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1,3-Dipolar Cycloadditions of Electrogenerated Activated Olefins to Nitrones. Use of 1-Arylsulfonylcyclobutenes in the Synthesis of New Isoxazolidines.

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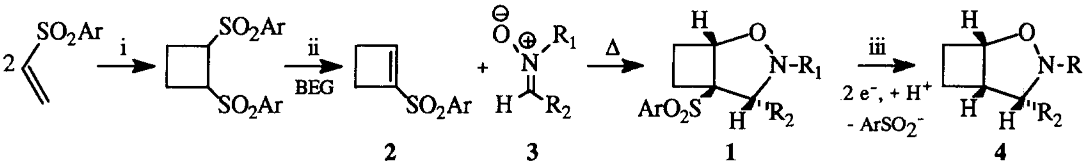
Abstract : Specifically electrogenerated 1-sulfonylcyclobutenes can be used in the facile synthesis of 2-oxa-3-azabicyclo[3,2,0]heptane by means of 1,3-dipolar cycloaddition to several nitrones followed by a cathodic cleavage. © 1998 Elsevier Science Ltd. All rights reserved.

The addition of activated olefins to nitrones according a 1,3-dipolar cycloaddition is known to be an easy method for the synthesis of isoxazolidines.[1] We wish hereby to report a new mode of formation for 2-oxa-3-azabicyclo[3.2.0]heptane **1** by condensation of cyclobutene **2** (here Ar = C_6H_5) exclusively electrochemically prepared,[2] to a wide palette of nitrones **3**.



i : Intentiostatic cyclodimerization at a platinum electrode in aprotic dimethylformamide[3]
ii : Elimination by mean of electrogenerated superoxide[2]
iii : Potentiostatic two electron reduction of **1** at a mercury pool cathode

Formation of **1** and its readily reduced form **4** by means of a specific cathodic cleavage of the sulfone illustrates a new facile mode of synthesis of bicyclic isoxazolidine. **1** was obtained in moderate to high yield (see Table 1). However, the C-S bond cleavage of **1** by cathodic means is effective only when R_1 is aliphatic.

1	R_1	R_2	Yields of **1** (%)	m.p. (°C) (EtOH)	^1H NMR 200 MHz in $CDCl_3$ (δ: ppm; *J*: Hz)
a	-tBu	-Ph	82	176	8.05 (d, 2H, *7*); 7.65 (m, 3H); 7.3 (m, 5H); 5.1 (m, 1H); 4.45 (s, 1H); 2.5-2.2 (m, 3H); 1.75 (m, 1H); 0.85 (s, 9H)
b	-Ph	-Ph-pOMe	50	148-149	7.85 (d, 2H, *7*); 7.6 (t, 1H, *7*); 7.5 (t, 2H, *7*); 7.2 (d, 2H, *9*); 7.1 (t, 2H, *8*); 6.95 (t, 1H, *8*); 6.85 (d, 2H, *8*); 6.8 (d, 2 H, *9*); 5.25 (m, 1H); 4.7 (s, 1H); 3.75 (s, 3H); 2.6-2.3 (m, 3H); 1.95 (m, 1H)
c	-Me	-Ph-pOMe	50	111-112	7.85 (d, 2H, *7*); 7.65 (t, 1H, *7*); 7.55 (t, 2H, *7*); 7.2 (d, 2H , *9*); 6.8 (d, 2H, *9*); 5 (m, 1H); 3.9 (s, 1H); 3.8 (s, 3H); 2.6 (s, 3H); 2.4-2 (m, 4H)
d	-Ph	-Ph	79	133-134	7.9 (d, 2H, *7*); 7.65 (t, 1H, *7*); 7.5 (t, 2H, *7*); 7.3 (m, 5H); 7.15 (t, 2H, *8*); 6.95 (t, 1H, *8*); 6.85 (d, 2H, *8*); 5.25 (m, 1H); 4.75 (s, 1H); 2.6-2.3 (m, 3H); 1.9 (m, 1H)
e	-Me	-Ph	59	98-99	7.85 (d, 2H, *7*); 7.7 (t, 1H, *7*); 7.55 (t, 2H, *7*); 7.25 (s, 5 H); 5.05 (m, 1H); 3.95 (s, 1H); 2.6 (s, 3H); 2.5-2 (m, 4H)
f	-Ph	-CO-Ph	80	138-139	7.65-7.55 (m, 4H); 7.45 (t, 2H, *9*); 7.35-7 (m, 9H); 5.3 (m , 1H); 5.2 (s, 1H); 2.85 (m, 1H); 2.6 (m, 2H); 2.3 (m, 1H)

Table 1 : Characteristics and yields of cycloadducts **1** isolated after heating to reflux during 4 h. an equimolar mixture of 1-phenylsulfonylcyclobutene (**2**) (5.10^{-2} M) and the corresponding nitrone **3** in 10 ml of toluene.

