Heterocyclic Mesomeric Betaines. Part 6.[1] Synthesis and a Cycloaddition of a Hetero Derivative of the 1-Methylenephenalene-3-methide Anion

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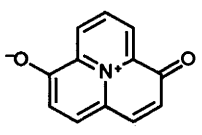
Synthesis of the cross-conjugated heterocyclic mesomeric betaine **4** is reported. This mesomeric betaine **4** is isoconjugate with the odd alternant hydrocarbon anion **5** (R = Ph). Cycloaddition of the betaine **4** with dimethyl acetylenedicarboxylate yields the 1,4-cycloadduct **14**.

Heterocyclic mesomeric betaines have been classified as conjugated, cross-conjugated, and pseudo-cross-conjugated systems.[2] These three systems are exemplified by the tricyclic structures **1**, **2** and **3**, respectively. No representative of these tricycles **1**, **2** and **3** has yet been synthesised. The synthesis of the betaine **4** is now reported. The compounds **2** and **4** are cross-conjugated heterocyclic mesomeric betaines[2] in which the positive and negative charges are *exclusively* restricted to separate parts of the π-electron system of these molecules. The cross-conjugated mesomeric betaines **2** and **4** are isoconjugate with the odd alternant hydrocarbon anions **5** (R = H or Ph).



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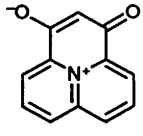

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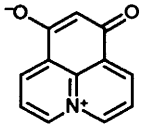

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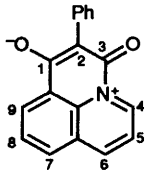

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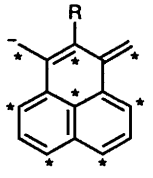

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The synthesis (Scheme 1) of the cross-conjugated heterocyclic mesomeric betaine **4** utilised the azaphenalenone **6** as the starting material.[3] Thermal condensation of diethyl 2-phenylmalonate and tetrahydroquinoline gave the enolic azaphenalenone **6** which gave one product **7** (83%) with benzenesulfonyl chloride–pyridine. The constitution of **7**, as a derivative of quinolin-2-one, was assigned by comparison of its spectroscopic properties [ν_{CO}(KBr)/cm^{-1} 1645; ^{13}C ($CDCl_3$) δ 161.3] with ^{13}C NMR spectra reported for *N*-methylquinolin-2-one [δ_{CO} 162.6] and *N*-methylquinolin-4-one [δ_{CO} 178.4].[4] Benzylic bromination, using *N*-bromosuccinimide (NBS) in carbon tetrachloride, gave the bromo derivative **8** (87%) which was transformed into the dehydro compound **11**, either by the sequence **8** → **9** → **11** involving base-catalysed {1,5-diazabicyclo[5.4.0]undec-7-ene (DBU)} elimination **8** → **9** (72%) followed by alkaline hydrolysis **9** → **11** (100%), or by the sequence **8** → **10** → **11** (87%) involving alkaline hydrolysis **8** → **10** followed by acid-catalysed dehydration **10** → **11**.

Dehydrogenation **11** → **12** (53%) was best achieved using triphenylcarbenium tetrafluoroborate as the hydride acceptor.[5] Deprotonation of the salt **12** with triethylamine gave the cross-conjugated heterocyclic mesomeric betaine **4** (90%) as deep purple crystals, m.p. 222 °C. The ^{1}H chemical shifts of the six aromatic hydrogen atoms (4-, 5-, 6-, 7-, 8- and 9-H) of the quinolinium group of the salt **12** [(CD_3CN) δ 10.10, 8.45, 9.62, 8.96/8.75, 8.22 and 8.75/8.96] and the betaine **4** [(CD_3SOCD_3) δ 10.12, 8.15, 9.20, 8.86/8.45, 8.04 and 8.45/8.86] show an instructive correspondence. This supports the cross-conjugated nature of the betaine **4** because the positive charge is clearly restricted to the quinolinium group in both structures **12** and **4**.

