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A versatile synthesis of new pyrimidinyl nitronyl nitroxides†

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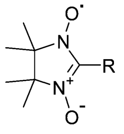
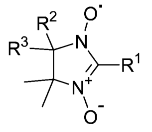
Pyrimidinyl nitronyl nitroxides where the bis-*N*-oxy fragment is included in a six-membered ring were prepared from diacetonamine by a sequence of reactions including a Grignard reaction, a Ritter reaction and oxidation of the intermediate pyrimidine; the properties of the 2-phenyl-substituted representative are fully described.

Imidazolidinyl nitronyl nitroxides[1] **1** have found various applications, such as trapping reagents for NO,[2] spin-labels,[3] versatile ligands for magnetic metal–organic complexes,[4–6] and building blocks for purely organic magnetic materials.[7] In the particular field of molecular magnetism structural modifications of these free radicals have provided a variety of molecular structures and crystal packings, leading to different intermolecular exchange interactions and thus to different magnetic ground states. However, except for a few examples such as **2**,[8] these modifications all use Ullmann's standard synthetic method,[1] and have been mainly restricted to the substituents at C_2.

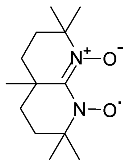
Although these structural variations, still the object of intense activity, are potentially infinite, modification of other parts of the molecule would also provide different possibilities for the construction of new magnetic materials. In particular, if polyfunctional materials were to be designed, it would be difficult to obtain diverse properties from a single substituent at C_2. Moreover, Ullmann's synthesis, based on the radical coupling of nitro compounds, is lacking in flexibility since it yields only symmetrical precursors. Other synthetic approaches leading to stable **3**,[9] or to unstable **4**,[10] seem difficult to adapt.



1
a: R = Ph



2	R^1	R^2	R^3
a:	Me	Ph	Ph
b:	Ar	Ar	NH_2



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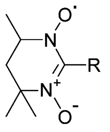

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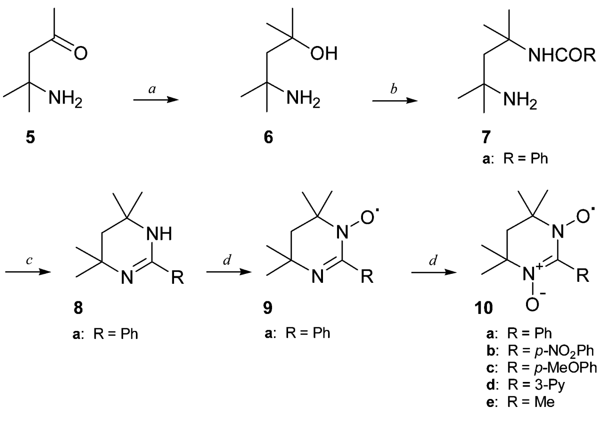
We report here a versatile stepwise synthesis of new nitronyl nitroxides **10** (Scheme 1) where the conjugated nitronyl nitroxide fragment is included in a six-membered ring and for which varied substitutions may be anticipated. The synthesis of the phenyl derivative is described as an example.

Freshly prepared diacetonamine **5** was reacted with methylmagnesium iodide to afford 4-amino-2,4-dimethyl-2-pentanol, **6**.[11] Replacement of the hydroxyl group by an amide function was performed through a Ritter reaction adapted from the one described for 2,4-dimethyl-2,4-pentanediol,[12] in which the major product of the reaction was a dihydro-oxazine. Since this indicated a nucleophilic attack of the remaining hydroxyl group on the first formed imidosulfate moiety, amino alcohol **6** was expected to yield a tetrahydropyrimidine through a similar intramolecular reaction.[13] However, when reacted with benzonitrile in H_2SO_4, **6** afforded the corresponding amino-benzamide **7a**. Attempts to hydrolyze the amide function in strongly basic medium gave phenyl-substituted **8a** (86% yield) and no traces of 2,4-diamino-2,4-dimethylpentane; alternatively, **7a** could be dehydrated to **8a** by azeotropic removal of water in toluene. **8a** was then oxidized with *m*CPBA as recently described for related heterocycles[14] to give, *via* the transient imino nitroxide **9a**, the highly stable nitronyl nitroxide **10a** in moderate yield (40%). Following the same synthetic scheme, **10b** (R = *p*-nitrophenyl, 60% yield), **10c** (R = *p*-methoxyphenyl, 40% yield), **10d** (R = 3-pyridyl, 30% yield) and **10e** (R = methyl, 10% yield) were also prepared.‡

The ESR spectra of these nitronyl nitroxides are quite similar to those of the imidazolinyl analogues.§ In comparison to **1a**, the UV-Visible spectra of **10a** in hexane and in ethanol solutions show a weak hypsochromic shift, an almost 100% larger absorption coefficient in the visible region and 50% smaller ones in the UV region.§

In the solid state **10a** crystallizes as dark blue needles.¶ The molecular structure (Fig. 1) exhibits the following structural features: i) the pyrimidine ring is in a half-chair conformation; ii) the C6–N1–C2–N3–C4 fragment is nearly planar; bond lengths are in the range found for five-membered analogs, *e.g.* **1a**,[15] and the valence angles are larger than in **1a**; iii) the plane of the phenyl ring makes an angle of 56.4(6)° (in comparison to 24.5 and 29.8 in **1a**)[15] with the plane of the ONCNO fragment, so that the molecule is frozen in a chiral conformation; iv) the shortest intermolecular contacts between neighboring NO groups are greater than 6.24 Å.