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Thus, structures **1a**, **1c** and **1e** afforded reduced compounds **4** since the two electron cleavage of the C-S bond[4] was checked to occur without inversion of configuration[5] (see Table 2). Contrarywise, when R_1 = aromatic, a fast degradation either by electrogenerated bases and/or at the level of the anion radical was found to occur and results are not reported here.

1	Substrate concentration (.10^{-2} M)	E app. (V) vs. Ag/AgI/I$^-$ 0.1 M	Electric consumption (F/mol)	Yields of **4** (%)	^{1}H NMR 200 MHz in $CDCl_3$ (δ: ppm; *J*: Hz)
a	4.3	- 1.8	2.02	61	7.25 (m, 5H); 4.7 (dt, 1H, *4 and 6*); 4.15 (d, 1H, *7*); 3.35 (m, 1H); 2.15 (m, 3H); 1.6 (m, 1H); 1.05 (s, 9H)
c	1.1	- 1.7	1.99	65	7.25 (d, 2H, *9*); 6.9 (d, 2H, *9*); 4.7 (dt, 1H, *5.5 and 5.5*); 3.8 (s, 3H); 3.45 (d, 1H, *7*); 3.35 (m, 1H); 2.7 (s, 3H); 2.25 (m, 3H); 1.7 (m, 1H)
e	0.9	- 1.7	1.96	53	7.3 (m, 5H); 4.65 (dt, 1H, *5.5 and 5.5*); 3.4 (d, 1H, *6.5*); 3.35 (m, 1H); 2.65 (s, 3H); 2.2 (m, 3H); 1.65 (m, 1H)

Table 2 : Experimental conditions allowing the conversion **1** to **4** by means of a potentiostatic cathodic reduction implying the use of a two-compartment cell. Total volume: about 10 ml of dimethylformamide containing Bu_4NBF_4 0.1 M. Used cathode: stirred mercury pool (area: 3 cm^2), anode: graphite rod (area: 3.8 cm^2). All the electrolyses are carried out under argon atmosphere. The disappearance of **1** in the cathodic compartment was followed by cyclic voltammetry, measuring the intensity of its irreversible peak.

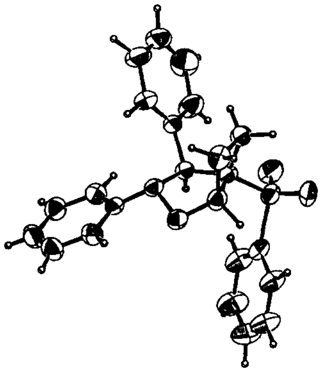

Figure 1 : ORTEP drawing of **1d**

References and notes :

1. a) Black D. St. C.; Crozier R. F.; Davis V. C.; *Synthesis*, **1975**, 205-221.
   b) Lebel N. A.; Whang J. J.; *J. Am. Chem. Soc.*,**1959**, *81*, 6334-6335.
   c) Tufariello J. J.; *1,3-Dipolar Cycloadditions*; Padwa A.; Ed.: John Wiley and Sons Ltd: New York, **1984**, 83-168.
2. 1-Phenylsulfonylcyclobutene was obtained from 1,2-diphenylsulfonylcyclobutane in the presence of superoxide ion which is produced by reduction on mercury pool cathode of dioxygen at - 0.5 V vs. Ag/AgI/I$^-$ 0.1 M in DMF : a) Delaunay J.; Orliac-Le Moing A.; Simonet J.; *New J. Chem.*; **1993**, *17*, 393-398. b) Delaunay J.; Orliac A.; Simonet J.; *Tetrahedron Lett.*, **1995**, *36*, 2083-2084.
3. Delaunay J.; Mabon G.; Orliac A.;Simonet J.; *Tetrahedron Lett.*, **1990**, *31*, 667-668.
4. Simonet J.; *The Chemistry of Sulphones and Sulfoxides*, Pataï S., Rappoport Z.,Stirling C. J. M., Ed.: John Wiley and Sons Ltd: New York,**1988**, 1001-1045.
5. The synthesis of **4e** was already reported using the 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hept-6-ene which was reduced by $NaBH_4$ after N-alkylation with trimethyloxonium tetrafluoroborate. Cerri A.; De Micheli C.; Gandolfi R.; *Synthesis*, **1974**, 710-712.