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Synthesis of Terminal-Biradical Compounds Consisting of Two *N*-Oxyl Groups Connected with Conjugated π-Systems

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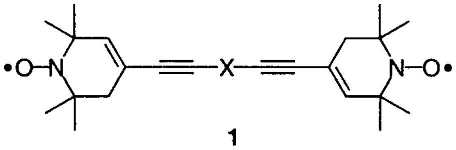
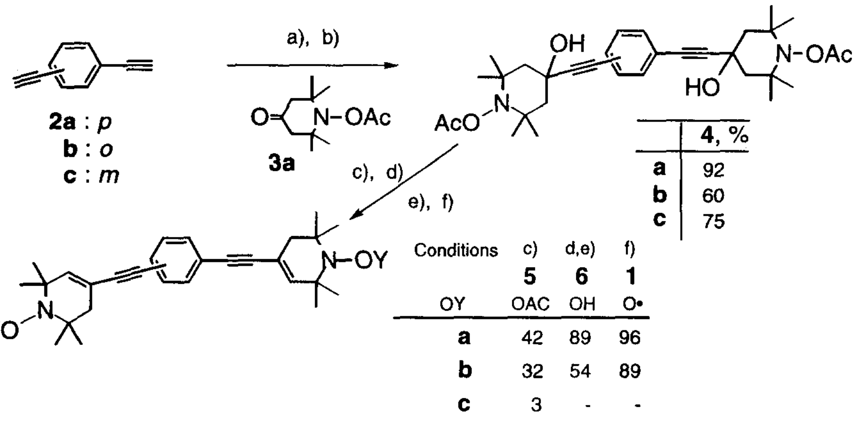
Abstract: Terminal-biradical compounds **1** having two *N*-oxyl groups connected with conjugated π-systems were synthesized by (1) addition of magnesium acetylide to 4-oxo-TEMPO, followed by dehydration, or (2) cross-coupling between acetylene and vinyl triflate derived from 4-oxo-TEMPO. © 1997 Elsevier Science Ltd.

The design and synthesis of molecular magnets are one of the current interests.[1] Essentials are how to increase the spin density and to regulate the direction of the spins. For latter purpose, the radicals are attempted to be joined by π-electron systems to allow to interact each other. Poly-radical compounds connecting the radicals by aromatic structure have been reported.[1a,b,d] However, the overlap of the aromatic π-orbital seems not so efficient as expected because of a steric repulsion. We planed to connect radicals by other type of π-system, *e.g.*, acetylenic and vinylic moieties. Herein, we describe preliminary synthetic results on terminal-biradical compounds **1** containing two *N*-oxyl groups connected with conjugated π-systems by (1) addition of magnesium acetylide to 4-oxo-TEMPO followed by dehydration, or (2) Pd-catalyzed cross-coupling between acetylene derivatives and vinyl triflate derived from 4-oxo-TEMPO.



1

Diacetylenes **2**, obtained by the cross-coupling of dibromobenzenes and 3-methyl-1-butyn-3-ol in the presence of a $PdCl_2(PPh_3)_2$–CuI catalyst followed by removal of the 2-propanol moiety with KOH in toluene at 100 °C, underwent metallation with ethylmagnesium bromide and subsequent reaction with *N*-acetoxy-2,2,6,6-tetramethylpiperidine[2] **3a** to give the corresponding diols **4** in 60~92% yields. The diols **4a**[3] and **4b** were converted to the terminal biradicals **1a** and **1b** by 1) acid-catalyzed dehydration[4] with *p*-TsOH, 2) basepromoted hydrolysis, and 3) oxidation with lead dioxide in good to moderate yields. In contrast, the dehydration of the *meta*-diol **4c** gave the corresponding dienediyne **5c** in poor yield (Scheme 1).



