d, 2H, *J*=7.5 Hz), 7.44–7.18 (m, 7H), 7.00 (d, 1H, *J*=16.2 Hz), 6.85 (t, 1H, *J*=7.5 Hz), 6.58 (d, 1H, *J*=7.5 Hz), 4.25 (br s, 1H, NH), 4.00 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 175.7 (s, C=O), 143.4 (s), 136.9 (s), 130.9 (d), 128.4 (d), 128.2 (d), 127.2 (d), 127.1 (d), 126.0 (d), 124.1 (s), 123.3 (d), 118.4 (d), 110.8 (d), 45.3 (t). MS *m*/*z*: 253 (M$^+$, 42.5%). Elemental analysis calcd $C_{16}H_{15}NO_2$ (M_r=253.30): C 75.87, H 5.97, N 5.53%; found C 76.25, H 5.79, N 5.83%.

*4.2.2.1.2. trans-N-{2-[2-(4-Methylphenyl)ethenyl]phenyl}aminoacetic acid, **13b**.* Yield 2.30 g (75.0%), white solid, mp 117–118 °C. UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 203 (13,736), 216 (13,425), 250 (11,987), 289 (12,522). IR (KBr) ν_{max}/cm^{-1}: ~3300–2500 (asos. COOH), 3428 (NH), 3023, 2918, 2754 (CH), 1727 (C=O). ^{1}H NMR (600 MHz, DMSO) δ ppm: 7.52 (d, 2H, *J*=7.8 Hz), 7.44 (d, 1H, *J*=7.8 Hz), 7.34 (d, 1H, *J*=16.2 Hz), 7.17 (d, 2H, *J*=7.8 Hz), 7.05 (t, 1H, *J*=7.8 Hz), 6.97 (d, 1H, *J*=16.2 Hz), 6.61 (t, 1H, *J*=7.8 Hz), 6.40 (d, 1H, *J*=7.8 Hz), 3.85 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ ppm: 172. 8 (s, CO), 145.3 (s), 136.6 (s), 135.0 (s), 129.2 (d), 128.6 (d), 128.3 (d), 126.5 (d), 125.8 (d), 123.2 (d), 122.5 (s), 116.6 (d), 110.5 (d), 44.8 (t), 20.9 (q). MS *m*/*z*: 267 (M$^+$, 49.7%). Elemental analysis calcd $C_{17}H_{17}NO_2$ (M_r=267.32): C 76.38, H 6.41, N 5.24%; found C 76.22, H 6.29, N 5.19%.

*4.2.2.1.3. trans-N-{2-[2-(4-Methylphenyl)ethenyl]phenyl}amino-(α-methyl)acetic acid, **14**.* Yield 3.07 g (95.0%), white solid, mp 115–118 °C. UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 203 (20,417), 215 (19,055), 253 (16,218), 289 (17,378), 349 (10,000). IR (KBr) ν_{max}/cm^{-1}: ~3300–2500 (asoc. COOH), 3407 (NH), 3020, 2978, 2922, 2875 (CH-ar), 1710 (CO). ^{1}H NMR (600 MHz, DMSO) δ ppm: 7.55 (d, 2H, *J*=8.0 Hz), 7.47 (d, 1H, *J*=7.8 Hz), 7.44 (d, 1H, *J*=16.0 Hz), 7.18 (d, 2H, *J*=8.0 Hz), 7.08 (t, 1H, *J*=7.5 Hz), 6.98 (d, 1H, *J*=16.0 Hz), 6.65 (t, 1H, *J*=7.5 Hz), 6.47 (d, 1H, *J*=7.8 Hz), 4.02 (q, 1H, *J*=7.3 Hz), 2.31 (s, 3H), 1.48 (d, 3H, *J*=7.4 Hz). ^{13}C NMR (150 MHz, DMSO) δ ppm: 176.5 (s, CO), 145.3 (s), 137.0 (s), 135.4 (s), 129.6 (d), 129.0 (d), 128.7 (d),

127.1 (d), 126.3 (d), 123.7 (d), 123.3 (s), 117.4 (d), 111.5 (d), 51.8 (d), 21.3 (q), 18.6 (q). MS *m*/*z*: 281 (M^+, 100%).

