Delocalized cationic azo dyes derived from
2-aminoselenazole-5-carbaldehyde

Maria A. Salvador,a Lucinda V. Reis,a P. Almeida,b and Paulo F. Santos*a*

aDepartamento de Química and Centro de Química - Vila Real,
Universidade de Trás-os-Montes e Alto Douro, Apartado 1013, 5001-801 Vila Real, Portugal
bDepartamento de Química and Unidade de I & D de Materiais Têxteis e Papelereiros,
Universidade da Beira Interior, 6201-001 Covilhã, Portugal
E-mail: psantos@utad.pt

Abstract
Several delocalized cationic azo dyes incorporating a selenazole ring have been prepared by
Knoevenagel condensation of an intermediate azo compound bearing a 5-formylselenazole group
with methylene bases derived from indolenine, benzothiazole, benzoselenazole, and quinoline.
All dyes display a strong absorption at around 700 nm, bathochromically shifted relative to their
thiazole analogues, and show a negative solvatochromic behavior.

Keywords: Azo dyes, delocalized, cationic, selenazole, solvatochromism

Introduction

More than half of all commercially available dyes are azo dyes.1 Only a few azo dyes absorb in
the near infrared (NIR),2 and among these, delocalized cationic dyes are rare.2f The majority of
NIR azo dyes display bathochromism of the thiazole ring3 incorporated in the chromophore.

Recently, we have reported the synthesis of some delocalized cationic azo dyes derived from
2-amino- and 2-amino-4-chlorothiazole-5-carbaldehyde2g,h with absorption in the long-
 wavelength region of the visible spectrum. Delocalized cationic azo dyes are a borderline case of
polymethine dyes.4 We anticipated that the substitution of sulfur by selenium would have a
bathochromic effect as observed with methine dyes derived from N,N-disubstituted 2-
aminothiazoles and 2-aminoselenazoles.5 Therefore, we synthesized several representative
eamples of delocalized cationic azo dyes based on Knoevenagel condensation of an azo
derivative 5 of 2-aminoselenazole-5-carbaldehyde (3) with heterocyclic methylene bases.
Results and Discussion

The synthetic strategy used to prepare the dyes described herein, i.e., the incorporation of a selenazole moiety into the chromophore, parallels that previously reported for their thiazole analogues. The selenazole features a diazotable amino group at C-2 to be coupled to an aromatic amine, and a formyl group at C-5, suitable to undergo Knoevenagel condensation with a cationic methylheterocycle.

Whereas several syntheses have been described for 2-aminothiazole-5-carbaldehyde, the selenium analogue appears to be unknown. The synthesis of 2-aminoselenazole-5-carbaldehyde (3) was accomplished in rather good yield by a modified Hantzsch method from bromomalonaldehyde (1) and selenourea (2) (Scheme 1). It is worthwhile mentioning that despite the desired structural diversity of 1,3-selenazoles due to the growing interest in their potential biological activities, only few syntheses of 5-acyl-2-amino-1,3-selenazoles have been reported. 2-Aminoselenazole-5-carbaldehyde (3) was subsequently diazotized with nitrosyl bisulfate in DMF, and the resulting diazonium salt 4 was coupled with N,N-diethylaniline to afford the azo dye 5 in 17% yield. Although different diazotization/coupling conditions were used, we were unable to improve the yield.

Finally, condensation of 5 with a quaternary heterocyclic salt 6a–d in the presence of pyridine furnished the delocalized cationic azo dyes 7a–d in poor to moderate yields.

All synthesized dyes display a strong absorption (ε > 10⁴ cm⁻¹M⁻¹) within the range of 684–744 nm (Table 1); the molar absorption coefficients are approximately 10 times smaller than those of the corresponding thiazole analogs. When compared to the latter, the maximum wavelength of absorption of the selenazole-derived dyes is bathochromically shifted from 9 to 30 nm, except in the case of dye 7b, for which a hypsochromic shift of 6 nm was observed. The largest bathochromic shift was observed for the quinoline-based dye 7d, while the lowest was displayed by dye 7c derived from benzoselenazole.
As with their thiazole counterparts, dyes 7a-d show negative solvatochromic behavior on passing from CH$_2$Cl$_2$ to DMSO, and from this to the even more polar MeOH.$^9$ The largest solvatochromic shift was observed for the indolenine dye 7a (60 nm).