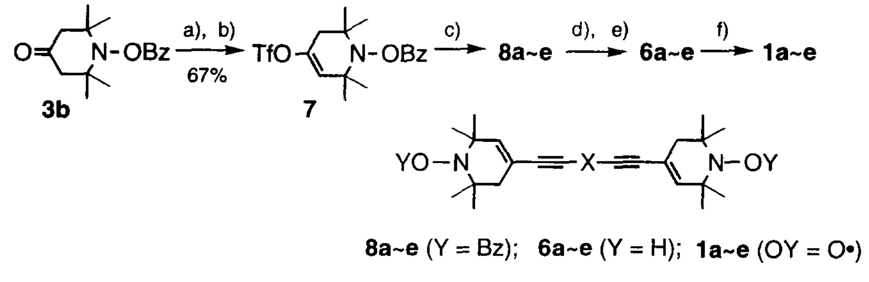
	4, %
a	92
b	60
c	75

Conditions	c)	d,e)	f)
	5	6	1
OY	OAC	OH	O•
a	42	89	96
b	32	54	89
c	3	-	-

Scheme 1

a) EtMgBr (2 equiv.), THF, room temp., 1 h; b) **3a** (2 equiv.), room temp., 20 h; c) *p*-TsOH (0.5 equiv.), PhH, reflux, 6 h; d) 1 M NaOH, MeOH, 50 °C ~ reflux, 6 h; e) H_3O^+; f) PbO_2, CH_2Cl_2, room temp., 10 h.

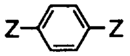
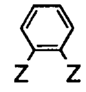
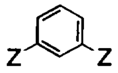
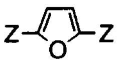
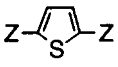
Therefore, more versatile methods are now required to develop for the synthesis of the desired compounds **1**. The different approaches to arrive at the targets are as follows: firstly, *N*-(benzyloxy)-2,2,6,6-tetramethylpiperidine **3b**[2] was allowed to convert into the corresponding vinyl triflate **7** (67% yield). Actually, this triflate is stable enough to store for a few months in a refrigerator. Cross-coupling[5] of **7** with diacetylene compounds **2** in the presence of triethylamine and a catalytic amount of $PdCl_2(PPh_3)_2$ in DMF gave the corresponding dienediyne **8** in good to moderate yields. Hydrolysis of **8** followed by oxidation afforded the desired biradical **1** (Scheme 2, Table 1).

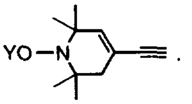


Scheme 2

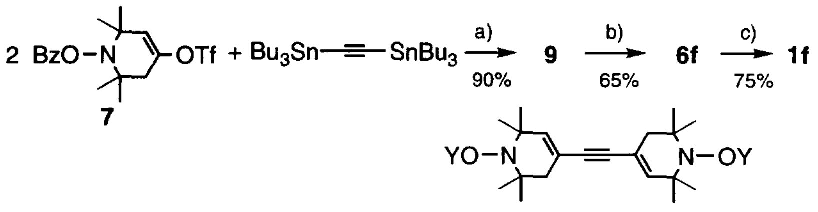
a) LDA, THF, -78 °C, 2 h; b) Tf_2NPh, 0 °C, 5 h; c) ≡-X-≡ (**2**, see Table 1), $PdCl_2(PPh_3)_2$, Et_3N, DMF, 50 °C, 2 ~ 4.5 h; d) 1 M NaOH, MeOH, 50 ~ 80 °C, 2.5 ~ 11 h; e) H_3O^+; f) PbO_2, CH_2Cl_2, room temp., 10 ~ 12 h.

Table 1. Synthesis of Biradicals **1** *via* Cross-Coupling of **7** with **2**, Hydrolysis of **8**, and Oxidation of **6**

	Compounds[a] Z-X-Z	Isolated Yield, %			**1**
		8 (Y = Bz)	**6** (Y = H)	**1** (OY = O•)	Mp., °C[b]
a		57	44	96	220 ~ 221 (decomp.)
b		54	45	89	47 ~ 48
c		70	43	81	147 ~ 149
d		59	72	74	164 ~ 165 (decomp.)
e		53	70	69	177 ~ 178 (decomp.)

a) Z =  . b) The melting points were not corrected.

