Phenyliodonium Derivatives from 4-Aminocoumarin and their Reactivity

Ioannis Papoutsis, Spyros Spyroudis* and Anastasios Varvoglis*

Laboratory of Organic Chemistry, Chemistry Department,
University of Thessaloniki, Thessaloniki 54006, Greece
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Dedicated to the memory of Professor Nicholas Alexandrou

The reaction of 4-aminocoumarin with [hydroxy(tosyloxy)iodo]benzene affords 4-amino-3-phenyliodoniocoumarin tosylate which upon basification is converted to the corresponding stable iodine-nitrogen 1,4-dipole. The reactivity of the latter is briefly discussed.

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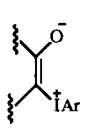
Aryliodonium phenolates of the general type **1** constitute an interesting class of iodine-oxygen 1,4-dipoles whose chemistry, as well as of other zwitterionic iodonium compounds, has been reviewed [1].



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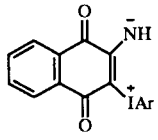
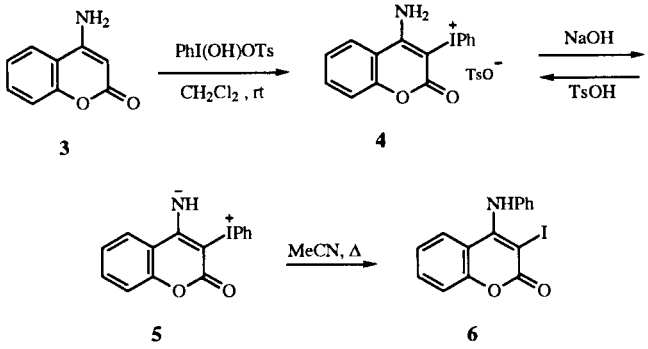


2

We have recently described the preparation and explored briefly the reactivity of a new class of iodine-nitrogen 1,4-dipoles, *i.e.* 3-aryliodonio-1,4-naphthoquinone-2-imides, **2**, resulting from the reaction of 2-aminonaphthoquinone with [hydroxy(tosyloxy)iodo]arenes [2].

Extending our studies to other systems containing the same β-keto-enamino functionality, we find that a related heterocyclic substrate, 4-aminocoumarin, **3**, forms analogous stable phenyliodonium derivatives. Treatment of **3** with [hydroxy(tosyloxy)iodo]benzene under mild conditions resulted in the formation of its 3-phenyliodonium tosylate, **4**, in high yield; upon basification, this was converted to its conjugated acid, *i.e.* the stable 1,4-dipole **5** (Scheme 1).

Scheme 1

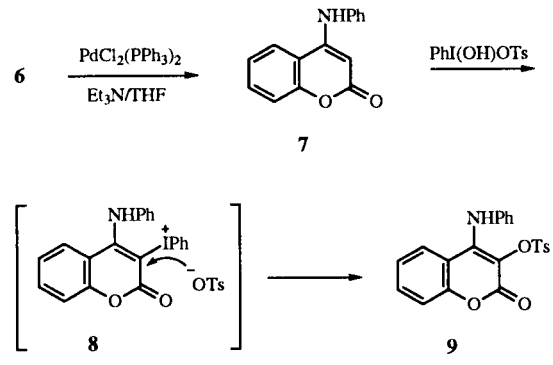


3 **4** **5** **6**

The characterization of these new phenyliodonium compounds was based on elemental analysis and spectral data (ir, nmr, ms) which were consistent with the proposed structures. In addition, **5** upon reaction with *p*-toluenesulfonic acid was converted back to **4**. Attempts to explore the reactivity of **5** (photochemical and thermal reactions with alkenes and alkynes) were not successful because isomerization prevailed, with formation of 3-iodo-4-phenylaminocoumarin, **6**. Indeed, this rearrangement which has been observed in several analogous 1,4-iodonium zwitterions derived from β-diketones [1], phenols [3,4] or enaminones [2], proceeded quantitatively in refluxing acetonitrile. Most likely, it constitutes another example of a Smiles-type rearrangement.

Deiodination of **6** was effected quantitatively upon treatment with $PdCl_2(PPh_3)_2$ in triethylamine and tetrahydrofuran. Unexpectedly, the resulting 4-phenylaminocoumarin, **7**, did not furnish a stable iodonium derivative similar to **4**, when it was treated with [hydroxy(tosyloxy)iodo]-benzene, but it was converted directly to 3-tosyloxy-4-phenylaminocoumarin, **9**, through the intermediacy of the tosylate **8** (Scheme 2). This reaction is a further demonstration of the superleaving group ability of phenyliodonio group [1] which enables this substitution with such a weak nucleophile under so mild conditions.

