Preparation of 9-Aryl (or Heteroaryl)methylidene-10-(methoxyimino)-phenanthrenes and their Thermal Electrocyclisation to Fused Quinolines

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o-Quinone methanide *N*-methoxyimines **6a-c**, **7a-c**, **11a-b** and **12a**, easily prepared from the reaction of 10-(methoxyimino)phenanthrene-9-one (**3**) with phosphonium salts **5a-c**, **10a-b** in the presence of lithium hydroxide, are thermally converted into dibenzo[f,h]quinolino[2,3-*x*]fused compounds **9a-c** and **13a-b**, in high yield.

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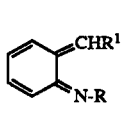
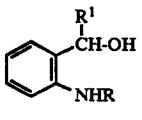
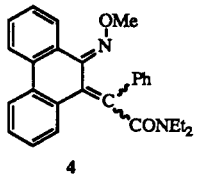
Unlike *o*-quinodimethanes [1], the *o*-quinone methanide imines, usually called azaxylylenes, have received little attention in organic synthesis, despite their potential in heterocyclic chemistry [2]. Both *N*- and *C*-functionalised azaxylylenes have been suggested as hetero-1,4-diene intermediates in some intra- and intermolecular Diels-Alder cycloadditions [3-7]. *C*-Phenylazaxylylene **1a** (R = H, R^1 = C_6H_5), formed as intermediate by flash vacuum pyrolysis (FVP) of compounds **2a-b** (a, R = H, R^1 = C_6H_5; b, R = COOBu^t, R^1 = C_6H_5) or of 4-phenyl-4*H*-dihydro-1,3-benzoxazin-2-one, was further converted to dihydroacridine and to acridine [6,8]. The thienyl derivative **2c**



1a-c



2a-c



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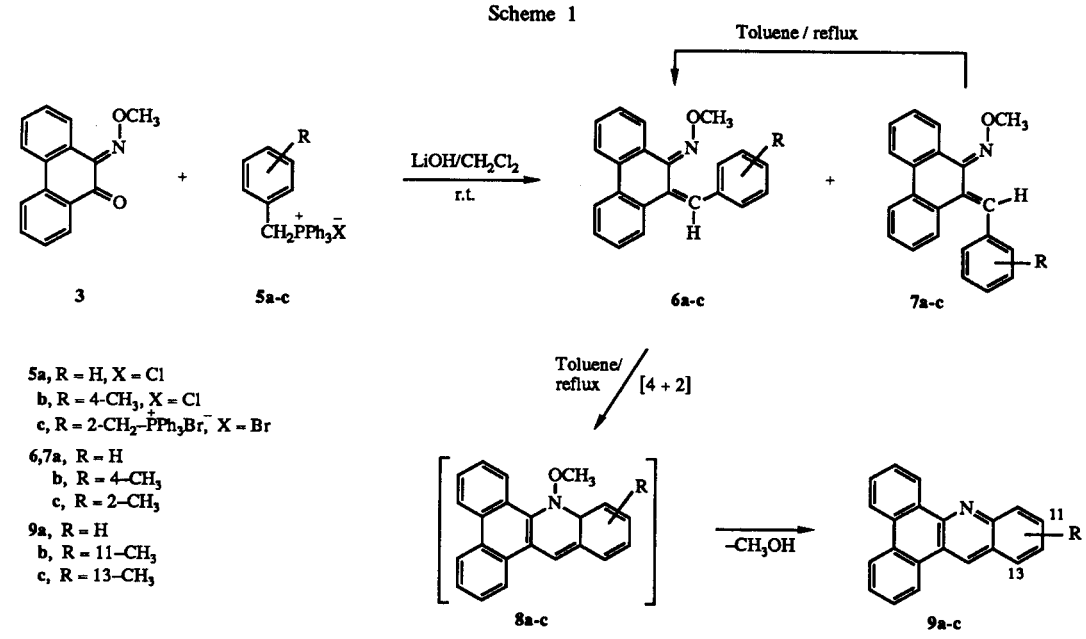
(R = COOBu^t, R^1 = 2-thienyl), prepared by addition of *o*-lithiated *t*-butoxycarbonylaniline to thiophene-2-carbaldehyde in 14% yield, was converted by FVP *via* the azaxylylene **1b** (R = H, R^1 = 2-thienyl) to thieno[3,2-*b*]-quinoline in 54% yield [6]. The *C,N*-bis-substituted azaxylylene intermediate **1c** (R = 4-Cl-C_6H_4, R^1 = C_6H_5), formed from the reaction of benzyne with *N*-benzylidene-4-chloroaniline, gave 2-chloro-10-phenylacridine derivatives, through electrocyclisation of the *N*-aryl group in **1c**, indicating that this group more readily adopts the required "inside" configuration, since only the *Z*-imine can cyclise [5]. Recently Elferink and Bos [9] reported that the reaction of 10-(methoxyimino)phenanthren-9-one (**3**) with *N,N*-diethylphenylethynamine gave the stable *E*- and *Z*-carboxamides **4**, which were then photochemically or /and thermally (>120°) converted into 14-(*N,N*-dimethylcarboxamido)dibenzo[*a,c*]acridine, through $E \rightleftharpoons Z$-isomerization, followed by electrocyclisation and further methanol elimination. Similar fused quinoline carboxamides were also prepared starting from 2-(methoxyimino)acenaphthen-1-one and 4,6-di-*t*-butyl-2-(methoxyimino)benzen-1-one.