The high-temperature magnetic susceptibility data follow a Curie–Weiss law ($C = 0.378\ \mathrm{cm^3\ K\ mol^{-1}}$, $\theta = -2.47$ K) and the negative Weiss constant suggests predominant antiferromagnetic interactions, as in **1a**.[7a,b]



Scheme 1 Synthesis of pyrimidinyl nitronyl nitroxides. *a*) MeMgI/diethyl ether; *b*) RCN/H_2SO_4; *c*) $Ba(OH)_2$/H_2O, 110 °C; *d*) *m*CPBA/THF, $NaIO_4$.

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† Electronic supplementary information (ESI) available: experimental procedures for the synthesis of **10a**. See http://www.rsc.org/suppdata/cc/b3/b309786b/

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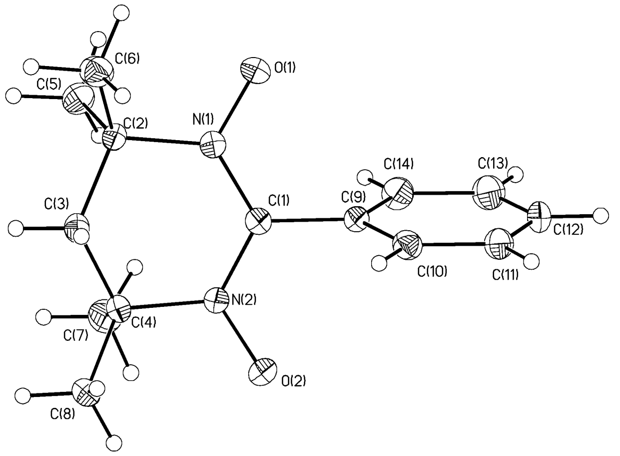

Fig. 1 X-Ray crystal structure of **10a**. Relevant structural parameters (Å, deg.) [and corresponding ones of **1a**]. O1–N1 = 1.298(1) [1.266(6)], O2–N2 = 1.288(1) [1.273(8)], N1–C1 = 1.347(2) [1.351(6)], N2–C1 = 1.351(2) [1.399(8)], C1–C9 = 1.485(2) [1.471(6)], O1–N1–C1 = 119.2(1) [127.4(5)], O2–N2–C1 = 119.2(1) [126.2(4)], N1–C1–N2 = 121.2(1) [108.9(4)].

This synthetic route may easily be extended to prepare pyrimidinyl nitronyl nitroxides: use of different nitriles allows substitutions at C_2, with the same possibilities as for the numerous imidazolidinyl nitronyl nitroxides; although rearrangements may occur in some Ritter reactions,[16] a choice of appropriate Grignard reagents and of β-aminoketones may provide access to pyrimidyl nitronyl nitroxides with various substituents at C4, C5 and C6. Furthermore, chiral magnetic materials[17] could be obtained starting from chiral molecules such as (1*R*,4*S*)-8-amino-*p*-menthanone.[18]

Notes and references

‡ *Melting points* (°C) for **10a**: 139–140; **10b**: 190–192; **10c**: 115–117; **10d**: 150–151; crystalline **10e** spontaneously decomposes at room temperature.

§ *Selected data*: *ESR*: a_X, (mT) H_2O: **9a**: a_N 0.38 and 1.00; **10a**, **10b**, **10c** and **10d**: a_N 0.79; **10e**: a_N 0.81, a_H 0.30. *UV-Vis* for **10a**, λ_{max}/nm (ε/mol^{-1} dm^3 cm^{-1}), *n*-hexane ($c = 4 \times 10^{-4}$ mol L^{-1}): 261 (7000), 355 (6900), 626 (935) [compare **1a**:[1c] 238 (8640), 266 (12850), 346 (9300), 362 (17700), 587 (407), 637 (450)]; EtOH (c = 4.3 10 $^{-4}$ mol L^{-1}): 258 (4500), 326 (7500), 596 (1500) [compare **1a**: 238 (9400), 263 (12 200), 360 (13 300), 588 (685)].

¶ *Crystal data* for **10a**: $C_{14}H_{19}NO$, M = monoclinic, $P2_1/n$, a = 6.243(1), b = 21.36(1), c = 9.998(1)Å, β = 96.862(2)°, V = 1323.9(2) Å^3, Z = 4, D (calc.) = 1.241 Mg m^{-3}, λ(Mo-Kα) = 0.71073 Å, T = 19 °C, 6664 reflections collected, 3093 independent reflections, full-matrix least squares on F^2, 239 parameters, final Rindices [$I > 2\sigma(I)$]: R_1 = 0.0405, wR_2 = 0.0879. CCDC 202737. See http://www.rsc.org/suppdata/cc/b3/b309786b/ for crystallographic data in CIF or other electronic format.

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