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REACTION OF 2,4-DINITROFLUOROBENZENE WITH ENEDIAMINES. SYNTHESIS OF CINNOLINES

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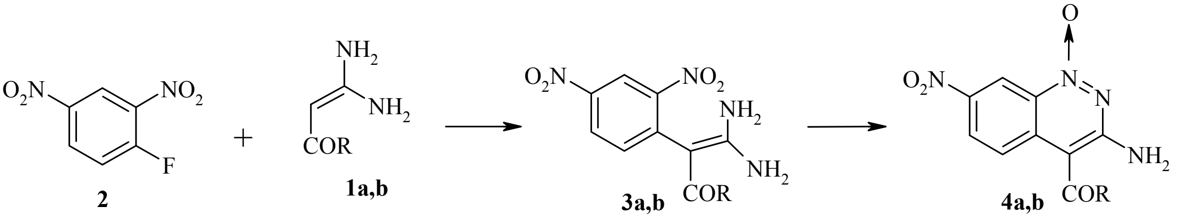
As we have shown previously, enediamines **1** can cyclocondense with aromatic electrophiles (aldehydes and esters) containing an active halogen atom in an *ortho* position to the electrophilic group to give condensed aminoazines [1-3]. The reaction occurs chemoselectively, the aromatic halogen atom being substituted by the carbon of the nucleophilic center of the enediamine and an amino group reacts with an exocyclic electrophilic group.

In this work we have studied the use of nitro as the electrophilic group. Similar cyclizations involving nitro and amino groups are well known [4-6].

The reaction of the enediamines **1** with 2,4-dinitrofluorobenzene (**2**) occurs smoothly at room temperature to give a high yield of the products of substitution of the fluorine atom by the α-carbon of the enediamine **3**. Subsequent cyclization at the nitro group in the presence of sodium hydride under the conditions reported in [7] gives the cinnoline 1-oxides **4**.



1, 3, 4 a R = OEt, **b** R = Ph

^1H and ^{13}C NMR spectra were taken on a Bruker DPX 300 instrument (300 and 75 MHz respectively) using DMSO-d_6 with the residual signals of the DMSO-d_5 (δ 2.50 ppm for ^1H) or DMSO-d_6 (δ 39.7 ppm for ^{13}C) as internal standards.

Reaction of 2,4-Dinitrofluorobenzene (2) with Enediamines 1. Enediamine **1** (1.1 eq.) was added to a solution of compound **2** (1 eq.) in dry DMF and stirred at room temperature for 20 h. It was then diluted with water and the precipitated crystals were filtered off and recrystallized from a mixture of ethanol and acetonitrile (4:1).

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Ethyl 3,3-Diamino-2-(2,4-dinitrophenyl)acrylate (3a). Yield 91%; mp 229-231ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.97 (3H, t, *J* = 7.0, CH_3); 3.80 (2H, q, *J* = 7.0, CH_2); 6.74 (4H, br. s, $2NH_2$); 7.64 (1H, d, *J* = 8.7, H-6); 8.30 (1H, d, *J* = 8.7, H-5); 8.58 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 14.98, 58.53, 75.09, 120.41, 126.97, 137.20, 140.82, 144.95, 150.62, 161.75, 166.84. Found, %: C 44.60; H 4.08; N 18.91. $C_{11}H_{12}N_4O_5$. Calculated, %: C 44.48; H 4.07; N 18.69.

3,3-Diamino-2-(2,4-dinitrophenyl)-1-phenylpropenone (3b). Yield 90%; mp 225-227ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.09 (9H, m, $2NH_2 + C_6H_5$); 7.45 (1H, d, *J* = 8.7, H-6); 8.18 (1H, dd, *J* = 8.7, *J* = 2.2, H-5); 8.50 (1H, d, *J* = 2.2, H-3). ^{13}C NMR spectrum, δ, ppm: 90.35, 120.78, 126.86, 128.08, 128.24, 128.79, 139.40, 141.74, 143.82, 146.01, 150.99, 162.99, 185.84. Found, %: C 54.92; H 3.71; N 16.98. $C_{15}H_{12}N_4O_5$. Calculated, %: C 54.98; H 3.68; N 17.06.

