Synthesis of Acenaphtho[1,2-*x*]heterocycles and Spiro[acenaphthylene 1-isoxazoles]

D. A. Lefkaditis, D. N. Nicolaides*, G. K. Papageorgiou and J. Stephanidou-Stephanatou

Laboratory of Organic Chemistry, University of Thessaloniki, GR-54006 Thessaloniki, Greece

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Methyl (*Z*)-(1,2-dihydro-2-oxo-1-acenaphthylenylidene)acetate **1** gives with hydroxylamine the oximes **2** and the pyrrole derivative **4**, whereas with hydrazines affords the pyridazinones **5** and **6**. A pyridazine derivative **8** is also isolated from the reaction of (1,2-dihydro-2-oxo-1-acenaphthylenylidene)acetone **7** with hydrazine hydrate. Reaction between the spiro-derivative **9** and hydroxylamine hydrochloride gives oxime **10**, whereas Wittig olefination of **9** with ylide **11** yields compound **12** which by reaction with 2,4,6-trimethylbenzonitrile oxide (**13**) affords the dispiro-derivatives **14**. Finally from the reaction of acenaphthylene-1,2-quinone (**17**) with the bisylide **16** the acenaphtho[1,2-*c*]thiophene (**18**) is formed.

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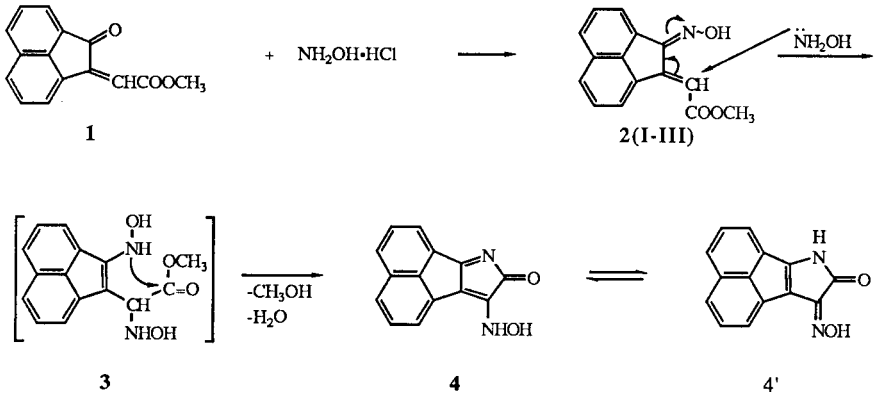
Recently we reported the preparation of some spiro[acenaphthylene-dioxazoles] and spiro[acenaphthylene-isoxazoles] by consecutive reactions of nitrile oxides and phosphorus ylides to acenaphthylene-1,2-quinone as well as their catalytic hydrogenation to new acenaphthylene derivatives [1]. We also reported some reactions of acenaphthylene-1,2-quinone monoxime with phosphorus ylides, which resulted in the formation of acenaphtho-[1,2-*x*]-fused systems [2]. Our continuous interest in the preparation and study of acenaphthylenes prompted us to extend our previous study on spiro[acenaphthyleneisoxazoles] and also to examine the reactions of some (carbonylmethylene)acenaphthenones with hydrazines and hydroxylamine.

Tsuge, Tashiro, and Shinkai prepared several alkylideneacenaphthenones by Wittig reaction of acenaphthylene-1,2-quinone with phosphorus ylides and studied the reactions of some of them with hydrazines [3,4]. The reactions of benzylidene-acenaphthenones with hydrazine hydrate gave 1-hydroxy-2-(hydrazinobenzyl)acenaphthylenes, whereas with phenylhydrazines the expected pyrazolines were obtained. In the case of phenacylideneacenaphthenone, the corresponding pyridazine and pyrazoline derivatives were isolated from the reactions with hydrazine hydrate and 2,4-dinitrophenylhydrazine, respectively.

