

## Generation of Radical Cations from Enamines and Their Addition to Unactivated Olefins

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Oxidation of unsaturated enamines by metallic salts produced radical cations which added intramolecularly to unactivated olefins, producing cyclized products in a highly efficient manner.

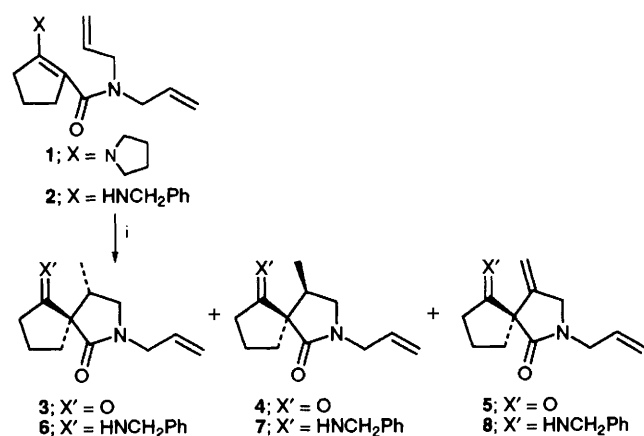
Enamines are widely used in organic synthesis as nucleophilic reagents in carbon-carbon bond-forming reactions.<sup>1</sup> Moreover, enamines can be used as electrophiles when they are oxidized to their corresponding radicals. Until now, these radical cations were produced only by electrochemical methods.<sup>2</sup>

We report here that enamines **1** and **2**, which have a redox potential of about 0.8 V vs. standard calomel electrode (SCE),<sup>3</sup> can be oxidized by two equivalents of metallic salts such as Co(OAc)<sub>2</sub>, AgOAc or CuCN or by one equivalent of Cu(OAc)<sub>2</sub>. The radical cation which is formed reacts intramolecularly with unactivated olefins, producing cyclized products in good yields. The reactions were performed at room temperature except for those involving Cu(OAc)<sub>2</sub> and CuCN which were run at 80 °C. The results are summarized in Table 1.

Since no azaspiro compounds were observed when the enamines were treated with a Lewis acid such as EtAlCl<sub>2</sub> or ZnCl<sub>2</sub>, an ene reaction can be excluded.<sup>4</sup> The formation of azaspiro compounds is assumed to proceed *via* the radical cation **B** (Scheme 1). This radical cyclizes to produce the corresponding radical **C** which is reduced to **D** by ethanol<sup>5</sup> in the presence of AgOAc,† CuCN† and Co(OAc)‡ or leads to the formation of **E** when Cu(OAc)<sub>2</sub> is used<sup>6</sup> (Scheme 1). Only one equivalent of Cu(OAc)<sub>2</sub> was necessary to obtain **5** (61%) and **8** (85%) from **1** and **2**, respectively. This is probably the

† A deposit of metal was observed on the wall of the flask.

‡ By analogy with the oxidation of diketones, Co<sup>II</sup> seems to act on enamines as an oxidizing agent; J. Iqbal, T. K. Praveen Kumar and S. Manogaran, *Tetrahedron Lett.*, 1989, **30**, 4701.

**Table 1** Oxidation of enamines by metallic salts in ethanol

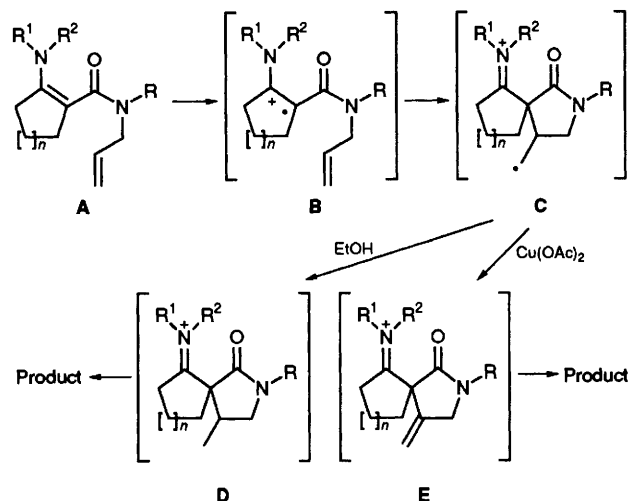
Starting material <sup>a</sup>	Metallic salt (equiv.)	Temp. <sup>b</sup>	Products (ratio)	Yield (%)
1	Co(OAc) <sub>2</sub> (2)	RT	3, 4 (95:5)	60
2	Co(OAc) <sub>2</sub> (2)	RT	6, 7 (45:55)	65
1	AgOAc (2)	RT	3, 4 (94:6)	51
2	AgOAc (2)	RT	6, 7 (46:54)	75
1	CuCN (2)	80 °C	3, 4 (95:5)	57
2	CuCN (2)	80 °C	6, 7 (43:57)	70
1	Cu(OAc) <sub>2</sub> (1)	80 °C	5	61
2	Cu(OAc) <sub>2</sub> (1)	80 °C	8	85

<sup>a</sup> Conditions for compound 1: metal salt, then H<sub>3</sub>O<sup>+</sup>; conditions for compound 2: metal salt. <sup>b</sup> RT = room temperature.

result of a dismutation of Cu<sup>I</sup> to Cu<sup>II</sup> (Cu<sup>I</sup> + Cu<sup>I</sup> → Cu<sup>II</sup> + Cu<sup>0</sup>).<sup>7</sup> The observed stereoselectivity is independent of the oxidants and is probably associated with steric effects as well as electrostatic effects.<sup>§</sup>

In cases where AgOAc is used to produce the azaspiro compounds, two competing mechanisms can be envisaged: a radical mechanism or an electrophilic mechanism. To verify if a radical mechanism was involved, 1 and 2 were treated with AgOAc (2 equiv.) and Cu(OAc)<sub>2</sub> (1 equiv.) at room temperature. Under these conditions, the azaspiro compounds 5 and 8 were obtained in yields of 57 and 82% respectively. These results allow one to propose that a radical cation of type B is involved in the oxidation of the enamine by AgOAc. Because Cu(OAc)<sub>2</sub> is unable to promote the reaction at room temperature, the initial reaction is initiated by AgOAc, with subsequent oxidation of the product radical by Cu(OAc)<sub>2</sub>.

§ The stereochemistry of 3, 4, 6 and 7 was established by X-ray analysis: J. Cossy and A. Bouzide, unpublished results.

**Scheme 1** Mechanism for the formation of the azaspiro products.

In summary, it has been demonstrated that the oxidation of enamines<sup>¶</sup> by various metallic salts can produce a radical cation which adds efficiently to unactivated olefins producing cyclized products.

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¶ This reaction is general as azaspiro compounds were obtained for *n* = 2 and for R = Me with similar yields.