Conjugated heterocyclic mesomeric betaines normally participate in 1,3-dipolar cycloadditions, whereas cross-conjugated heterocyclic mesomeric betaines participate in 1,4-dipolar cycloadditions. The study of the cycloadditions of cross-conjugated heterocyclic mesomeric betaines has previously been limited to those cross-conjugated systems which are isoconjugate with even alternant hydrocarbon dianions.[2]

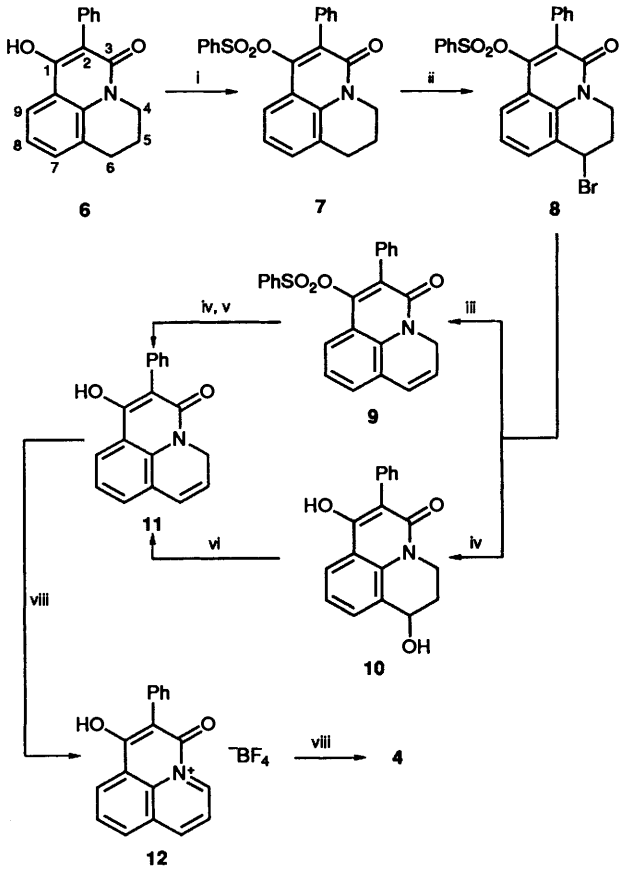
Cycloaddition of the betaine **4** with dimethyl acetylenedicarboxylate provides the first example of the cycloaddition of a cross-conjugated system isoconjugate with an odd alternant hydrocarbon anion **5** (R = Ph). Treatment of the salt **12** with triethylamine in the presence of dimethyl acetylenedicarboxylate yields a product of 1,4-cycloaddition (Scheme 2). The direct cycloadduct would have the constitution **13**, but structure **13** for the product is clearly eliminated by its ^{1}H NMR spectrum. The base-catalysed prototropic rearrangement **13** → **14** yields the product **14** which is firmly characterised by the singlet signal (δ 5.79; 2-H) in its ^{1}H NMR spectrum.

Experimental

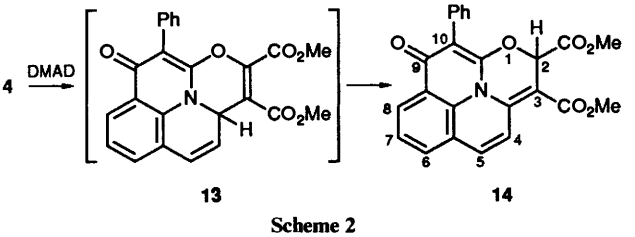
General experimental directions are given in Part 1.[6] *J*-Values are given in Hz.

1-*Hydroxy*-2-*phenyl*-5,6-*dihydro*-3a-*azaphenalen*-3(4H)-*one* **6**.—Diethyl 2-phenylmalonate (25 cm^3) and 1,2,3,4-tetrahydroquinoline (25 cm^3) were heated under reflux (6.5 h). Ethanol was removed by distillation and the solid residue was then washed with diethyl ether giving the title compound **6** (28.9 g, 52%), m.p. 222–228 °C (lit.,[3] 220–222 °C) which was used directly, δ_H(CF_3CO_2H) 8.35 (1 H, d, *J* 8, 9-H), 7.87 (1 H, d, *J* 8, 7-H), 7.80–7.75 (4 H, m), 7.60–7.50 (2 H, m), 4.67 (2 H, m, 4-H), 3.30 (2 H, m, 6-H) and 2.44 (2 H, m, 5-H).