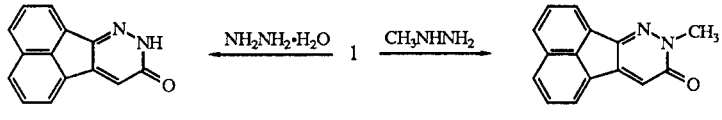
The studied reactions of (carbonylmethylene)acenaphthenones **1**, **7** with hydroxylamine hydrochloride and

Scheme 1



1 2(I-III) 3 4 4'

Scheme 2



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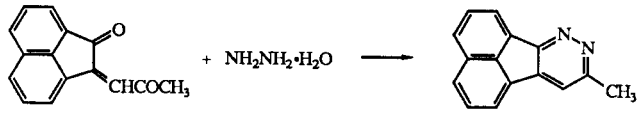
hydrazines and the products obtained are depicted in Schemes 1, 2 and 3. Treatment of methyl (*Z*)-(1,2-dihydro-2-oxo-1-acenaphthylenylidene)acetate (**1**) with hydroxylamine hydrochloride in boiling pyridine (Scheme 1) afforded three stereoisomeric methyl (1,2-dihydro-2-hydroxyimino-1-acenaphthylenylidene)acetates [**2(I-III)**] in 40% total yield and straw coloured crystals of a compound in 5% yield, to which the structure of 9-hydroxylamino-8*H*-acenaphtho[1,2-*b*]pyrrol-8-one (**4**) or its tautomeric form 8,9-dihydro-9-hydroxyimino-7*H*-acenaphtho-[1,2-*b*]pyrrol-8-one (**4'**) could be assigned on the basis of its spectral data and elemental analysis. A further attack of hydroxylamine to the methylene carbon atom of **2** (Michael addition), followed by intramolecular nucleophilic attack of the oximino-nitrogen to the carbonyl carbon of **3** and subsequent alcohol elimination and dehydration, can account for the formation of compound **4**. Oximes **2(I-II)** were also obtained previously by treatment of acenaphthylene-1,2-quinone monoxime with ethoxycarbonylmethylenetriphenylphosphorane **11** [2].

Treatment of (1,2-dihydro-2-oxo-1-acenaphthylenylidene)acetone **7** and of the benzophenone analog with hydroxylamine hydrochloride afforded (1,2-dihydro-2-hydroxyimino-1-acenaphthylenylidene)acetone and the corresponding benzophenone derivative in 31% (mp 179-181°) and 52% yield (mp 173-175°) respectively [5].

When compound **1** was treated with hydrazine hydrate or methylhydrazine the expected pyridazinones **5** and **6** were obtained in 52% and 59% yield respectively (Scheme 2). However, the reaction of **1** with phenylhydrazine resulted unexpectedly [5] in the formation of 2-phenylhydrazono-1-acenaphthenone, possibly by a reductive cleavage reaction [4], whereas the reaction of **1** with benzoylhydrazine afforded methyl (2-benzoylhydrazono-1,2-dihydro-1-acenaphthylenylidene)acetate in 31% yield (mp 178-180°) [5].

Treatment of compound **7** with hydrazine hydrate gave 9-methylacenaphtho[1,2-*c*]pyridazine (**8**) in 78% yield (Scheme 3). All other reactions of **7** and of the benzophenone analog with the above hydrazines resulted in the formation of complicated reaction mixtures and all efforts for their separation by chromatographic methods failed [5].