4.2.2.2. Preparation of trans-N-{2-[2-(4-methylphenyl)ethenyl] phenyl}amino-(α-phenyl)acetic acid, ***15****.* In a suspension of **12** (0.25 g, 0.7 mmol) and NaOH (0.04 g, 1.1 mmol) dissolved in water (20 mL), ethanol (15 mL) was added and reaction mixture was heated for 24 h at reflux, after which time the reaction mixture was homogeneous. Volume was reduced by evaporation to~1/3 V, then the reaction mixture was extracted with dichloromethane (3×5 mL). The aqueous layer was acidified to pH 4 with concentrated hydrochloric acid. A white solid precipitated from the solution and was collected by filtration. Yield on **15** is 183 mg (76.0%); white solid, mp 191–193 °C. IR (KBr) ν_{max}/cm^{-1}: ~3300–2500 (asoc. COOH), 3436 (NH), 3028, 2914 (CH), 1707 (CO). ^{1}H NMR (300 MHz, DMSO) δ ppm: 7.56–7.52 (m, 4H), 7.44–7.29 (m, 5H), 7.20 (d, 2H, *J*=7.9 Hz), 7.01 (d, 1H, *J*=15.6 Hz), 6.99 (t, 1H, *J*=7.9 Hz), 6.55 (t, 1H, *J*=7.9 Hz), 6.46 (d, 1H, *J*=7.9 Hz), 5.17 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ ppm: 172.8 (s, CO), 143.5 (s), 138.4 (s), 136.7 (s), 134.6 (s), 129.4 (d), 129.2 (d), 128.4 (d), 128.3 (d), 127.7 (d), 127.4 (d), 126.5 (d), 126.4 (d), 123.6 (s), 123.1 (d), 117.4 (d), 112.0 (d), 59.7 (d, CH), 20.8 (q, CH_3). MS *m*/*z*: 344 (M^++1, 100%).

4.2.3. Preparation of sydnones ***3–5****.*

4.2.3.1. Preparation of trans-3-{2-[2-phenylethenyl]phenyl}sydnone, ***3a****.* A suspension of **13a** (400 mg, 1.6 mmol) and sodium nitrite (165 mg, 2.4 mmol) in water (1 mL) was cooled down and stirred at 0 °C for 1 h. Then the reaction mixture was acidified to pH 4 by the dropwise addition of concentrated hydrochloric acid. A light brown solid precipitated from the solution. The mixture was stirred for additional 3 h with cooling at 0 °C and then dichloromethane (5 mL) was added. The organic layer was separated and combined with additional dichloromethane extracts (3×5 mL), dried, and concentrated. Acetic anhydride (2 mL) was added to the residue and reaction mixture was put on dark place for seven days. Then water (50 mL) was added with stirring and cooling on the ice bath. After neutralization with $Na_2CO_3 \cdot H_2O$, dichloromethane (10 mL) was added. The organic layer was separated and combined with additional dichloromethane extraction (3×5 mL), dried, and concentrated. Sydnone was isolated from crude mixture by column chromatography using dichloromethane as eluent. Compound **3a**: 392 mg (92.7%), white solid, mp 125–127 °C; TLC R_f=0.24 (CH_2Cl_2). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 223 (17,326), 298 (30,724). IR (KBr) ν_{max}/cm^{-1}: 3145 (CH-syd), 1752 (CO-syd). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.90 (d, 1H, *J*=7.98 Hz), 7.67 (m, 1H, *J*=7.98 Hz), 7.50–7.27 (m, 7H), 7.21 (d, 1H, *J*=16.2 Hz), 6.86 (d, 1H, *J*=16.1 Hz), 6.57 (s, 1H, H-Syd). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 168.3 (s, CO-syd), 135.4 (s), 134.2 (d), 132.6 (s), 132.0 (d), 131.9 (s), 128.6 (d), 128.5 (d), 128.6 (d), 126.8 (d), 126.6 (d), 125.1 (d), 119.5 (d), 97.8 (d, *C*-syd). MS *m*/*z*: 264 (M^+, 35.6%), 234 (87.3%), 206 (100%), 178 (45.8%). Elemental analysis calcd $C_{16}H_{12}N_2O_2$ (M_r=264.28): C 72.72, H 4.58, N 10.60%; found C 72.73, H 4.46, N 10.57%.

