Pergamon

Tetrahedron Letters 40 (1999) 1895–1898

TETRAHEDRON
LETTERS

Pyridine-based Nitronyl Nitroxides as Versatile Synthons for the Synthesis of Elongated Ethynyl-Bridged Radicals

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Received 25 November 1998; accepted 6 January 1999

Abstract: We report the preparation of multi-component molecules based on pyridine-, bipyridine- and pyrene-substituted nitronyl nitroxide (NIT) radicals. The synthetic protocol is based on a Pd(0) promoted cross-coupling reaction between 6-BrPyNIT and either 6-HC≡CPyNIT, diethynyl substituted bipyridines, or 1-ethynylpyrene derivatives. The magnetic properties and X-ray structures of the pyridine (Py) and pyrene-based bi- and monoradicals are described briefly. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Numerous stable free radicals have been employed in a variety of studies requiring spin labels, MRI imaging, antioxidants, or magnetic materials.[1] The nitroxide family of radicals has been widely studied because of readily available synthetic procedures allowing the preparation of functionalized molecules.[2] Surprisingly, functionalization of NIT radicals is less developed, despite much synthetic effort and appealing magnetic properties.[3] We have shown recently that alkyne-substituted NIT-radicals display interesting magnetic properties since macroscopic organization of these radicals can be achieved *via* hydrogen bonded networks.[4] Others have found that polymeric magnetic materials can be produced by topochemical polymerization of radicaloid-diacetylenic prototypes.[5]

In an ongoing project aimed at further illustrating the potentiality of alkyne-NIT building blocks we have found that Heck-type cross-coupling reactions between a NIT-radical bearing a halogeno function and an ethynyl functionalized partner is effective for the preparation of novel ethynyl-bridged biradicals. We describe herein a synthetic rational for functionalization of various pyridine, bipyridine and pyrene derivatives with NIT-appendages. The key **6-BrPyNIT** building block was prepared in four steps from 2,6-dibromopyridine, while **6-HC≡CPyNIT** is obtained in two steps using a Pd(0)-promoted Heck-type reaction (Scheme 1).[4b] Cross-coupling of these compounds at 80 °C led to the precipitation of **1**, which was isolated by flash chromatography. It is noteworthy that, under these conditions, only 5% of the product is reduced, while additional recovery of the biradical is possible via PbO_2 oxidation.

Compound **2**, bearing a diacetylenic spacer, was obtained by precipitation during an oxidative homocoupling reaction catalyzed by copper salts in the presence of molecular oxygen.[6] Corresponding imino-nitroxide (IM) radicals were prepared by deoxygenation with HNO_2 followed by reoxidation of the N-hydroxyimidazoline with PbO_2 [7] (see Table for selected analytical data).

Compound **1** crystallizes in the monoclinic $C_c(9)$ space group, the molecular structure being shown in Fig. 1a together with the magnetic behaviour (Fig. 1b).

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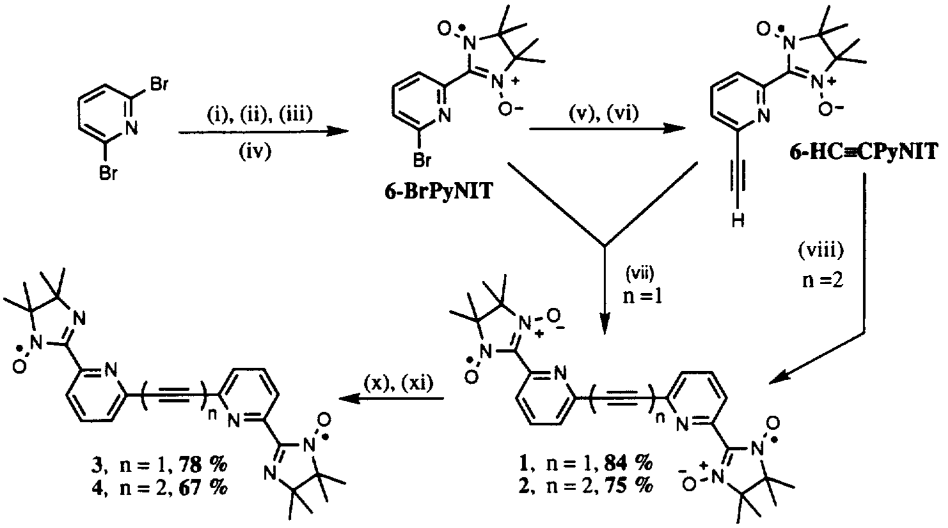
PII: S0040-4039(99)00069-6



(i) *n*-BuLi/Et_2O -78 °C; (ii) DMF; (iii) 2,3-bis(hydroxyamino)-2,3-dimethybutane/CH_3OH; (iv) $NaIO_4/H_2O/CH_2Cl_2$; (v) TMSC≡CH, $[Pd^0(PPh_3)_4]$, C_6H_6/*i*-Pr_2NH; (vi) KF/CH_3OH; (vii) $[Pd^0(PPh_3)_4]$, C_6H_6/*i*-Pr_2NH; (viii) CuCl/O_2/pyridine; (x) HNO_2/DMF; (xi) PbO_2.

