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SYNTHESIS AND ELECTROCHEMICAL PROPERTIES OF THE UNKNOWN N,N-BISHETEROARYL AMINES BEARING A FUSED HETEROCYCLE AS N-SUBSTITUENT

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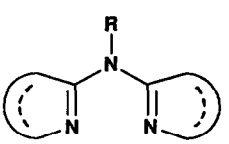
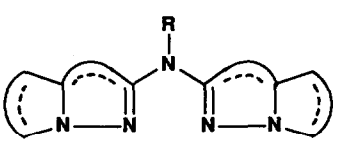
Abstract. The first preparation of N,N-bisheteroaryl amines bearing a fused heterocycle as N-substituent, from the iminophosphorane derived from 3-amino-4-phenylthiazoline-2(3*H*)-thione by sequential treatment with alkyl isocyanates and tetrafluoroboric acid is described. Its electrochemical behaviour shows that these compounds can act as organic electron transfer agents in indirect electrolysis.

Current interest in the chemistry of N,N-bisheteroaryl amines **I** has continued to grow because of the behaviour of this type of compound as ligands[1]; also some boron chelates synthesized from 2-dipyridyl amine show antivirial activity[2]. Recent studies on the metabolites of the sponge *Clathrina clathrus* revealed the presence of compounds type **I** with two imidazole rings[3]. However, there have been no reports dealing with the preparation of N,N-bisheteroaryl amines type **II**, in which the N-linked rings are fused heterocyclic rings, to the best of our knowledge.

We report herein the first preparation of compounds type **II**, bearing thiadiazolo[2,3-*b*][1,3,4]thiadiazole moieties as N-heterocyclic substituents, based on the strategy shown in the scheme.



I



II

The starting iminophosphorane **1** was readily available from 3-amino-4-phenylthiazoline-2(3*H*)-thione[4] and triphenylphosphine dibromide. When a dichloromethane solution of **1** was treated with methyl isocyanate at room temperature the thiadiazolo[2,3-*b*][1,3,4]thiadiazole derivative **3a** was obtained in almost pure form. Reaction of the related alkyl isocyanates also resulted in smooth formation of the derivatives **3b-3f** in *ca.* 45% yields[5], confirming the generality of the reaction. However, reaction of iminophosphorane **1** with alkyl isothiocyanates in dichloromethane at room temperature led to the zwitterionic derivatives **4**; ^{1}H and ^{13}C n.m.r. data confirmed the proposed structure and rule out the alternative structures 2,4-dialkyl-5-(4-phenyl-2-thiazolylthio)-1,2,4-triazoline-3-thione and N,4-dialkyl-3-(4-phenyl-2-thiazolylthio)-1,2,4-thiadiazolin-5-imine[6]. The formation of **3** can be rationalized in terms of a initial aza Wittig-type reaction between the isocyanate and the iminophosphorane **1** to give a carbodiimide as highly reactive

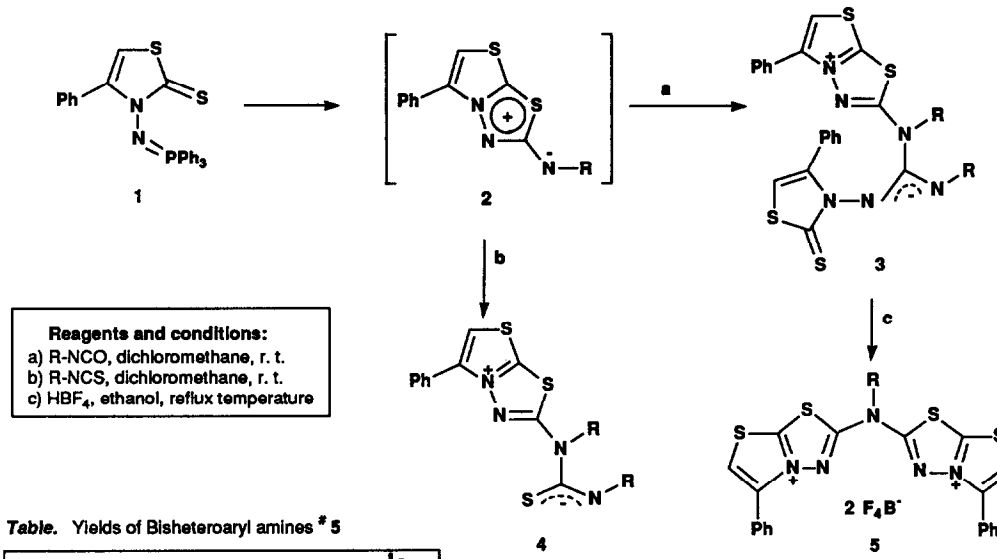


Table. Yields of Bisheteroaryl amines # 5

5	R	%	mp °C
a	CH_3	85	281-283
b	C_2H_5	91	239-241
c	n-C_3H_7	93	274-276
d	i-C_3H_7	87	224-226
e	c-C_6H_{11}	81	204-206
f	H	86	280-282

All new compounds described here had spectral and microanalytical properties in agreement with the assigned structures.