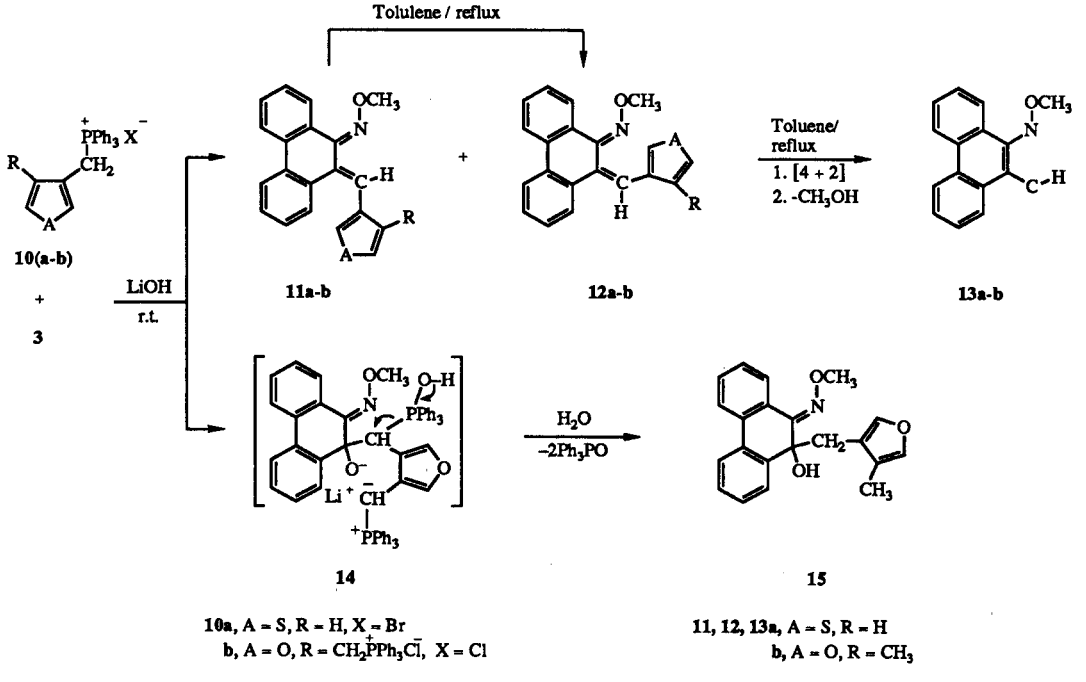
Our continuous interest in the reactions of phosphorus ylides with *o*-quinones [10] and *o*-quinone monoximes [11] and also in the chemistry of compound **3** [12] prompted us to examine the title reactions, depicted in Schemes 1,2.