### Table 1. Yields and Vis spectral data for azo dyes 7

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield (%)</th>
<th>$\lambda_{\text{max}}$ [nm] (log $\varepsilon$)</th>
<th>$\lambda_{\text{max}}$ [nm]</th>
<th>$\lambda_{\text{max}}$ [nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>20</td>
<td>CH$_2$Cl$_2$ 744 (4.73)</td>
<td>DMSO 687</td>
<td>MeOH 684</td>
</tr>
<tr>
<td>7b</td>
<td>13</td>
<td>684 (4.76)</td>
<td>648</td>
<td>645</td>
</tr>
<tr>
<td>7c</td>
<td>17</td>
<td>702 (4.63)</td>
<td>651</td>
<td>645</td>
</tr>
<tr>
<td>7d</td>
<td>13</td>
<td>687 (4.36)</td>
<td>642</td>
<td>639</td>
</tr>
</tbody>
</table>

In conclusion, a modified Hantzsch method was used to prepare, in rather good yield, 2-aminoselenazole-5-carbaldehyde (3), a novel member of the limited family of the biologically important 5-acyl-2-amino-1,3-selenazoles. The Knoevenagel condensation of an azo derivative of 3 with methylene bases generated in situ from benzoazolium and quinolinium salts 6 was then used to prepare several new delocalized cationic azo dyes. The so formed dyes display strong absorption around 700 nm, which is, in general, bathochromically shifted in relation to that of the known thiazole analogues.

### Experimental Section

#### General Procedures.

All reagents were of the highest purity available, purchased from Sigma-Aldrich Company, and were used as received. Bromomalonaldehyde (1)$^{10}$ and the quaternary ammonium salts 6a–d were prepared according to the literature.$^{11}$ Reactions were monitored by thin-layer chromatography using 0.25 mm aluminium-backed silica-gel plates (Merck 60 F$_{254}$). Melting points were measured in open capillary tubes in a Büchi 530 melting point apparatus. IR spectra were recorded on a Mattson 5000 FT IR spectrophotometer. UV/Vis spectra were performed on a Perkin-Elmer Lambda 6 instrument. $^1$H and $^{13}$C NMR spectra were recorded on Bruker ARX 400 or ACP 250 spectrometers. Chemical shifts are reported with respect to the solvent or TMS as internal standard. Fast Atom Bombardment High Resolution mass spectra (FABHRMS) were determined on a Micromass AutoSpec M spectrometer, operating at 70 eV, using a matrix of 3-nitrobenzyl alcohol (3-NBA).

2-Aminoselenazole-5-carbaldehyde (3). To a suspension of bromomalonaldehyde (1) (5.00 g, 33.11 mmol) in water (108 mL), vigorously stirred under N$_2$, was added selenourea (2) (4.16 g, 33.11 mmol). The mixture was stirred at room temperature for 24 h, then poured onto ice and neutralized with aqueous ammonia (25%). The precipitated product was collected by filtration under reduced pressure, washed with cold water and dried under reduced pressure over P$_2$O$_5$ to
afford chromatographically pure 3. Upon concentration of the filtrate under reduced pressure, an additional crop of product with same purity could be obtained. Orange-reddish solid (3.08 g, 53%); mp 183 °C (dec.). Rf 0.56 (MeOH). IR (KBr): \( \tilde{\nu}_{\text{max}} \) 3360 (w), 3274 (w), 3065 (w), 2838 (w), 1613 (s), 1532 (w), 1495 (s), 1396 (m), 1297 (w), 1206 (s), 1042 (w), 789 (w), 644 cm\(^{-1}\) (w). \(^1\)H NMR (400.13 MHz, CDCl\(_3\)): \( \delta \) 9.59 (s, 1H, CHO), 8.55 (br s, 2H, NH\(_2\), exchanging with D\(_2\)O), 7.89 (s, 1H, H-4). \(^13\)C NMR (100.61 MHz, CDCl\(_3\)): \( \delta \) 131.4 (C-5), 156.3 (C-4), 177.2 (C-2), 182.8 (CHO). FABHRMS (3-NBA): Calcd. for C\(_4\)H\(_5\)N\(_2\)O\(_8\)Se: 174.9575; found: 174.9575. Calcd for C\(_4\)H\(_5\)N\(_2\)O\(_8\)Se [M+H]+: 176.9567; found: 176.9565.