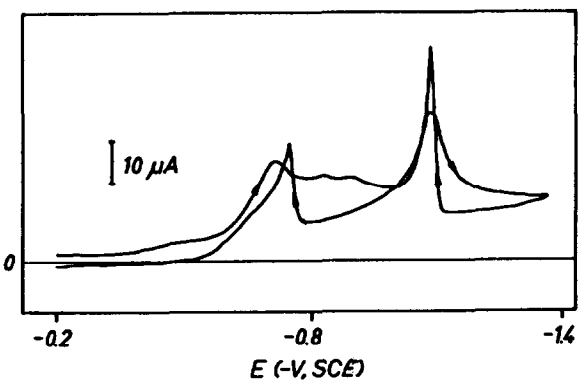
intermediate which cleanly undergoes cyclization to give a mesoionic aminide[7] **2**. Dimerization occurrs by nucleophilic attack of the exocyclic nitrogen atom of the aminide **2** on the C-2 of the second molecule of aminide. The formation of **4** can be understood by nucleophilic attack of the intermediate aminide **2** on the sp-hybridized carbon atom of the second molecule of isothiocyanate. Accordingly with these results, it is worth mentioning that the order of reactivity of the mesoinoic alkyl aminides **2** (carbodiimide valence tautomers[8]) towards heterocumulenes is the following: isothiocyanates> isocyanates, being this scale inverse to the observed in previously reported[9] nucleophilic reactions on these heterocumulenes.

Compounds **3** underwent cyclization followed by elimination of the corresponding amine by the action of tetrafluoroboric acid in ethanol at reflux temperature to give **5** in good yields[10] (81-91%); this conversion was found to be general when R was a primary or secondary alkyl group, however for **3f** (R= t-Bu) a concomitant dealkylation occurred and the unsubstituted derivative **5f** was obtained in 86% yield.

Presumably the conversion **3** → **5** involves protonation of the exocyclic guanidino moiety followed by intramolecular nucleophilic attack of the thiocarbonyl group of the thiadiazole ring on the central carbon atom of the guanidino group followed by elimination of the amine.

An important goal in electroorganic synthesis is the indirect reduction through redox catalysis process which allows to the reduction at very negative potentials of a number of functional groups which do not exhibit voltammetric waves[11]. Voltammetric and polarographic analyses of the electrochemical behaviour

of compounds **5** clearly show the ability of this type of compounds to act as redox catalyst (mediator) in indirect reductions. Cyclic voltammograms of **5** show two cathodic peaks at about -0.72, and -1.08 v *vs* SCE respectively. The anodic trace rises above the cathodic trace in the region of the maxima (inverted peak[12]) at about -1.09, and -0.75 v *vs* SCE. Polarographic measurements also show a sharp rise of cathodic current at the foot of the wave (catalytic maximum[13]). In order to study the nature of the two-electron reduction product of compounds **5**, work is in progress on the electroreduction of single models such as 2-arylamino thiadiazolo[3,2-b][1,3,4]thiadiazolium salts.



Cyclic Voltammogram of **5c** (10^{-3} N); dry DMF-$LiClO_4$; Hg electrode; 25°C; sweep rate:25 mV s^{-1}

Acknowledgements:
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5. General Procedure: To a solution of iminophosphorane **1** (1 mmol) in dry dichloromethane (15 ml) was added dropwise under nitrogen the appropriate isocyanate (1 mmol). The reaction mixture was stirred at room temperature for 16h. The separated solid was collected by filtration and recrystallized