4.2.3.2. Preparation of trans-3-{2-[2-(4-methylphenyl)ethenyl] phenyl}sydnone, ***3b*** *from* ***13b****.* A suspension of **13b** (1.08 g, 4.1 mmol) in water (25 mL) and hydrochloric acid (1.5 mL) was cooled down and stirred at 0 °C for 2 h. Then a suspension of sodium nitrite (423 mg, 6.2 mmol) in water (3 mL) was added dropwise. Reaction mixture was stirred with cooling for 1 h and then additional amount of sodium nitrite (141 mg in 3 mL of water) was added and cooling with stirring was continued for an hour. Then dichloromethane (15 mL) was added and the organic layer was separated and combined with additional dichloromethane extracts (3×10 mL), dried, and concentrated. Acetic anhydride (5 mL) was added in residue, and reaction mixture was put on dark place for seven days. Then water (100 mL) was added with stirring and cooling in ice bath. After neutralization with $Na_2CO_3 \cdot H_2O$, dichloromethane (15 mL) was added. The organic layer was separated and combined with additional dichloromethane extracts (3×10 mL), dried, and concentrated. Sydnone **3b** was isolated from the crude mixture by column chromatography using dichloromethane as eluent. Spectroscopic data of isolated **3b** are identical with literature data:[3] 1.04 g (91.4%), yellow solid, mp 162–164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.89 (d, 1H, *J*=8.1 Hz), 7.64 (m, 1H, *J*=7.95 Hz), 7.48–7.46 (d, 2H), 7.33 (d, 2H, *J*=8.2 Hz), 7.17 (d, 2H, *J*=8.2 Hz), 7.17 (d, 1H, *J*=16.2 Hz), 6.80 (d, 1H, *J*=16.2 Hz), 6.55 (s, 1H, CH-syd), 2.36 (s, 3H, CH_3).

4.2.3.3. General procedure for the preparation of sydnones ***4*** *and* ***5****.* We have found that the compounds **4** and **5** could be prepared from corresponding esters, **11** and **12**, respectively, without isolation and purification of their acids (**14**, **15**), and nitroso derivatives (**17**, **18**). After hydrolysis of esters (1 mmol, the procedure is described in 4.2.2.) and extraction with dichloromethane, to the aqueous layer $NaNO_2$ (3 equiv calculated on amount of starting ester) was added. After stirring for 30 min the reaction mixture was put in an ice bath and acidified to pH 4 by dropwise addition of concentrated hydrochloric acid. A light brown solid precipitated from the solution. The mixture was stirred with cooling for additional 3 h and then dichloromethane was added. The organic layer was separated and combined with additional dichloromethane extracts, dried, and concentrated. Acetic anhydride was added in residue and reaction mixture was put on dark place for 7 days. Then water (50 mL) was added with stirring and cooling on the ice bath. After neutralization with $Na_2CO_3 \cdot H_2O$, dichloromethane (20 mL) was added. The organic layer was separated and combined with additional dichloromethane extracts (3×15 mL), dried, and concentrated. Sydnones were isolated from crude mixture by column chromatography using dichloromethane.