2-(4-Diethylaminophenylazo)selenazole-5-carbaldehyde (5). To a solution of 2-aminoselenazole-5-carbaldehyde (3) (1.5 g, 8.6 mmol) in DMF (28.5 mL) were added concentrated H\(_2\)SO\(_4\) (2.8 mL) and NaNO\(_2\) (591 mg, 8.6 mmol), and the mixture was stirred at 0 °C for about 1 h. To the resulting diazonium salt solution was gradually added a solution of \( N, N \)-diethylaniline (1.4 mL, 8.6 mmol) in DMF (85.5 mL), and the mixture was stirred at r.t. for 1 h. The mixture was then poured into water and thoroughly extracted with CHCl\(_3\). The organic extracts were combined, washed sequentially with 1% aqueous NaHCO\(_3\) and water, and dried over anhydrous Na\(_2\)SO\(_4\). Removal of the solvent at reduced pressure yielded a residue, which was purified by column chromatography (silica gel, petroleum ether/\( \text{Et}_2\)O 9:1 \(\rightarrow\) 1:1) and recrystallized from \( \text{Et}_2\)O/CHCl\(_3\)/\(n\)-hexane. Purple crystals (491 mg, 17%); mp 136–137 ºC. Rf 0.68 (CH\(_2\)Cl\(_2\)/MeOH 95:5). Vis (CH\(_2\)Cl\(_2\)): \( \lambda_{\text{max}} \) (log \( \varepsilon \)) 561 (4.58) nm. IR (KBr): \( \tilde{\nu}_{\text{max}} \) 2973 (w), 2919 (w), 1657 (m), 1600 (s), 1543 (w), 1448 (w), 1414 (w), 1326 (m), 1304 (s), 1260 (m), 1219 (m), 1120 (s), 1072 (m), 1006 (m), 882 (w), 828 (w), 715 cm\(^{-1}\) (w). \(^1\)H NMR (250.13 MHz, CDCl\(_3\)) \( \delta \) 1.24 (t, 6H, \( J = 7.1 \) Hz, CH\(_3\)), 3.48 (q, 4H, \( J = 7.1 \) Hz, CH\(_2\)), 6.66, 6.70 (AA’, 2H, ArH), 7.87, 7.91 (BB’, 2H, ArH), 8.47 (s, 1H, =CHN), 9.82 (s, 1H, CHO). FABHRMS (3-NBA): Calcd for C\(_{14}\)H\(_{17}\)N\(_4\)O\(_8\)Se: 335.0575; found: 335.0564. Calcd. for C\(_{14}\)H\(_{17}\)N\(_4\)O\(_8\)Se [M+H]+: 337.0568; found: 337.0565.

Synthesis of dyes 7a–d. General procedure
A solution of a quaternary ammonium salt 6 (1.0 mmol) and the azo dye 5 (0.34 g, 1.0 mmol) in EtOH (ca 15 mL) containing pyridine (1.5 mL) was stirred between r.t. and 40–50 ºC until complete consumption of the starting azo dye (6–46 h). The temperature was carefully controlled to avoid the decomposition of both the starting material and the reaction product. The reaction mixture was then cooled, and Et\(_2\)O was added. The resulting dark-blue solid was collected by filtration under reduced pressure, washed several times with Et\(_2\)O, dissolved in CHCl\(_3\) and the solution washed with water. The organic layer, after being separated by decantation, was dried over anhydrous Na\(_2\)SO\(_4\) and evaporated to dryness. The resulting residue was recrystallized from CHCl\(_3\)/MeOH/\( \text{Et}_2\)O until a chromatographically pure material was obtained (1–3 times).