2-*Phenyl* 1-*Phenylsulfonyloxy*-5,6-*dihydro*-3a-*azaphenalen*-3(4H)-*one* **7**.—Benzenesulfonyl chloride (22 cm^3) was added dropwise (30 min) to an ice-cooled, stirred solution of the



Scheme 1 *Reagents:* i, $PhSO_2Cl$–pyridine; ii, NBS–CCl_4; iii, DBU; iv, KOH–MeOH; v, aq. HCl; vi, AcOH–H_2SO_4; vii, $[Ph_3C^+][^-BF_4]$; viii, Et_3N



Scheme 2

preceding compound **6** (46.5 g) in pyridine (100 cm^3). After warming to room temperature (1 h), the mixture was poured into cold dilute hydrochloric acid. The precipitate was collected, washed and crystallised from chloroform–ethanol to give the *title compound* **7** (58.1 g, 83%) as colourless rhombs, m.p. 204–206 °C (Found: C, 68.8; H, 4.8; N, 3.2; S, 8.0%; $M^{+\cdot}$, 417. $C_{24}H_{19}NO_4S$ requires C, 69.0; H, 4.6; N, 3.4; S, 7.7%; *M*, 417); ν_{max}(KBr)/cm^{-1} 1645, 1590, 1365, 1190, 1080 and 750; δ_H 8.02 (1 H, d, *J* 7, 9-H), 7.60–7.10 (12 H, m), 4.25 (2 H, br t, *J* 6, 4-H), 3.02 (2 H, br t, *J* 6, 6-H) and 2.17 (2 H, m, 5-H); $\delta_C(CDCl_3)$ 161.3, 150.6, 136.2, 135.8, 133.6, 131.7, 130.6 (two C), 128.7, 127.8, 127.6, 127.4, 124.9, 124.5, 123.1, 121.9, 117.2, 43.0, 27.5 and 20.4.

6-Bromo-2-phenyl 1-Phenylsulfonyloxy-5,6-dihydro-3a-azaphenalen-3(4H)-one **8**.—The preceding compound **7** (15.1 g), *N*-bromosuccinimide (6.8 g), dibenzoyl peroxide (~10 mg), and carbon tetrachloride (70 cm^3) were heated under reflux (3 h). After cooling, the mixture was diluted with dichloromethane (50 cm^3) and the organic layer was separated and treated with aqueous sodium hydroxide and then water. It was then dried (Na_2SO_4) and evaporated to give a residue which was recrystallised from methyl cyanide to yield the *title compound* **8** (15.6 g, 87%) as pale yellow rhombs, m.p. 152–153 °C (decomp.) [Found: C, 58.0; H, 3.8; Br, 16.1; N, 3.0; S, 6.7%; *m/z* 415 (M – HBr). $C_{28}H_{18}BrNO_4S$ requires C, 58.1; H, 3.7; Br, 16.1; N, 3.0; S, 6.7%; *M*, 496]; ν_{max}(KBr)/cm^{-1} 1645, 1585, 1360, 1190 and 760; δ_H 8.13 (1 H, d, *J* 7, 9-H), 7.70–7.10 (12 H, m), 5.65 (1 H, br s, 6-H), 4.98 (1 H, br d, *J* 12, 4-H), 4.12 (1 H, dt, *J* 12 and 3, 4-H), 2.64 (1 H, m, 5-H) and 2.42 (1 H, m, 5-H).