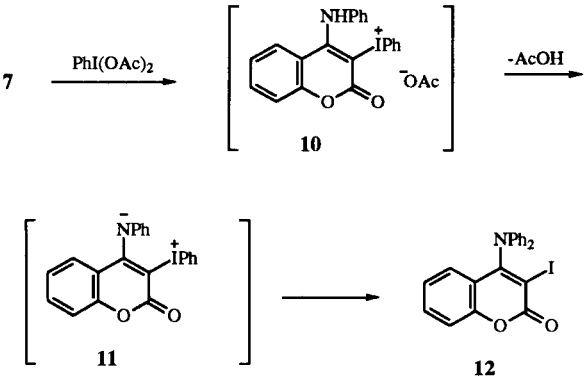
Scheme 2



6 **7** **8** **9**

Interestingly enough, when 4-phenylaminocoumarin, **7**, was treated with (diacetoxyiodo)benzene, 4-diphenylamino-3-iodocoumarin, **12**, was the only isolable product (Scheme 3). The reaction, no doubt, proceeds through the phenyliodonium acetate, **10**, which is converted *in situ* to

Scheme 3



the the corresponding dipole, **11**; this upon phenyl migration affords compound **12.**

In conclusion, we have shown that stable iodine-nitrogen 1,4-dipoles can be obtained from heterocyclic compounds bearing the β-enaminoketone functionality. Our future research will be extended to other similar heterocyclic systems.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. The ir spectra were determined on a Perkin-Elmer 1370 spectrometer. The ^{1}H nmr spectra were recorded on Bruker AW 80 MHz and AM 300 MHz spectrometers using tetramethylsilane as an internal standard. The ms spectra were recorded on a VG TS-250 instrument.

Compound **3**, 4-aminocoumarin, was prepared from the reaction of 4-hydroxycoumarin with ammonium acetate [5].

Preparation of 4-Amino-3-phenyliodoniocoumarin Tosylate (**4**).

[Hydroxy(tosyloxy)iodo]benzene (1.96 g, 5 mmoles) was added to a stirring suspension of 4-aminocoumarin **3** (0.805 g, 5 mmoles) in dichloromethane (30 ml). After one hour at room temperature the resulting white solid was filtered, washed repeatedly with dichloromethane and dried *in vacuo* to yield 2.542 g (95%) of the tosylate **4**, mp 194-196°; ir (nujol): ν_{max} 3340, 3210, 1680, 1645, 1180, 1160 cm^{-1}; ^{1}H nmr (80 MHz) (deuteriochloroform/trifluoroacetic acid): δ 8.36-7.13 (m, 13H), 2.39 (s, 3H); ms: m/z 363 (M^+-TsOH, 60), 331 (M^+-PhI, 58), 204 (92), 176 (100), 155 (61).

Anal. Calcd. for $C_{22}H_{18}INO_5S$: C, 49.36; H, 3.39; N, 2.62. Found: C, 49.39; H, 3.69; N, 2.48.

Preparation of 3-Phenyliodoniocoumarin-4-imide (**5**).

A solution of aqueous sodium hydroxide (8 ml, 2%, 4 mmoles) was added to the tosylate **4** (1.07 g, 2 mmoles). After half an hour stirring at room temperature the resulting yellow solid was filtered, washed successively with water and diethyl ether and dried *in vacuo* to yield 0.668 g (92%) of the dipole **5**, mp 93-95°; ir (nujol): ν_{max} 3450, 1620, 1595 cm^{-1}; ^{1}H nmr (80 MHz) (deuteriochloroform/trifluoroacetic acid): δ 8.32-7.31 (m, aromatic H); ms: m/z 363 (M^+, 44), 236 (57), 170 (100), 77 (75).

Anal. Calcd. for $C_{15}H_{10}INO_2$: C, 49.61; H, 2.78; N, 3.86. Found: C, 49.37; H, 2.61; N, 3.68.

Preparation of 3-Iodo-4-phenylaminocoumarin (**6**).