A methylene chloride solution of benzyltriphenylphosphonium chloride (**5a**) and monoxime **3** was treated at room temperature with aqueous 0.5*M* lithium hydroxide for 10 days to give the expected Wittig products *Z*-(**6a**) and *E*-10-benzylidene-9-(methoxyimino)phenanthrene (**7a**) in 18% and 10% yield respectively (Scheme 1). By a similar treatment of **3** and the salt **5b** for 10 days compounds **6b** (22%) and **7b** (16%) were obtained. When a solution of **3** and *o*-xylenebis(triphenylphosphonium bromide) (**5c**) was similarly treated for 4 days products **6c** (19%) and **7c** (15%) were obtained, through a Wittig olefination of only one ylide group generated from salt **5c** and subsequent hydrolysis of the second. The reactions were monitored by tlc, following the disappearance of **3**. Treatment of a solution of **3** and 3-thenyltriphenylphosphonium bromide (**10a**) with lithium hydroxide for 24 hours under the same conditions gave an oily mixture of compounds **11a-12a** in 58% total yield (Scheme 2). Effords to separate the mixture by chromatographic methods failed. The ^{1}H nmr spectrum of the mixture exhibited two singlets at δ 3.82 and 3.98 in a 2:3 ratio, for the N-OCH_3 protons of the two isomers present. On the base of the observation that the methoxy protons of *Z*-isomers **6a-c** resonate at a higher field than those of the corresponding *E*-isomers **7a-c**, it can be considered that the isomers **12a**:**11a** were isolated in a 2:3 molar ratio. The suggested configurations of the isolated isomers were confirmed by their cyclisation experiments, discussed below. Finally, by a similar treatment of the bis-salt **10b**, in the presence of **3** for 15 days, only the *E*-isomer **11b** (5%) was obtained, through a normal Wittig mono-olefination along with the unexpected com-

Scheme 1



Scheme 2



pound **15** (2%), as it is depicted in Scheme 2. A partial convertion of the initially formed corresponding monobetaine, by addition of water, to the intermediate **14**, followed by further hydrolysis of its phosphonium groups can account for the formation of compound **15**. A similar deviation, giving the hydrolysed, parallel to the normal Wittig product, has been recently reported by us for a reaction of phenanthrene-9,10-quinone [13].

When to a solution of compounds **3** and **10** (in a 2:1 molar ratio) in dry dimethylformamide, heated at 90°, under nitrogen, a dry ethanolic solution of lithium ethoxide was added within 1 hour and the reaction mixture was subsequently heated for 100 hours, 12-methyldibenzo[f,h]-furo[2,3-*b*]quinoline (**13b**) was obtained in 21% yield, obviously through a further thermal electrocyclisation of the initially formed compounds **11b** and/or **12b**, followed by

methanol elimination (Scheme 2). The reaction between **3** and **5c** under these dry conditions afforded compounds **6c** (4%) and **7c** (2%), along with 13-methyldibenzo[a,c]-acridine (**9c**) (13%), from the partial thermal cyclisation -ethanol elimination of the former isomers (Scheme 1). It is of interest to be noticed that the reaction of the salt **5c** with acenaphthylene-1,2-quinone monoxime under the same conditions resulted in the formation of benzo[*k*]-fluoranthene, *via* a Wittig and a "Wittig type" reaction of its carbonyl and oximino groups with the corresponding bis-ylide, formed from **6c** [11].

In order to study further the applicability of the above observed interesting electrocyclisation, we heated in refluxing toluene solutions of the prepared *o*-quinone methanide *N*-methoxy imines. Compounds **6a**, **6b** and **6c** were directly converted into dibenzo[**a,c**]acridines **9a** [14] (93%), **9b** (41%) and **9c** (44%) respectively, as it was found by tlc examination of the reaction mixture, and in agreement with the proposed *Z*-configuration. Compounds **9a** (89%), **9b** (38%) and **9c** (41%) were also obtained by heating solutions of **7a**, **7b** and **7c** respectively, via their prior isomerisation to isomers **6a**, **6b** and **6c**, as was detected by tlc examination. Similarly, the mixture of compounds **11a**, **12a** was converted into dibenzo[*f,h*]thieno-[2,3-*b*]quinoline (**13a**) in 88% yield. Compound **11b** was also isomerised to **12b** and finally to **13b** (62%).