2-Phenyl 1-Phenylsulfonyloxy-3a-azaphenalen-3(4H)-one **9**.—A solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (3 cm^3) in dichloromethane (10 cm^3) was added dropwise (20 min) to a stirred solution of the preceding compound **8** (5.5 g) in dichloromethane (20 cm^3) at room temperature. After 2 h the solution was shaken with dilute hydrochloric acid, and then with water, dried (K_2CO_3), and evaporated. Fractionation by column chromatography (silica gel, CH_2Cl_2) gave the *title compound* **9** (3.3 g, 72%) as pale yellow, feathery needles, m.p. 190–192 °C (decomp.) from methyl cyanide (Found: C, 69.4; H, 4.4; N, 3.3; S, 7.5%; $M^{+\cdot}$, 415. $C_{24}H_{17}NO_4S$ requires C, 69.4; H, 4.1; N, 3.4; S, 7.7%; *M*, 415); ν_{max}(KBr)/cm^{-1} 1645, 1585, 1360, 1190 and 1080; δ_H 7.90 (1 H, t, *J* 5, 9-H), 7.60–7.10 (12 H, m), 6.51 (1 H, dt, *J* 10 and 2, 6-H), 6.02 (1 H, dt, *J* 10 and 4, 5-H) and 4.90 (2 H, m, 4-H).

1-Hydroxy-2-phenyl-3a-azaphenalen-3(4H)-one **11**.—*Method A.* The preceding compound **9** (1.0 g) and potassium hydroxide (250 mg) in methanol (10 cm^3) were heated under reflux (1.5 h). The mixture was then cooled, poured into water, and acidified to give a precipitate (660 mg, 100%) which was collected. Crystallisation from ethanol gave the *title compound* **11** as tan plates, m.p. 225–230 °C (Found: $M^{+\cdot}$, 275.0950. $C_{18}H_{13}NO_2$ requires *M*, 275.0947); δ_H 7.78 (1 H, dd, *J* 8 and 2, 9-H), 7.60–7.10 (7 H, m), 6.51 (1 H, dt, *J* 10 and 2, 6-H), 6.03 (1 H, dt, *J* 10 and 4, 5-H) and 4.88 (2 H, br dd, *J* 4 and 2, 4-H).

Method B. The bromo compound **8** (2.2 g) and potassium hydroxide (1.0 g) in methanol (10 cm^3) were heated under reflux (1.5 h). The mixture was then cooled and poured into iced, dilute hydrochloric acid. Extraction (CH_2Cl_2) yielded 1,6-dihydroxy-2-phenyl-5,6-dihydro-3a-azaphenalen-3(4H)-one **10** (1.3 g) which was directly dehydrated; δ_H 8.01 (1 H, dd, *J* 8 and 2, 9-H), 7.70–7.20 (7 H, m), 6.28 (1 H, br s, OH), 4.58 (1 H, dt, *J* 14 and 4, 4-H), 4.48 (1 H, m, 6-H), 3.97 (1 H, dt, *J* 9 and 4, 4-H), 2.38 (1 H, m, 5-H) and 2.08 (1 H, m, 5-H). Compound **10** (1.1 g) in acetic acid (5 cm^3) and concentrated sulfuric acid (4 drops) was heated (1 h) in an oil-bath (100 °C). Water was added to the cooled solution and extraction (CH_2Cl_2) yielded the *title compound* **11** (900 mg, 87%), identical with that produced by method A.

1-Hydroxy-3-oxo-2-phenyl-3aλ⁵-azaphenalen-3a-ium Tetrafluoroborate **12**.—The azaphenalenone **11** (5.5 g) and triphenylcarbenium tetrafluoroborate (6.6 g) in dichloromethane (30 cm^3) were stirred (1 h) at room temperature. After the mixture had cooled, the precipitate was collected to yield the *title compound* **12** (3.85 g, 53%) as a rust-coloured powder, m.p. >210 °C (decomp.) [Found: *m/z* 273.0787. $C_{18}H_{11}NO_2$ (*M* – HBF_4) requires *m/z*, 273.0790]; ν_{max}(KBr)/cm^{-1} 1720, 1630 and 1605; $\delta_H(CD_3CN)$ 10.10 (1 H, d, *J* 6, 4-H), 9.62 (1 H, d, *J* 8, 6-H), 8.96 (1 H, d, *J* 8, 7-H or 9-H), 8.75 (1 H, d, *J* 8, 7-H or 9-H), 8.45 (1 H, dd, *J* 8 and 6, 5-H), 8.22 (1 H, t, *J* 8, 8-H), 7.55 (5 H, br s) and 6.0–5.0 (1 H, br s, OH).