2-{2-[2-(4-Diethylaminophenylazo)selenazo-5-yl]vinyl}-1-ethyl-3,3-dimethyl-3\(^{\text{H}}\)-indolium iodide (7a). Dark-green solid. (38 mg, 20%); mp 184 ºC (dec.). Rf 0.51 (CH\(_2\)Cl\(_2\)/MeOH 9:1). Vis (CH\(_2\)Cl\(_2\)): \( \lambda_{\text{max}} \) (log \( \varepsilon \)) 744 (4.73). IR (KBr): \( \tilde{\nu}_{\text{max}} \) 2971 (w), 1598 (m), 1572 (s), 1534 (m), 1463 (w), 1242 (s), 1206 (m), 1164 (w), 1108 (s), 1067 (s), 1040 (m), 1004 (w), 940 (w), 879 (w), 768
cm⁻¹ (w). ¹H NMR (400.13 MHz, DMSO-d₆): δ 1.22 (t, 6H, J = 6.9 Hz, CH₃), 1.42 (t, 3H, J = 7.1 Hz, CH₂), 1.79 (s, 6H, CH₃), 3.63 (br q, 4H, J = 6.9 Hz, CH₂), 4.63 (br q, 2H, J = 7.1 Hz, CH₂), 7.02, 7.04 (AA', 2H, ArH), 7.17 (d, 1H, J = 15.4 Hz, =CHC), 7.59–7.64 (m, 2H, ArH), 7.83–7.88 (m, 4H, ArH), 8.70 (d, 1H, J = 15.4 Hz, =CHC), 8.79 (s, 1H, =CHN). ¹³C NMR (100.61 MHz, DMSO-d₆): δ 12.7 (CH₃), 13.6 (CH₃), 25.6 (C(CH₃)₂), 41.7 (C(CH₃)₂), 45.2 (CH₂), 51.9 (CH₂), 113.2, 114.7, 123.0, 129.0, 129.1, 139.0, 140.5, 142.8, 143.7, 147.0, 153.9, 156.7, 179.8, 190.4. FABHRMS (3-NBA): Calcd. for C₂₇H₃₂N₅Se: 504.1831; found: 504.1853. Calcd. for C₂₇H₃₂N₅Se⁺ [M⁺]$: 506.1823; found: 506.1836.

2-[2-[2-(4-Diethylaminophenylazo)selenazol-5-yl]vinyl]-3-ethylbenzothiazol-3-ium iodide (7b). Dark-green solid (126 mg, 20%); mp 173 °C (dec.). Rf 0.46 (CH₂Cl₂/MeOH 9:1). Vis (CH₂Cl₂): λmax (log ε) 684 (4.76). IR (KBr): νmax 2970 (w), 1592 (m), 1574 (m), 1537 (w), 1443 (w), 1414 (w), 1253 (s), 1206 (m), 1069 (s), 1034 (w), 1005 (w), 826 (w), 784 cm⁻¹ (w). ¹H NMR (400.13 MHz, DMSO-d₆): δ 1.22 (t, 6H, J = 7.1 Hz, CH₃), 1.47 (t, 3H, J = 8 Hz, CH₂), 3.61 (br q, 4H, J = 7.1 Hz, CH₂), 4.91 (br q, 2H, J = 7.1 Hz, CH₂), 6.97, 6.99 (AA', 2H, ArH), 7.61 (d, 1H, J = 15.2 Hz, =CHC), 7.76–7.88 (m, 4H, ArH), 8.25 (d, 1H, J = 8.2 Hz, ArH), 8.42–8.49 (m, 2H, ArH and =CHC), 8.57 (s, 1H, =CHN). ¹³C NMR (100.61 MHz, DMSO-d₆): δ 12.3 (CH₃), 13.8 (CH₃), 44.1 (CH₃), 44.7 (CH₂), 112.6, 114.1, 116.2, 124.1, 128.0, 129.3, 137.9, 140.6, 142.0, 153.2, 188.6. FABHRMS (3-NBA): Calcd. for C₂₄H₂₆N₅Se: 494.1082; found: 494.1080. Calcd. for C₂₄H₂₆N₅Se⁺ [M⁺]: 496.1074; found: 496.1076.