All new compounds exhibited spectral data and elemental analysis in accord with their assigned structures.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The ^{1}H nmr spectra were recorded with carbon tetrachloride or deuteriochloroform as solvent on a Bruker Model AW 80 (80 MHz) spectrometer, with tetramethylsilane as the internal standard. Mass spectra were determined with a Hitachi Perkin-Elmer RMU-6L spectrometer. The ionization energy was maintained at 70 eV. Microanalyses were performed on a Perkin-Elmer 240 B CHN analyser. Earlier reported procedures were used for the preparation of the phosphonium salts **5a** [15], **5b** [16], **5c** [17], **10a** [18] and **10b** [19].

General Procedure for the Reaction of 10-(Methoxyimino)phenanthren-9-one (**3**) with Phosphonium Salts **5a-c** and **10a-b**.

Procedure A.

A solution of the appropriate salt **5a-c** or **10a-b** (1.2 mmoles) and the monoxime **3** (0.237 g, 1 mmole) in methylene chloride (25 ml) was stirred vigorously, Freshly prepared aqueous lithium hydroxide (0.5*M*, 5 ml) was added as one portion to the mixture and the two-phase system was stirred at room temperature until an almost complete consumption of the monoxime **3** was observed on tlc (10 days for salts **5a**, **5b** and **10b**, 4 days for **5c**, 24 hours for **10a**). The mixture was then poured into water (20 ml) and extracted with methylene chloride (2 x 20 ml). The organic extract was dried (sodium sulfate), the solvent removed under reduced pressure and the residue was separated by preparative tlc on silica gel (hexane). According to this general procedure the following products were prepared:

E-10-Benzylidene-9-(methoxyimino)phenanthrene (**7a**).

This compound was obtained from **5a** (yellow crystals, 32 mg, 10%), mp 221-223° (carbon tetrachloride); ^{1}H nmr (carbon tetrachloride): δ 4.07 (s, 3 H), 7.02 (s, 1 H), 7.10-8.02 (m, 12 H), 8.35-8.49 (m, 1 H); ms: m/z (%) 311 (M^+, 42), 296 (11), 280 (100), 279 (55), 190 (11), 105 (30).

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.75; H, 5.55; N, 4.46.

Z-10-Benzylidene-9-(methoxyimino)phenanthrene (**6a**).

This compound was also obtained from **5a** (eluted from the slower moving band) (yellow crystals, 56 mg, 18%), mp 145-147° (carbon tetrachloride); ^{1}H nmr (carbon tetrachloride): δ 3.83 (s, 3 H), 7.05 (s, 1 H), 7.12-8.03 (m, 12 H), 8.26-8.40 (m, 1 H); ms: m/z (%) 311 (M^+, 37), 296 (11), 280 (100), 279 (32), 190 (14), 105 (11).

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 85.03; H, 5.60; N, 4.27.

E-10-(4-Methylbenzylidene)-9-(methoxyimino)phenanthrene (**7b**).

This compound was obtained from **5b** (oil, 53 mg, 16%); ^{1}H nmr (deuteriochloroform): δ 2.29 (s, 3 H), 4.05 (s, 3 H), 6.93-8.02 (m, 12 H), 8.33-8.55 (m, 1 H); ms: m/z (%) 325 (M^+, 29), 324 (7), 310 (8), 295 (21), 294 (93), 293 (100), 292 (19), 278 (9), 277 (8).

Anal. Calcd. for $C_{23}H_{19}NO$: C, 84.89; H, 5.88; N, 4.30. Found: C, 85.18; H, 5.61; N, 4.05.

Z-10-(4-Methylbenzylidene)-9-(methoxyimino)phenanthrene (**6b**).

This compound was also obtained from **5b** (eluted from the slower moving band) (yellow crystals, 72 mg, 22%), mp 155-157° (ethanol); ^{1}H nmr (deuteriochloroform): δ 2.34 (s, 3 H), 3.67 (s, 3 H), 6.93-8.05 (m, 12 H), 8.27-8.47 (m, 1 H); ms: m/z (%) 325 (M^+, 2), 324 (0.5), 310 (0.4), 295 (4), 294 (29), 293 (100), 292 (18), 278 (1).

Anal. Calcd. for $C_{23}H_{19}NO$: C, 84.89; H, 5.88; N, 4.30. Found: C, 85.10; H, 5.72; N, 4.32.

E-10-(2-Methylbenzylidene)-9-(methoxyimino)phenanthrene (**7c**).