Scheme 3



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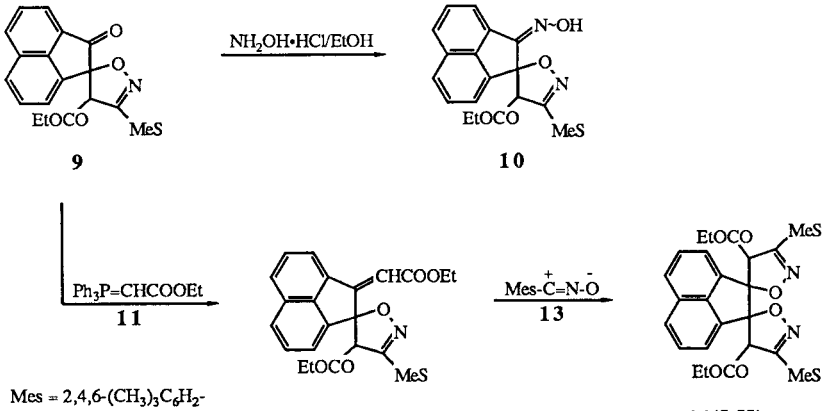
In connection with the above results we studied the reactions of ethyl 2-oxo-3'-(2,4,6-trimethylphenyl)spiro[acenaphthylene-1(2*H*),5'(4'*H*)-isoxazole]-4'-carboxylate **9** [1] with hydroxylamine and also with ylide **11**, as it is depicted in Scheme 4. From the reaction of **9** with hydroxylamine hydrochloride ethyl 2-hydroxyimino-3'-(2,4,6-trimethylphenyl)spiro[acenaphthylene-1(2*H*),5'(4'*H*)-isoxazole]-4'-carboxylate (**10**) was isolated in a sole stereoisomeric form and in 45% yield. Treatment of **9** with **11** in refluxing dichloromethane for 48 hours afforded an oily mixture of two stereoisomeric ethyl (3'-(2,4,6-trimethylphenyl)-4'-ethoxycarbonylspiro[acenaphthylene-1(2*H*)-,5'(4'*H*)-isoxazole]-2-ylidene)acetates [**12(I-II)**] in 97% yield. The ^{1}H nmr spectrum of the isomeric mixture exhibited for the 4'-H two singlets at δ 5.02 and 4.90 in 2:1 ratio and also two (2:1) quartets at δ 3.34 and 3.72 and two (2:1) triplets at δ 0.25 and 0.83 for the ethyl protons of the 4'-ethoxycarbonyl substituent. All efforts to separate the isomers by chromatographic methods failed. However, when the same reaction was carried out in refluxing ethanol for 17 hours and the reaction mixture was allowed to stand at room temperature crystals of the major isomer

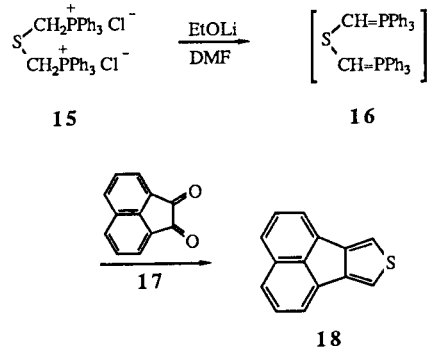
Scheme 4



12(I) precipitated in 41% yield. Further reaction of this isomer **12(I)** with 2,4,6-trimethylbenzonitrile oxide (**13**) afforded a mixture of two stereoisomeric dispiro-derivatives **14(I,II)** in a ratio of 5:1 as was deduced by the ^{1}H nmr, which showed two singlets for the 2,6-methyl protons of the aryl substituents at δ 2.47 and 2.40 (5:1 ratio) and two singlets at δ 2.27 and 2.29 (5:1 ratio) for the 4-methyl protons. All efforts to separate the mixture by chromatographic methods failed.

Finally, we wish to report the synthesis of acenaphtho-[1,2-*c*]thiophene (**18**) according to the reaction sequence shown in Scheme 5. Bis-Wittig reaction of acenaphthylene-1,2-quinone (**17**) with the bis-ylide **16** derived *in situ* from the dimethylthioether-a,a'-triphenylphosphonium dichloride (**15**) [6] afforded compound **18** in 5% yield. It is also noteworthy that from the reaction of phenanthrene-9,10-quinone with the salt **15** under the same reaction conditions the phenanthro[9,10-*b*]furan was isolated in 8% yield [7].

Scheme 5



15 16 17 18

EXPERIMENTAL

Melting points were determined with a Kofler Hot-stage apparatus and are uncorrected. The ir spectra were obtained with a Perkin-Elmer Model 297 spectrophotometer. The ^{1}H nmr spectra were recorded on a Varian A60A (60 MHz) or on a Bruker Model AW80 (80 MHz) spectrometer, with tetramethylsilane as the internal standard. Mass spectra were determined on 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. Petroleum ether refers to the fraction of bp 40-60°. Earlier reported methods were used for the preparation of compounds **7** [3], **9** [1] and **15** [6].