Cyclization of 2,4-Dinitrophenyl-substituted Enediamines 3 to Cinnoline N-Oxides 4. Sodium hydride (60% suspension in mineral oil, 1.2 eq.) was added to a solution of enediamine **3** (1 eq.) in dry DMF with stirring and cooling in ice. Stirring was continued at room temperature for 24 h, aqueous acetic acid (2 eq.) was added, and the precipitated crystals were filtered off and recrystallized from acetonitrile.

Ethyl 3-Amino-7-nitrocinnoline-4-carboxylate 1-Oxide (4a). Yield 68%; mp 247-249ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.39 (3H, t, *J* = 7.3, CH_3); 4.43 (2H, q, *J* = 7.3, CH_2); 8.16 (2H, s, NH_2); 8.39 (1H, dd, *J* = 9.3, *J* = 2.0, H-6); 8.69 (1H, d, *J* = 9.3, H-5); 8.95 (1H, d, *J* = 2.0, H-8). ^{13}C NMR spectrum, δ, ppm: 14.92, 62.36, 90.75, 118.51, 127.09, 127.23, 132.90, 137.18, 143.83, 158.63, 166.16. Found, %: C 47.24; H 3.86; N 20.04. $C_{11}H_{10}N_4O_5$. Calculated, %: C 47.49; H 3.62; N 20.14.

3-Amino-4-benzoyl-7-nitrocinnoline 1-Oxide (4b). Yield 56%; mp 224-226ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.31 (1H, d, *J* = 9.4, H-5); 7.52 (4H, m, NH_2 + *m*-C_6H_5); 7.70 (1H, t, *J* = 7.3, *p*-C_6H_5); 7.87 (2H, d, *J* = 7.3, *o*-Ph); 8.15 (1H, dd, *J* = 9.4, *J* = 2.2, H-6); 8.97 (1H, d, *J* = 2.2, H-8). ^{13}C NMR spectrum, δ, ppm: 101.85, 118.92, 126.06, 126.44, 129.88, 130.54, 132.25, 134.99, 136.95, 138.21, 144.04, 156.07, 194.06. Found, %: C 58.44; H 3.42; N 18.33. $C_{15}H_{10}N_4O_4$. Calculated, %: C 58.07; H 3.25; N 18.06.

REFERENCES

1. D. V. Dar'in, S. I. Selivanov, P. S. Lobanov, and A. A. Potekhin, *Khim. Geterotsikl. Soedin.*, 1036 (2004). [*Chem. Heterocycl. Comp.*, **40**, 888 (2004)].
2. S. G. Ryazanov, S. I. Selivanov, D. V. Dar'in, P. S. Lobanov, and A. A. Potekhin, *Zh. Org. Khim.*, **44**, 292 (2008).
3. D. V. Dar'in, S. G. Ryazanov, S. I. Selivanov, P. S. Lobanov, and A. A. Potekhin, *Khim. Geterotsikl. Soedin.*, 589 (2008).[*Chem. Heterocycl. Comp.*, **44**, 461 (2008)].
4. G. B. W. Ligthart, D. Guo, A. L. Spek, H. Kooijman, H. Zuilhof, and R. P. Sijbesma, *J. Org. Chem.*, **73**, 111 (2008).
5. S. S. Shinde, A. Maroz, M. P. Hay, and R. F. Anderson, *J. Am. Chem. Soc.*, **131**, 5203 (2009).
6. A. Slevin, T. Koolmeister, and M. Scobie, *Chem. Commun.*, 2506 (2007).
7. M. Scobie and G. Tennant, *J. Chem. Soc. Chem. Commun.*, 2451 (1994).