4.2.3.3.1. trans-4-Methyl-3-{2-[2-(4-methylphenyl)ethenyl]phenyl}sydnone, ***4****.* Yield 172 mg (58.8%); white solid, mp 146–147 °C; TLC R_f=0.18 (CH_2Cl_2). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 203 (22,909), 231 (14,125), 312 (28,184). IR (KBr) ν_{max}/cm^{-1}: 3060, 3033, 2995, 2945, 2912 (CH), 1733 (CO-syd). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.92 (d, 1H, *J*=7.9 Hz), 7.67 (t, 1H, *J*=7.7 Hz), 7.49 (t, 1H, *J*=7.7 Hz), 7.37 (d, 1H, *J*=7.9 Hz), 7.31 (d, 2H, *J*=8.0 Hz), 7.17–7.20 (m, 3H), 6.58 (d, 1H, *J*=16.1 Hz), 2.37 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 168.7 (s, CO-syd), 139.4 (s), 134.2 (d), 133.5 (s), 132.5 (s), 131.8 (d), 130.6 (s), 129.2 (d), 127.9 (d), 126.5 (d), 126.3 (d), 125.9 (d), 118.0 (d), 106.4 (s, *C*-syd), 20.8 (q), 6.9 (q). MS *m*/*z*: 292 (M^+, 100%), 248 (11), 207 (60). Elemental analysis calcd $C_{18}H_{16}N_2O_2$ (M_r=292): C 73.95, H 5.52, N 9.58%; found C 73.79, H 5.60, N 9.64%.

4.2.3.3.2. trans-4-Phenyl-3-{2-[2-(4-methylphenyl)ethenyl]phenyl}sydnone, ***5****.* Yield 64 mg (18.0%), white solid, mp 132–133 °C; R_f=0.46 (CH_2Cl_2). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 233 (15,169), 315 (22,959). IR (KBr) ν_{max}/cm^{-1}: 2925 (CH), 1737 (CO). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.86 (d, 1H, *J*=7.8 Hz), 7.66 (t, 1H, *J*=7.8 Hz), 7.45 (t, 1H, *J*=7.8 Hz), 7.42 (d, 1H, *J*=7.8 Hz), 7.28–7.27 (m, 2H), 7.21–7.19 (m, 5H), 7.13 (d, 2H, *J*=7.8 Hz), 7.02 (d, 1H, *J*=16.0 Hz), 6.62 (d, 1H, *J*=16.0 Hz), 2.34 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 167.1 (s, CO-syd), 139.3 (s), 134.8 (d), 134.5 (s), 133.3 (s), 132.5 (d), 132.4 (s), 129.7 (d), 128.9 (d), 128.9 (d), 128.7 (d), 127.2 (d), 127.1 (d), 126.9 (d), 126.6 (d), 124.7 (s), 119.0 (d), 109.5 (s, *C*-syd), 21.52 (q). MS *m*/*z*: 355 (M^++1, 32%). Elemental analysis calcd $C_{23}H_{18}N_2O_2$ (M_r=354): C 77.95, H 5.12, N 7.90%; found C 77.62, H 5.32, N 8.01%.

4.3. Irradiation experiments

4.3.1. Irradiation of ***3a*** *and* ***3b****.* A solution of **3a** or **3b** in benzene or acetonitrile (**3a**: 5.0×10^{-3} M; **3b**: 4.7×10^{-3} M) was purged with argon for 15 min and irradiated at 300 nm in a Rayonet reactor in

a quartz tube for 60 min. Solvent was removed in vacuum and the oily residue subjected to chromatography on silica gel column and thin layer chromatography using dichloromethane and/or dichloromethane/diethyl ether (9.8/0.2) mixture as eluent affording quinoline **19a**[14] and **19b**,[14] respectively, and aminostilbenes **9a**/**9b**.

*4.3.2. Irradiation of trans-**4**.* A solution of *trans*-**4** (50 mg, 0.17 mmol) in benzene (38 mL) was purged with argon for 15 min and irradiated at 300 nm in a Rayonet reactor in a quartz tube for 40 min. The solvent was removed in vacuo and the oily residue subjected to chromatography on silica gel column using dichloromethane and/or dichloromethane/diethyl ether (9.8/0.2) mixture as eluent. Quinoline **20** and benzodiazepine **7** were isolated.