from dichloromethane/diethyl ether (1:1) to give **3**: **3a** (40%) mp. 170-172°C. ^{1}H n.m.r. (200 MHz, $CDCl_3$+TFA) δ 2.57 (s br, 3H), 3.64 (s, 3H), 6.59 (s, 1H), 6.78 (s br, 1H, NH), 7.40-7.58 (m, 8H), 7.79-7.84 (m, 2H), 7.88 (s, 1H). ^{13}C n.m.r. (50 MHz, $CDCl_3$+TFA) δ 29.40 (CH_3), 36.59 (CH_3), 107.44, 119.27, 125.49 (q), 128.16, 128.78 (CH x 2), 129.09 (q), 129.20, 130.06, 131.43, 140.75 (q), 143.81 (q), 155.79 (q), 158.65 (q), 166.77 (q), 179.37 (q). **3c** (41%) mp.172-173°C. ^{1}H n.m.r. (200 MHz, $CDCl_3$+TFA) δ 0.73 (t, 3H, J=7.4 Hz), 0.77 (t, 3H, J=7.3 Hz), 1.40-1.50 (m, 2H), 1.60-1.78 (m, 2H), 2.60-2.90 (m, 2H), 4.20 (t, 2H, J=7.2 Hz), 6.65-(s, 1H), 7.35-7.54 (m, 8H), 7.65 (s, 1H), 7.69-7.78 (m, 2H), 7.91 (s br, 1H, NH). ^{13}C n.m.r. (50 MHz, $CDCl_3$+TFA) δ 29.40 (CH_3), 10.58 (CH_3), 11.24 (CH_3), 20.23 (CH_2), 22.34 (CH_2), 45.01 (CH_2), 51.50 (CH_2), 107.60, 121.78, 125.88 (q), 127.80, 128.50, 128.85 ,128.95, 129.34 (q), 129.75, 130.84, 139.39 (q), 143.53 (q), 154.44 (q), 158.80 (q), 166.63 (q), 178.88 (q).

6. Compound **4** (R=Et): 38% yield, mp. 148-150°C. ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 1.36 (t, 3H, J=7.3 Hz), 1.40 (t, 3H, J=7.0 Hz), 3.72 (q, 2H, J=7.3 Hz), 4.75 (q, 2H, J=7.0 Hz), 7.46-7.60 (m, 3H), 7.74 (s, 1H), 7.92-7.97 (m, 2H). ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 12.49 (CH_3), 14.87 (CH_3), 43.76 (CH_2), 44.13 (CH_2), 117.19 (C-6), 126.51 (C_i), 128.12 (C_m), 128.94 (C_o), 130.77 (C_p), 139.90 (C-5), 159.89 (C-7a), 162.00 (C=S), 168.02 (C-2). Values assigned by decoupling methods and 2D ^{1}H-^{13}C correlation techniques. The fact that compound **4** (R=C_6H_5-CH_2) undergoes S-methylation by the action of the Meerwein´s reagent excludes the alternative structure 1,2,4--thiadiazolin-5-imine and the ^{1}H n.m.r. spectrum of **4** (R=CH_3) in $CDCl_3$+TFA which shows one methyl group as a singlet at δ 3.92 ppm and the other one as a doublet at δ 3.19 ppm (J=4.4 Hz) clearly rules out the structure 1,2,4-triazoline-3-thione.
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10. Compound **5a.** ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 4.01 (s, 3H, CH_3N), 7.64-7.73 (m, 6H), 7.96-8.05 (m, 4H), 8.50 (s, 2H, H-6 x 2). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 40.59 (CH_3N), 123.70 (C-6), 126.32 (C_i), 128.32 (CH), 129.26 (CH), 130.92 (C_p), 139.62 (C-5), 160.92 (C-7a), 165.95 (C-2).

    Compound **5c**. ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 1.03 (t, 3H, J=7.3 Hz), 1.90-2.01 (m, 2H), 4.40 (t, 2H, J=6.8 Hz), 7.64-7.71 (m, 6H), 7.94-8.03 (m, 4H), 8.47 (s, 2H, H-6 x 2). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 11.01 (CH_3), 19.60 (CH_2), 56.26 (CH_2), 123.57 (C-6), 126.40 (C_i), 128.38 (CH), 129.27 (CH), 131.00 (C_p), 139.69 (C-5), 161.01 (C-7a), 165.45 (C-2).

    Compound **5f**. ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 3.15 (s br, 1H, NH), 7.58-7.65 (m, 6H), 7.98-806 (m, 4H), 8.28 (s, 2H, H-6 x 2). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 121.07 (C-6), 127.16 (C_i), 128.23 (CH), 129.03 (CH), 130.45 (C_p), 138.99 (C-5), 156.75 (C-7a), 169.65 (C-2).
    Values assigned by decoupling methods and 2D ^{1}H-^{13}C correlation techniques.
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