2-[2-[2-(4-Diethylaminophenylazo)selenazol-5-yl]vinyl]-3-ethylbenzoselenazol-3-ium iodide (7c). Dark-brownish solid (114 mg, 17%); mp 209 °C (dec.). Rf 0.51 (CH₂Cl₂/MeOH 9:1). Vis (CH₂Cl₂): λmax (log ε) 702 (4.63). IR (KBr): νmax 2971 (w), 2924 (w), 1600 (m), 1568 (s), 1538 (m), 1442 (w), 1416 (w), 1379 (w), 1247 (s), 1198 (m), 1113 (s), 1072 (s), 1006 (m), 880 (w), 775 cm⁻¹ (w). ¹H NMR (400.13 MHz, DMSO-d₆): δ 1.21 (t, 6H, J = 6.8 Hz, CH₃), 1.43 (t, 3H, J = 7.1 Hz, CH₂), 3.59 (br q, 4H, J = 6.8 Hz, CH₂), 4.88 (br q, 2H, J = 7.1 Hz, CH₂), 6.95, 6.98 (AA', 2H, ArH), 7.59 (d, 1H, J = 14.9 Hz, =CHC), 7.68 (t, 1H, J = 8.0 Hz, ArH), 7.79–7.81 (m, 3H, ArH), 8.21 (d, 1H, J = 8.0 Hz, ArH), 8.44 (d, 1H, J = 8.0 Hz, ArH), 8.54–8.58 (m, 2H, =CHC and =CHN). ¹³C NMR (100.61 MHz, DMSO-d₆): δ 12.6 (CH₃), 14.1 (CH₃), 45.0 (CH₂), 45.2 (CH₂), 112.9, 117.2, 117.9, 127.3, 127.9, 129.0, 130.1, 138.5, 142.1, 142.3, 143.9, 153.4, 153.7, 179.2, 188.8. FABHRMS (3-NBA): Calcd. for C₂₄H₂₆N₅Se: 540.0534; found: 540.0538. Calcd. for C₂₄H₂₆N₅Se⁺ [M⁺]: 542.0526; found: 542.0515. Calcd. for C₂₄H₂₆N₅Se⁺ [M⁺]: 544.0519; found: 544.0536.

2-[2-[2-(4-Diethylaminophenylazo)selenazol-5-yl]vinyl]-1-ethylquinolinium iodide (7d). Dark-green solid (80 mg, 13%); mp 193 °C (dec.). Rf 0.44 (CH₂Cl₂/MeOH 9:1). Vis (CH₂Cl₂): λmax (log ε) 687 (4.36). IR (KBr): νmax 2971 (w), 1584 (s), 1502 (w), 1410 (w), 1329 (w), 1256 (m), 1206 (m), 1115 (s), 1072 (m), 1006 (w), 826 (w), 759 cm⁻¹ (w). ¹H NMR (400.13 MHz, DMSO-d₆): δ 1.20 (t, 6H, J = 7.0 Hz, CH₃), 1.55 (t, 3H, J = 7.0 Hz, CH₃), 3.56 (br q, 4H, J = 7.0 Hz, CH₂), 5.09 (br q, 2H, J = 7.0 Hz, CH₂), 6.91, 6.93 (AA', 2H, ArH), 7.40 (d, 1H, J = 15.0 Hz, =CHC), 7.76, 7.78 (BB', 2H, ArH), 7.92 (t, 1H, J = 7.5 Hz, ArH), 8.16 (t, 1H, J = 7.5 Hz, ArH),
8.32 (d, 1H, J = 7.5 Hz, ArH), 8.40 (s, 1H, =CHN), 8.53–8.56 (m, 3H, ArH and =C\text{H}C), 9.00 (d, 1H, J = 8.9 Hz, ArH). $^{13}$C NMR (100.61 MHz, DMSO-$d_6$): $\delta$ 12.5 (CH$_3$), 14.0 (CH$_3$), 44.8 (CH$_2$), 46.4 (CH$_2$), 112.6, 118.8, 119.9, 120.8, 128.0, 128.8, 130.2, 135.0, 138.0, 139.3, 141.0, 142.0, 143.7, 151.7, 153.0, 154.1, 187.4. FABHRMS (3-NBA): Calcd. for C$_{26}$H$_{28}$N$_5$\textsuperscript{78}Se: 488.1518; found: 488.1519. Calcd. for C$_{26}$H$_{28}$N$_5$\textsuperscript{80}Se [M$^+$]: 490.1510; found: 490.1508.

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References