Scheme 1

The dihedral angle between the NIT and the pyridine rings is 52° and all other angles and distances lie in the range expected for such radicals. Radicals are organised in chains of dimers with short NO--O'N' distances (*ca* 3.6 Å) and with an orientation favourable for antiferromagnetic interaction. The product of molar susceptibility and temperature (χT) shows a monotonous decrease with lowering T and a good fit of the experimental data was obtained using the Bleaney-Bowers[8] law with a mean-field approximation estimated by a Weiss temperature θ (solid line shown in Fig. 1b). A singlet-triplet splitting of $2J/k_B$ = -10 K and θ = -3 K were calculated (J = magnetic exchange coupling constant).

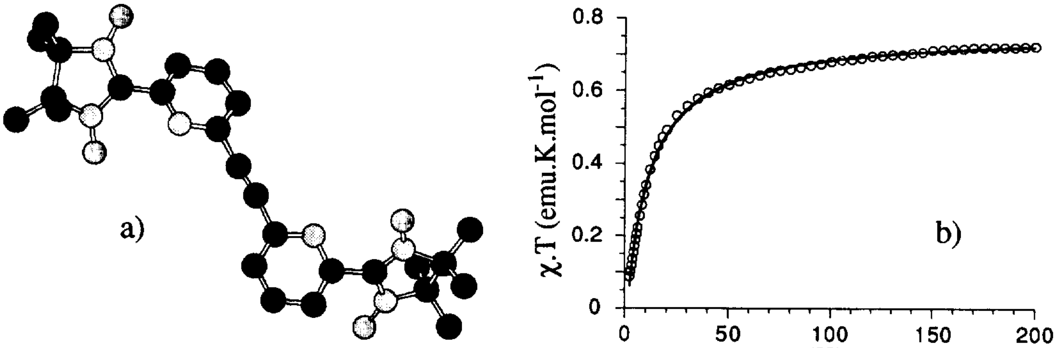
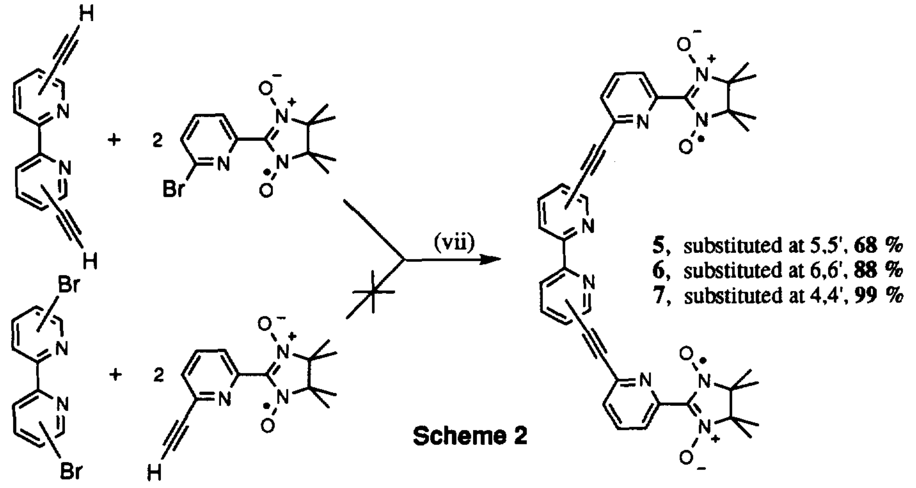


Figure 1

In view of the originality of this synthetic protocol in the NIT/IM radical domain and in order to generalize the process we have prepared three elongated bis-NIT radicals bearing a Py-C≡C-bpy-C≡C-Py spacer. Compounds **5**,**6**,**7** were prepared by cross-coupling of **6-BrPyNIT** with bpy-substituted ethynyl derivatives[9] in the presence of low valent "Pd(0)" as catalyst (Scheme 2). It should be noted that cross-coupling the other way round using **6-HC≡CPyNIT** and halogeno-substituted bpy ligands does not afford the target molecules. The strong withdrawing effect of a NIT radical deactivates the terminal alkyne function and inhibits the catalytic processes, while the bromine in **6-BrPyNIT** is readily activated to favour cross-coupling reactions.