The other acetylene derivatives **1f** and **1g** bearing the dehydropiperidinyl radical moiety attached to the both side of acetylene were synthesized by use of the Pd-catalyzed cross-coupling reaction. 1,2-Bis(tributylstannyl)ethyne was coupled[6] with the triflate **7** in the presence of Pd catalyst to afford dienyne **9** in 90% yield. Hydrolysis followed by oxidation gave the desired biradical **1f** (Scheme 3).

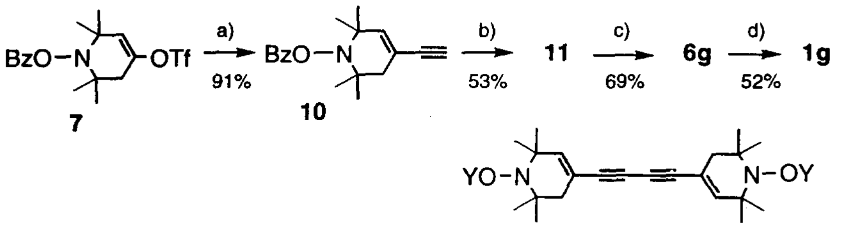


Scheme 3

9 (Y = Bz); **6f** (Y = H); **1f** (OY = O•)

a) $Pd(PPh_3)_4$, LiCl, THF, 60 °C, 2.5 h; b) 1 M NaOH, MeOH, 70 °C, 5 h;
c) PbO_2, CH_2Cl_2, room temp., 15 h.

Cross-coupling of the triflate **7** with tributylstannylethyne afforded the enyne **10** in 91% yield. Pd-catalyzed homo-coupling[7] of **10**, followed by hydrolysis and oxidation, gave the desired biradical **1g** (Scheme 4).



Scheme 4

11 (Y = Bz); **6g** (Y = H); **1g** (OY = O•)

a) ≡-$SnBu_3$, $Pd(PPh_3)_4$, LiCl, THF, 60 °C, 2 h; b) $Pd(PPh_3)_4$, CuI, NEt_3, $ClCH_2COCH_3$, PhH, room temp.; c) 1 M NaOH, MeOH, 80 °C, 8 h; d) PbO_2, CH_2Cl_2, room temp., 14 h.

In conclusion, we have synthesized the terminal biradicals **1** by addition of magnesium arenedi(acetylide) to 4-oxo-TEMPO, followed by dehydration. We also now offer the vinyl triflate **7** as a new versatile intermediate for the preparation of *N*-oxyl-dehydropiperidine derivatives by cross-coupling between acetylene or stannylacetylene compounds. Spin-spin interaction between radicals in **1** was observed by electrochemical and spectroscopic measurements. The detail will be submitted elsewhere. Korshak reported the synthesis of polymer material derived from diol analog of **1g** and suggested that control of the superstructure of the polymer is critical to manifest high ferromagneticity.[8] Further extended investigations are continued in our laboratories.

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References and Notes

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2. These TEMPO derivatives **3a** and **3b** are prepared from commercially available 4-oxo-2,2,6,6-tetramethylpiperidine *N*-oxyl through reduction of *N*-oxyl ($PhNHNHPh/CH_2Cl_2$, room temp., 1 h, 95%), and protection of the *N*-hydroxyl group with Ac_2O/Py/cat. DMAP/THF (room temp., 2.5 h, **3a**, 90%) or $Bz_2O/Py/CH_2Cl_2$ (0 °C, 5 h, **3b**, 98%).
3. *p*-Disubstituted diacetate **4a** was also prepared (isolated yield: 95%) from cross-coupling of 1-acetoxy-4-ethynyl-4-hydroxy-2,2,6,6-tetramethylpiperidine, derived from *N*-acetyloxy-4-oxo-TEMPO **3a**, and *p*-diiodobenzene in the presence of catalytic amount of CuI and $PdCl_2(PPh_3)_2$ in NEt_3 at room temperature. However, no desired **4a** could be obtained from cross-coupling with *p*-dibromobenzene.
4. Mesylation (MsCl/pyridine(/CH_2Cl_2)) and tosylation (*p*-TsCl/pyridine(/CH_2Cl_2)) did not proceed at all.
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