Methyl (*Z*)-(1,2-Dihydro-2-oxo-1-acenaphthylenylidene)acetate (**1**).

To a solution of carbomethoxymethylenetriphenylphosphorane [8] (4.2 g, 12.5 mmoles) in ethanol (150 ml) acenaphthylene-1,2-quinone (2.3 g, 12.5 mmoles) was added. The reaction mixture was stirred at room temperature for 2 hours and then filtered to give yellow crystals of compound **1** (2.23 g, 75%), mp 168-170° (ethanol); ir (Nujol): 1720, 1710, 1635 cm^{-1}; ^{1}H nmr (60 MHz, DMSO-d$_6$): δ 3.88 (s, 3H), 6.77 (s, 1H), 7.42-9.01 (m, 6H); ms: m/z (%) 238 (M$^+$, 100), 207 (72), 179 (53), 151 (70).

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23. Found: C, 75.50; H, 4.11.

9-Hydroxylamino-8*H*-acenaphtho[1,2-*b*]pyrrol-8-one (**4**) or 8,9-Dihydro-9-hydroxyimino-7*H*-acenaphtho[1,2-*b*]pyrrol-8-one (**4'**).

A solution of compound **1** (952 mg, 4 mmoles) and hydroxylamine hydrochloride (438 mg, 6.4 mmoles) in pyridine (150 ml) was refluxed for 15 minutes. Water was then added and the reaction mixture was extracted with chloroform. The organic layer was dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel with hexane/ethyl acetate (increasing amounts). Methyl (1,2-dihydro-2-hydroxyimino-1-acenaphthylenylidene)acetate [**2(I)**] was eluted first, as yellow crystals (253 mg, 25%), mp 178-179.5° (lit [2] mp 178-179.5°). A second isomer **2(II)** was then isolated, as orange crystals (81 mg, 8%), mp 125-127° (lit [2] mp 125-127°). The isomer **2(III)** was eluted third as yellow crystals (71 mg, 7%), mp 173-175° (ether/hexane); ir (Nujol): 3400, 1720 cm^{-1}; ^{1}H nmr (60 MHz, DMSO-d$_6$): δ 4.05 (s, 3H), 7.25-8.33 (m, 7H); ms: m/z (%) 253 (M$^+$, 100), 238 (24), 207 (18), 194 (52), 193 (77).

Anal. Calcd. for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.37; N, 5.53. Found: C, 70.88; H, 4.20; N, 5.61.

Finally compound **4** (or **4'**) was eluted as straw coloured crystals (47 mg, 5%), mp 251-253° (ethanol); ir (Nujol): 3440, 3250, 3160, 1700 cm^{-1}; ^{1}H nmr (60 MHz, DMSO-d$_6$): δ 7.43 (br s, 1H), 7.50-8.47 (m, 6H); ms: m/z (%) 236 (M$^+$, 53), 192 (100), 165 (28), 164 (35).

Anal. Calcd. for $C_{14}H_8N_2O_2$: C, 71.18; H, 3.41; N, 11.86. Found: C, 71.12; H, 3.88; N, 11.71.

8*H*-Acenaphtho[1,2-*c*]pyridazin-9-one (**5**).

A solution of compound **1** (238 mg, 1 mmole) and hydrazine hydrate (55 mg, 1.1 mmoles) in chloroform (5 ml) was refluxed for 24 hours. By cooling the reaction mixture yellow crystals of compound **5** were precipitated (115 mg, 52%), mp 300° (dimethyl sulfoxide); ir (Nujol): 3120, 1655, 1640 cm^{-1}; ms: m/z (%) 220 (M$^+$, 100), 192 (37), 164 (66), 163 (57).

Anal. Calcd. for $C_{14}H_8N_2O$: C, 76.36; H, 3.66; N, 12.72. Found: C, 76.04; H, 3.75; N, 12.48.

8-Methyl-8*H*-acenaphtho[1,2-*c*]pyridazin-9-one (**6**).