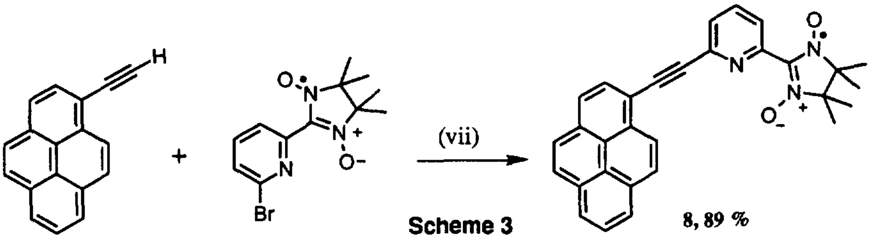


5, substituted at 5,5', **68 %**
6, substituted at 6,6', **88 %**
7, substituted at 4,4', **99 %**

Scheme 2

Product	Isolated Yield (%)	IR (cm^{-1})$^{a)}$	UV-Vis λ nm, (ε, M^{-1} cm^{-1}) $^{b)}$	MS $^{c)}$	C; H; N Found (calc.)
1	84	1361	562 (700)	491.2	63.46 (63.66); 6.01 (6.16); 16.91 (17.13)
2	75	1367	560 (680)	517.2	65.15 (65.36); 5.62 (5.88); 16.21 (16.33)
3	78	1562/1370	422 (310)	458.1	68.05 (68.10); 6.41 (6.59); 18.02 (18.33)
4	67	1559/1369	424 (500)	482.2	69.47 (69.69); 6.03 (6.27); 17.32 (17.41)
5	68	1366	565 (620)	671.0	68.07 (68.25); 5.38 (5.43); 16.62 (16.76)
6	88	1362	565 (580)	669.3	68.11 (68.25); 5.29 (5.43); 16.57 (16.76)
7	99	1361	565 (600)	669.3	68.02 (68.25); 5.35 (5.43); 16.69 (16.76)
8	89	1370	568 (750)	459.3	78.33 (78.58); 5.02 (5.28); 8.99 (9.16)

a) ν_{NO} and $\nu_{C=N}$ stretching vibration measured in KBr pellets; b) n→π* absorption band measured in CH_2Cl_2; c) obtained by FAB$^+$ using *meta*-nitrobenzylalcohol as matrix and correspond to m/z, $[M+H]^+$.



Scheme 3

8, **89 %**

Owing to the increasing interest of aromatic polycyclic derivatives as potent nucleic acid intercalators we decided to investigate the cross-coupling of 1-ethynylpyrene[10] with **6-BrPyNIT** and were able to isolate **8** in excellent yield (Scheme 3). The X-ray molecular structure of **8** and magnetic data are depicted in Fig. 2. The pyridine ring is tilted from the almost planar ethynylpyrene fragment by 34°, while the NIT radical forms an angle of *ca* 30°.

The χT product at rt is equal to 0.387 emu.K.mol^{-1}, a value close to that one expected for an isolated $S = 1/2$ spin system. At low temperature, antiferromagnetic interactions are effective and χ follows a Curie-Weiss law over the entire temperature range (θ = - 0.8 K) as shown in Fig. 2b. The head-to-tail arrangement of the radicals in the crystal packing is in keeping with the antiferromagnetic behaviour.

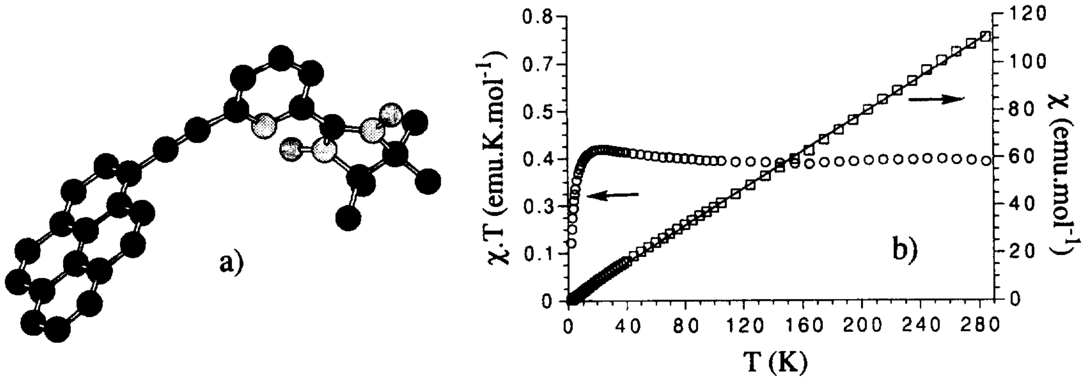


Figure 2

In summary, we have developed a flexible approach to the synthesis of NIT mono- or bis-radicals through a protocol easily amenable for large-scale preparation. The mild conditions involved and the good obtained overall yields make this sequence a novel and convenient synthetic route to this class of compounds. Further elaboration of this strategy for the synthesis of nucleoside-grafted radicals, as well as polymeric materials, is currently under way in our laboratory. Complete magneto-structural correlations for all new radicals will be reported elsewhere.

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