A suspension of the dipole **5** (0.363 g, 1 mmole) in acetonitrile (15 ml) was refluxed for three hours. The resulting solution was evaporated to dryness and the remaining crude solid was recrystallized from ethanol to afford 0.29 g (80%) of coumarin **6**, mp 181-182°; ir (nujol): ν_{max} 3300, 1675, 1585 cm^{-1}; ^{1}H nmr (80 MHz) (deuteriochloroform): δ 7.69-6.73 (m, aromatic H); ms: m/z 363 (M^+, 92), 236 (56), 77 (100).

Anal. Calcd. for $C_{15}H_{10}INO_2$: C, 49.61; H, 2.78; N, 3.86. Found: C, 49.78; H, 2.90; N, 3.85.

Deiodination of **6** to 4-Phenylaminocoumarin (**7**).

A catalytic amount of $PdCl_2(PPh_3)_2$ (0.035 g, 0.05 mmole) was added to a solution of iodocoumarin **6** (0.363 g, 1 mmole) in tetrahydrofuran (10 ml) and triethylamine (5 ml) and the mixture was stirred at room temperature until the disappearance of **6** (3 hours, monitored by tlc). After removal of the solvent, the residue was chromatographed on column (silica gel, hexane-ethyl acetate 2:1) to yield 4-phenylaminocoumarin **7** (0.178 g, 75%), mp 266-267° (ethanol) (lit [6] mp 267-268°); ir (nujol): ν_{max} 3280, 1655, 1610, 1585 cm^{-1}; ^{1}H nmr (80 MHz) (deuteriochloroform/deuterated dimethyl sulfoxide): δ 8.76 (s br, 1H, NH), 8.20-7.20 (m, 9H), 5.54 (s, 1H, H-3).

Compound **6** was in all respects identical to 4-phenylaminocoumarin prepared from 4-hydroxycoumarin and aniline, according to the literature method [6].

Preparation of 3-Tosyloxy-4-anilinocoumarin (**9**).

[Hydroxy(tosyloxy)iodo]benzene (0.784 g, 2 mmoles) was added to a stirring suspension of 4-phenylaminocoumarin **6** (0.474 g, 2 mmoles) in chloroform (15 ml). After 24 hours at room temperature the solvent was removed and the residue was chromatographed on column (silica gel, hexane-ethyl acetate from 10:1 to 2:1). Iodobenzene was eluted first. The second fraction was recrystallized from ethanol to afford 0.245 g of coumarin **9** (67% yield, based on reacted **6**), mp 196-198°; ir (nujol): ν_{max} 3300, 1670, 1170 cm^{-1}; ^{1}H nmr (300 MHz) (deuteriochloroform): δ 7.97 (d, J = 8.4 Hz, 2H), 7.46 (m, 1H), 7.24-7.39 (m, 7H), 7.20 (m, 1H), 7.07 (d, J = 8.4 Hz, 2H), 7.01 (m, 1H), 2.44 (s, 3H); ^{13}C nmr (75 MHz) (deuteriochloroform): δ 21.8, 114.6, 117.6, 123.0, 123.5, 125.3, 125.9, 126.3, 128.9, 129.4, 129.7, 131.9, 132.3, 140.3, 145.1, 146.0, 153.0, 159.0.

Anal. Calcd. for $C_{22}H_{17}NO_5S$: C, 64.85; H, 4.21; N, 3.44. Found: C, 64.68; H, 4.31; N, 3.58.

Unreacted 4-phenylaminocoumarin (0.261 g) was the third fraction.

Preparation of 4-Diphenylamino-3-iodocoumarin (**12**).

(Diacetoxy)iodobenzene (0.966 g, 3 mmoles) was added to a stirring suspension of 4-phenylaminocoumarin **7** (0.237 g, 1 mmole) in dichloromethane (15 ml). After one day at room temperature the resulting solution was evaporated and the residue was chromatographed on column (silica gel, hexane-ethyl acetate 10:1). After a small amount of iodobenzene, 4-diphenylamino-3-iodocoumarin **12** (0.307 g, 70%) was eluted and recrystallized from ethanol, yellow crystals, mp 247-248°; ir (nujol): ν_{max} 1695, 1580 cm^{-1}; ^{1}H nmr (80 MHz) (deuteriochloroform): δ 7.54-7.00 (m, aromatic H); ms: m/z 439 (M^+ 28), 312 (M^+-I, 81), 77 (100).

Anal. Calcd. for $C_{21}H_{14}INO_2$: C, 57.42; H, 3.21; N, 3.19. Found: C, 57.41; H, 3.11; N, 3.20.

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