3-Oxo-2-phenyl-3aλ⁵-azaphenalen-3a-ium-1-olate **4**.—Triethylamine (0.1 cm^3) was added at room temperature to a stirred suspension of the salt **12** (500 mg) in dichloromethane (5 cm^3). Evaporation of the mixture gave a deep purple residue which was fractionated by column chromatography (silica gel;

CH_2Cl_2–MeCN, 1:1) to give the *title compound* **4** (340 mg, 90%) as deep purple, lustrous needles, m.p. 222 °C (Found: $M^{+\bullet}$, 273.0767. $C_{18}H_{11}NO_2$ requires *M*, 273.0790); ν_{max}(KBr)/cm^{-1} 1675, 1625, 1600, 1390, 1335 and 775; δ_H[$^2H_6$]DMSO + trace [$^2H_5$]pyridine) 10.12 (1 H, dd, *J* 6 and 2, 4-H), 9.20 (1 H, dd, *J* 8 and 2, 6-H), 8.86 (1 H, dd, *J* 7 and 2, 7-H or 9-H), 8.45 (1 H, *J* 8 and 2, 7-H or 9-H), 8.15 (1 H, *J* 8 and 6, 5-H), 8.04 (1 H, dd, *J* 8 and 7, 8-H) and 7.57–7.14 (5 H, m).

Reaction of the Cross-conjugated Heterocyclic Mesomeric Betaine **4** *with Dimethyl Acetylenedicarboxylate.*—Pyridine (0.02 cm^3) was added at room temperature to a stirred mixture of the salt **12** (700 mg) and dimethyl acetylenedicarboxylate (DMAD) (800 mg) in dichloromethane (10 cm^3). After 8 h, evaporation and fractionation of the residue by column chromatography (silica gel, CH_2Cl_2–MeOH, 95:5) gave *dimethyl 9-oxo-10-phenyl-2H,9H-1-oxa-10b-azapyrene-2,3-dicarboxylate* **14** (230 mg, 28%) as yellow needles, m.p. 158 °C (from methanol) (Found: C, 66.4; H, 4.3; N, 3.2%. $C_{24}H_{17}NO_6 \cdot H_2O$ requires C, 66.5; H, 4.3; N, 3.2%) (Found: $M^{+\bullet}$, 415.1043. $C_{24}H_{17}NO_6$ requires *M*, 415.1056); ν_{max}(KBr)/cm^{-1} 1755, 1700 and 1630; δ_H 8.45 (1 H, dd, *J* 7.5 and 2, 8-H), 8.40 (1 H, d, *J* 10, 5-H), 7.63 (1 H, dd, *J* 7.5 and 2, 6-H), 7.48 (1 H, m, 7-H), 7.48–7.38 (6 H, m), 7.24 (1 H, d, *J* 10, 4-H), 5.79 (1 H, s, 2-H), 3.85 (3 H, s, CO_2Me) and 3.73 (3 H, s, CO_2Me).

References

1 Part 5, W. D. Ollis, C. A. Ramsden and S. P. Stanforth, *J. Chem. Soc., Perkin Trans. 1*, 1989, 965.
2 W. D. Ollis, S. P. Stanforth and C. A. Ramsden, *Tetrahedron*, 1985, **41**, 2239.
3 F. J. Kaemmerer and K. Perry, *Ger. Pat.*, 2 443 567 (*Chem. Abstr.*, 1976, **85**, P5700t).
4 G. M. Coppola, A. D. Kahle and M. J. Shapiro, *Org. Magn. Reson.*, 1981, **17**, 242; J. L. G. Ruano, C. Pedregal and J. H. Rodriguez, *Heterocycles*, 1991, **32**, 2151.
5 D. H. R. Barton, P. D. Magnus, J. A. Garbarino and R. N. Young, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2101.
6 Part 1, W. D. Ollis, C. A. Ramsden and S. P. Stanforth, *J. Chem. Soc., Perkin Trans. 1*, 1989, 945.

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