*4.3.2.1. 2-Methyl-3-(4-methyphenyl)quinoline, **20**.* Yield 4 mg (10.0%); yellow oil, TLC R_f=0.19 (9.8/0.2 CH_2Cl_2/Et_2O). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 214 (37,802), 232 (38,984), 320 (4616). IR (neat) ν_{max}/cm^{-1}: 3053, 2920 (CH). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 8.06 (d, 1H, J=8.0 Hz), 7.95 (s, 1H), 7.78 (d, 1H, J=8.0 Hz), 7.69 (t, 1H, J=8.0 Hz), 7.50 (t, 1H, J=8.0 Hz), 7.30 (d, 2H, J=8.3 Hz), 7.29 (d, 2H, J=8.3 Hz), 2.67 (s, 3H, CH_3) 2.45 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 157.6 (s), 147.0 (s), 137.4 (s), 137.0 (s), 136.0 (d), 135.8 (s), 129.2 (d), 129.1 (d), 129.1 (d), 128.5 (d), 127.4 (d), 127.0 (s), 126.0 (d), 24.6 (q, CH_3), 21.2 (q, CH_3). MS m/z: 233 (M^+, 100%). Elemental analysis, calcd for $C_{17}H_{15}N$ (M_r=233.12): C 87.52, H 6.48, N 6.00%; found C 87.31, H 6.02, N 6.13%.

*4.3.2.2. 3-Methyl-4-(4-methylphenyl)-1H-1,2-benzodiazepine, **7**.* Yield 16 mg (39.0%); oily matter; TLC R_f=0.10 (9.8/0.2 CH_2Cl_2/Et_2O). IR (KBr) ν_{max}/cm^{-1}: 3324 (NH), 3023, 2921, 2852 (CH). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.24–7.19 (m, 6H), 7.09 (t, 1H, J=7.8 Hz), 7.04 (s, 1H), 6.85 (d, J=7.8 Hz), 6.50 (br s, NH), 2.38 (s, 3H, CH_3) 1.88 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 162.3 (s), 156.3 (s), 148.1 (s), 143.5 (s), 137.8 (s), 135.3 (d), 131.2 (s), 129.7 (d), 129.5 (d), 129.3 (d), 127.7 (d), 124.7 (d), 120.2 (d), 21.4 (q, CH_3), 21.2 (q, CH_3). MS m/z: 248 (M^+, 100%).

*4.3.3. Irradiation of trans-**5**.* A solution of **5** (50 mg, 0.14 mmol) in benzene (41 mL) was purged with argon for 15 min and irradiated at 350 nm in a Rayonet reactor in a Pyrex tube for 20 min. The solvent was removed in vacuo and the oily residue subjected to chromatography on silica gel column using dichloromethane and/or dichloromethane/diethyl ether (9.8/0.2) mixture as eluent affording 4-(4-*Methylphenyl*)-3-*phenyl*-1*H*-1,2-*benzodiazepine*, **8**: 43 mg (67.0%), yellow solid, mp 147–148 °C; R_f=0.18 (CH_2Cl_2). UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 245 (20,585), 290 (15,994). IR (KBr) ν_{max}/cm^{-1}: 3318 (NH), 3055, 3016, 2912, 2852 (CH). ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.47 (s, 1H), 7.38 (d, 2H, J=7.6 Hz), 7.27 (d, 1H, J=7.6 Hz), 7.21 (t, 1H, J=7.6), 7.16–7.10 (m, 6H), 7.01 (d, 2H, J=7.6 Hz), 6.88 (d, 1H, J=7.6 Hz), 6.81 (br s, 1H, NH), 2.25 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 163.5 (s), 149.2 (s), 141.7 (s), 137.6 (s), 137.5 (s), 137.5 (d), 136.7 (s), 131.5 (s), 129.8 (d), 129.8 (d), 129.3 (d), 128.8 (d), 128.8 (d), 128.1 (d), 127.4 (d), 125.2 (d), 120.6 (d), 21.3 (q, CH_3). MS m/z: 311 (M^++1, 100%). Elemental analysis, calcd for $C_{22}H_{18}N_2$ (M_r=310): C 85.13, H 5.85, N 9.03%; found C 84.91, H 5.53, N 9.04%.