A solution of compound **1** (298 mg, 1.25 mmoles) and methylhydrazine (69 mg, 1.5 mmoles) in chloroform (5 ml) was refluxed for 2 days. The reaction mixture was left to cool, and upon addition of acetone (2 ml) compound **6** precipitated (173 mg, 59%), mp 203-205° (methylene chloride/hexane); ir (Nujol): 3050, 1660, 1620 cm^{-1}; ^{1}H nmr (60 MHz, deuteriochloroform): δ 3.90 (s, 3H), 7.22 (s, 1H), 7.60-8.05 (m, 6H); ms: m/z (%) 234 (M$^+$, 89), 206 (40), 191 (7), 177 (24), 163 (100).

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 77.23; H, 4.26; N, 11.57.

9-Methylacenaphtho[1,2-*c*]pyridazine (**8**).

A solution of compound **7** (222 mg, 1 mmole) and hydrazine hydrate (55 mg, 1.1 mmoles) in chloroform (5 ml) was refluxed for 24 hours. The solvent was evaporated under reduced pressure, and the residue was chromatographed on silica gel with ethyl acetate/ethanol (10:1) as eluant to give colorless crystals of com-

pound **8** (170 mg, 78%), mp 116-118° (ethyl acetate/hexane); ir (Nujol): 1610 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 2.82 (s, 3H), 7.60-8.17 (m, 6H), 8.33-8.57 (m, 1H); ms: m/z (%) 218 (M^+, 100), 203 (1), 190 (17), 189 (70).

Anal. Calcd. for $C_{15}H_{10}N_2$: C, 82.54; H, 4.62; N, 12.84. Found: C, 82.76; H, 4.61; N, 12.64.

Ethyl 2-Hydroxyimino-3'-(2,4,6-trimethylphenyl)spiro[acenaphthylene-1(2*H*),5'(4'*H*)-isoxazole)-4'-carboxylate (**10**).

A solution of ethyl 2-oxo-3'-(2,4,6-trimethylphenyl)spiro[acenaphthylene-1(2*H*),5'(4'*H*)-isoxazolo]-4'-carboxylate (**9**) [1] (413 mg, 1 mmole) and aqueous hydroxylamine (51 mg, 1 mmole) in ethanol (10 ml) was stirred at room temperature for 72 hours to give a precipitate of compound **10** (192 mg, 45%), mp 205-206° (ethanol); ir (Nujol): 3200, 1740 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 0.38 (t, J = 7 Hz, 3H), 2.27 (s, 3H), 2.56 (s, 6H), 3.57 (q, J = 7 Hz, 2H), 5.31 (s, 1H), 6.87 (s, 2H), 7.30-7.45 (m, 1H), 7.50-8.00 (m, 5H) and 9.25 (br s, 1H); ms: m/z (%) 428 (M^+, 13), 410 (53), 364 (15), 337 (11), 267 (50), 221 (40), 194 (33), 180 (80), 161 (100), 130 (54), 91 (46).

Anal. Calcd. for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.79; H, 5.61; N, 6.50.

Ethyl (3'-(2,4,6-Trimethylphenyl)-4'-ethoxycarbonylspiro[acenaphthylene-1(2*H*),5'(4'*H*)-isoxazole]-2-ylidene)acetates [**12(I,II)**].

A solution of compound **9** (413 mg, 1 mmole) and ethoxycarbonylmethylenetriphenylphosphorane (**11**) (348 mg, 1 mmole) in ethanol (10 ml) was heated at reflux for 17 hours. By cooling the reaction mixture colorless crystals of compound **12(I)** were precipitated (200 mg, 41%), mp 140-143°; ir (Nujol): 1740, 1720, 1640 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 0.26 (t, J = 7 Hz, 3H), 1.34 (t, J = 7 Hz, 3H), 2.25 (s, 3H), 2.50 (s, 6H), 3.34 (q, J = 7 Hz, 2H), 4.30 (q, J = 7 Hz, 2H), 5.02 (s, 1H), 6.53 (s, 1H), 6.91 (s, 2H), 7.50-8.00 (m, 5H), 8.92-9.08 (m, 1H); ms: m/z (%), 484 (12), 483 (M^+, 31), 4.78 (19), 438 (3), 410 (5), 364 (4), 322 (38), 249 (100), 221 (50), 161 (27).