This compound was obtained from **5c** (oil, 48 mg, 15%); ^{1}H nmr (carbon tetrachloride): δ 2.29 (s, 3 H), 3.92 (s, 3 H), 6.65-7.90 (m, 12 H), 8.24-8.40 (m, 1 H); ms: m/z (%) 325 (M^+, 11), 310 (18), 294 (100), 293 (59), 279 (36), 278 (18).

Anal. Calcd. for $C_{23}H_{19}NO$: C, 84.89; H, 5.88; N, 4.30. Found: C, 85.02; H, 5.90; N, 4.12.

Z-10-(2-Methylbenzylidene)-9-(methoxyimino)phenanthrene (**6c**).

This compound was also obtained from **5c** (eluted from the slower moving band) (yellow crystals, 63 mg, 19%), mp 112-114° (ethanol); ^{1}H nmr (carbon tetrachloride): δ 2.30 (s, 3 H), 3.58 (s, 3 H), 6.60-7.92 (m, 12 H), 8.12-8.28 (m, 1 H); ms: m/z (%) 325 (M^+, 21), 310 (23), 294 (100), 293 (23), 279 (26), 278 (26).

Anal. Calcd. for $C_{23}H_{19}NO$: C, 84.89; H, 5.88; N, 4.30. Found: C, 84.69; H, 6.01; N, 4.21.

E-(**11a**) and *Z*-10-Thenylidene-9-(methoxyimino)phenanthrene (**12a**).

These compounds were obtained from **10a** as an oily mixture (0.184 g, 58%); ^{1}H nmr (carbon tetrachloride): δ 3.82 (s), 3.98 (s), 6.65-8.10 (m), 8.10-8.42 (m); ms: m/z 317 (M^+).

E-10-(4-Methyl-3-furylmethylidene)-9-(methoxyimino)phenanthrene (**11b**).

This compound was obtained from **10b** (yellow crystals, 19 mg, 6%), mp 147-149° (ethanol); ^{1}H nmr (carbon tetrachloride): δ 1.75 (s, 3H), 3.98 (s, 3 H), 6.55 (s, 1 H), 6.72-7.88 (m, 9 H), 8.12-8.32 (m, 1 H); ms: m/z (%) 315 (M^+, 31), 284 (100), 256 (49), 254 (24), 241 (6), 228 (8).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 80.02; H, 5.49; N, 4.01.

10-Hydroxy-10-(4-Methyl-3-furylmethyl)-9-(methoxyimino)phenanthrene (**15**).

This compound was also obtained from **10b** (eluted from the slower moving next band) (oil, 10 mg, 3%); ^{1}H nmr (carbon tetrachloride): δ 1.55 (s, 3 H), 2.60 (s, 2 H), 3.84 (s, 3 H), 4.04 (brs, 1 H), 6.90 (s, 2 H), 7.00-7.89 (m, 7 H), 7.93-8.08 (m, 1 H); ms: m/z (%) 333 (M^+, 0.2), 316 (0.4), 302 (9), 238 (100), 219 (4), 206 (47), 178 (27), 152 (11), 95 (12).

Anal. Calcd. for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.81; H, 5.77; N, 4.39.

Procedure B.

A solution of the monoxime **3** (0.237 g, 1 mmole) and the appropriate bis-phosphonium salt **5c** or **13b** (0.5 mmole, dried at 100°/0.2 mm Hg over phosphorus pentoxide) in dry dimethylformamide (20 ml) was stirred under nitrogen for 1 hour at 90° while a solution of lithium ethoxide (from 20 mg of lithium) in ethanol (6 ml) was added dropwise. The mixture was stirred at 90° for a further 100 hours and then cooled to room temperature, poured into crushed ice (*ca* 25 g) and extracted with ether (5 x 30 ml). The extract was washed with water (3 x 20 ml), dried (sodium sulfate) and concentrated under reduced pressure. The residue was roughly chromatographed on silica gel with methylene chloride-hexane (7:3) as eluant and the obtained fraction of products was further separated by preparative tlc on silica gel [methylene chloride-hexane (0.5:9.5)]. According to this procedure the following products were prepared:

13-Methyldibenzo[*a*,*c*]acridine (**9c**).