4.4. Synthesis of 2,3-disubstituted quinolines, 20 and 21, by the method in literature[13]

In a flask purged with N_2, *o*-nitrobenzaldehyde (0.500 g, 0.0033 mol), methylbenzyl ketone (0.0033 mol, for **20**) or deoxybenzoin (0.0033 mol, for **21**), respectively, was added followed by anhydrous ethanol (20 mL). $SnCl_2$ (3.138 g, 0.0165 mol), $ZnCl_2$ (2.249 g, 0.0165 mol), and approximately 0.5 g molecular sieves (3A) were added to the solution. The mixture was then heated at 70 °C under an atmosphere of nitrogen for 4 h. The reaction was then cooled to room temperature and rendered basic (pH 8) with 10% aq sodium bicarbonate (50 mL). The mixture was extracted with ethyl acetate (3×20 mL). The organics were combined and washed thoroughly with saturated NaCl (aq), dried over $MgSO_4$, and filtered. Following reduction of the solvent in vacuo, the material remaining was subjected to chromatography on silica gel using dichloromethane as eluent.

2-*Methyl*-3-*phenylquinoline*, **20**: 220 mg (28.6%) (physical and spectroscopic data given in 4.3.2.).

2,3-*Diphenylquinoline,* **21**: 300 mg (23.9%), colorless solid, mp 81–82 °C. UV (EtOH) λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 208 (40,956), 235 (39,406), 258 (34,686), 329 (6017). IR (neat) ν_{max}/cm^{-1}: 3057, 3034, 2922 (CH). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 8.21 (d, 1H, J=8.4 Hz), 8.16 (s, 1H), 7.85 (d, 1H, J=8.1 Hz), 7.73 (t, 1H, J=7.9 Hz), 7.56 (t, 1H, J=7.4 Hz), 7.47–7.43 (m, 2H), 7.30–7.22 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 158.6 (s), 147.5 (s), 140.6 (s), 140.2 (s), 137.7 (d), 134.7 (s), 130.2 (d), 129.9 (d), 129.8 (d), 129.6 (d), 128.4 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.4 (d), 127.4 (s), 126.9 (d). MS m/z: 382 (M^++1, 100%), 251 (8%). Elemental analysis, calcd for $C_{21}H_{15}N_2$ (M_r=381): C 89.65, H 5.37, N 4.98%; found C 89.63, H 5.48, N 5.06%.

4.5. Decomposition of benzodiazepine 7

During the purification and isolation of **7** on silica gel column and thin layer chromatography the amount of **7** was rapidly decreasing in favor of *E*-**24** formation: (*E*)-1-(3*H*-*indazol*-3-*ylidene*)-1-(*p*-*tolyl*)*propan*-2-*one*, **24**: ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm: 7.47 (d, 1H, J=7.0 Hz, H-2), 7.41 (t, d, 1H, J=7.0 Hz, H-4), 7.32 (d, 2H, J=8.1 Hz, H-10), 7.27–7.24 (m, 3H, H-11, and H-3), 7.15 (d, 1H, J=7.0 Hz, H-5), 2.39 (s, 3H, CH_3), 2.31 (s, 3H, $COCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm: 196.1 (s, CO), 153.5 (s, C-8), 145.6 (s, C-7), 137.1 (s, C-12), 133.1 (d, C-4), 132.9 (s), 130.0 (s), 128.9 (d, C-10), 128.5 (d, C-11), 128.2 (d, C-3), 121.6 (d, C-2), 118.8 (d, C-5), 20.8 (q, CH_3), 12.1 (q, $COCH_3$). MS m/z: 263 (M^++H, 100%).

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Supplementary data

^{1}H and ^{13}C NMR spectra of compounds **4**, **5**, **7**, **8**, **20**, and NOE of **8**, HMBC of **24**. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.10.013. These data include MOL files and InChIKeys of the most important compounds described in this article.

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