Anal. Calcd for $C_{30}H_{29}NO_5$: C, 74.51; H, 6.05; N, 2.90. Found: C, 74.31; H, 5.91; N, 3.01.

When the reaction described above between compounds **9** and **11** was carried out in refluxing methylene chloride for 48 hours, after evaporation of the solvent in a rotary evaporator and column chromatography [silica gel, petroleum ether/methylene chloride (60:40 up to 20:80)] of the residue an oily mixture of compound **12(I)** and of its geometrical isomer **12(II)** was obtained (470 mg, 97%); ^1H nmr (60 MHz, deuteriochloroform): δ 0.26 (t, J = 7 Hz), 0.83 (t, J = 7 Hz), 1.34 (t, J = 7 Hz), 2.25 (s), 2.5 (s), 3.34 (q, J = 7 Hz), 3.72 (q, J = 7 Hz), 4.30 (q, J = 7 Hz), 4.90 (s), 5.02 (s), 6.53 (s), 6.91 (s), 7.35-8.00 (m), 8.92-9.08 (m).

Diethyl 3,3''-Bis(2,4,6-trimethylphenyl)dispiro[isoxazole-5(4*H*),1'-(2'*H*)-acenaphthylene-2',5''(4''*H*)isoxazole]-4,4''-dicarboxylates [**14(I,II)**].

A solution of compound **12** (483 mg, 1 mmole) and 2,4,6-trimethylbenzonitrile oxide (161 mg, 1 mmole) in dry methylene chloride (10 ml) was refluxed for 72 hours. The solvent was removed on a rotary evaporator, and the residue was chromatographed on silica gel, eluting with increasing proportions of methylene chloride in hexane (from 1:1 up to 9:1) to give a mixture of two diastereomeric compounds **14(I,II)** as colorless crystals (418 mg, 65%), mp 219-222° (petroleum ether/methylene chloride); ir (Nujol): 1740, 1610 cm^{-1}; ^1H nmr (80 MHz, deuteriochloroform): δ 0.61 (t, J = 7 Hz, 6H), 2.27 (s, 6H), 2.47 (s, 12H), 3.48 (q, J = 7 Hz, 2H), 3.61 (q, J = 7 Hz, 2H), 5.45 (s, 2H), 6.92 (s, 4H), 7.40-7.90 (m, 6H); ms: m/z 483 (M^+-MesCNO).

Anal. Calcd. for $C_{40}H_{40}N_2O_6$: C, 74.51; H, 6.25; N, 4.35. Found: C, 74.64; H, 6.08; N, 4.30.

Efforts to separate the mixture by preparative tlc or by fraction crystallization (from several solvents) failed.

Acenaphtho[1,2-*c*]thiophene (**18**).

A solution of the quinone **17** (2.72 g, 1.5 mmoles) and the bisphosphonium salt **15** (9.83 g, 1.5 mmoles), dried at 105°/0.1 torr over phosphorus pentoxide, in dry dimethyl formamide (400 ml) was stirred under nitrogen for 3 hours at room temperature while a solution of lithium ethoxide (4.1 g, 7.8 mmoles) in ethanol (90 ml) was added dropwise. The mixture was stirred for a further 21 hours and then poured into a mixture of concentrated hydrochloric acid (400 ml) and ice (*ca* 300 g) and extracted with ether (4 x 100 ml) and then with chloroform (2 x 150 ml). The combined extracts were washed with water (4 x 250 ml) dried (sodium sulfate) and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel with petroleum ether containing increasing amounts of chloroform to give compound **18** (155 mg, 5%), mp 82-83° (petroleum ether/chloroform); ir (Nujol): 3080, 1605 cm^{-1}; ^1H nmr (80 MHz, deuteriochloroform): δ 7.29 (s, 2H), 7.41-7.82 (m, 6H); ms: m/z (%) 209 (40), 208 (M^+, 100), 176 (5), 164 (36), 163 (48), 104 (36).

Anal. Calcd. for $C_{14}H_8S$: C, 80.76; H, 3.78. Found: C, 80.67; H, 3.96.

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