This compound was obtained from **5c** (from the faster moving band) (colorless crystals, 39 mg, 13%), mp 228-231° (methylene chloride); ^{1}H nmr (deuteriochloroform): δ 2.82 (s, 3 H), 7.27-7.85 (m, 7 H), 8.30-8.72 (m, 3 H), 9.40 (s, 1 H), 9.56-9.75 (m, 1 H); ms: m/z (%) 294 (71), 293 (M^+, 100), 292 (52), 278 (10), 277 (10).

Anal. Calcd. for $C_{22}H_{15}N$: C, 90.07; H, 5.15; N, 4.77. Found: C, 90.08; H, 4.98; N, 4.69.

The next band gave compound **6c** (12 mg, 4%) and the slower moving band gave compound **7c** (7 mg, 2%), identical in all respects with compounds **6c**, **7c** described above.

12-Methyldibenzo[*f*,*h*]furo[2,3-*b*]quinoline (**13b**).

This compound was obtained from **10b** (colorless crystals, 60 mg, 21%), mp 193-195° (methylene chloride); ^{1}H nmr (deuteriochloroform): δ 2.30 (s, 3 H), 7.21 (s, 1 H), 7.41-7.84 (m, 4 H), 8.35-8.67 (m, 3 H), 8.76 (s, 1 H), 9.14-9.37 (m, 1 H); ms: m/z (%) 283 (M^+, 100), 282 (3), 256 (6), 255 (14), 254 (16), 253 (6), 240 (6), 226 (12).

Anal. Calcd. for $C_{20}H_{13}NO$: C, 84.78; H, 4.63; N, 4.94. Found: C, 84.52; H, 4.81; N, 4.87.

Thermal Electrocyclisation of compounds **6a-c**, **7a-c**, **11a-b** and **12a**.

General Procedure.

A solution of the appropriate *Z*-[**6a-c**, **12a**] or *E*-methylidenemethoxyimine [**7a-c**, **11a-b**] (0.1 mmole) in toluene (3 ml) was heated under reflux for 3 days. After evaporation of the solvent under reduced pressure, the residue was triturated with methylene chloride and hexane. According to this procedure the following products were prepared:

Dibenzo[*a*,*c*]acridine (**9a**).

This compound was obtained from **6a** (26 mg, 93%) and also from **7a** (25 mg, 89%), mp 203-205° (methylene chloride-hexane) (lit [14], mp 206°).

11-Methyldibenzo[*a*,*c*]acridine (**9b**).

This compound was obtained from **6b** (colorless crystals, 12 mg, 41%), mp 185-187° (methylene chloride-hexane); ^{1}H nmr (deuteriochloroform): δ 2.62 (s, 3 H), 7.26-8.16 (m, 7 H), 8.42-8.71 (m, 3 H), 9.11 (s, 1 H), 9.39-9.59 (m, 1 H); ms: m/z (%) 294 (50), 293 (M^+, 100), 292 (15), 278 (11).

Anal. Calcd. for $C_{22}H_{15}N$: C, 90.07; H, 5.15; N, 4.77. Found: C, 90.12; H, 5.23; N, 4.81.

The same product **9b** (11 mg, 38%) was also obtained from **7b**.

13-Methyldibenzo[*a*,*c*]acridine (**9c**).

This compound was obtained from **6c** (13 mg, 44%) and also from compound **7c** (12 mg, 41%).

Dibenzo[*f*,*h*]thieno[2,3-*b*]quinoline (**13a**).

This compound was obtained from the mixture of compounds **11a-12a** (colorless crystals, 23 mg, 81%), mp 191-193° (methylene chloride-hexane); ^{1}H nmr (deuteriochloroform): δ 7.46 (d, J = 6.4 Hz, 1 H), 7.56-7.90 (m, 5 H), 8.44-8.74 (m, 3 H), 8.95 (s, 1 H), 10.86-11.11 (m, 1 H); ms: m/z (%) 286 (23), 285 (M^+, 100), 284 (14), 283 (9).

Anal. Calcd. for $C_{19}H_{11}NS$: C, 79.97; H, 3.88; N, 4.91. Found: C, 79.91; H, 3.62; N, 4.93.

12-Methyldibenzo[*f*,*h*]furo[2,3-*b*]quinoline (**13b**).

This compound was obtained from **11b** (17 mg, 62%).

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