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Generation of Cation Radicals from Enamines and Their Reactions with Olefins

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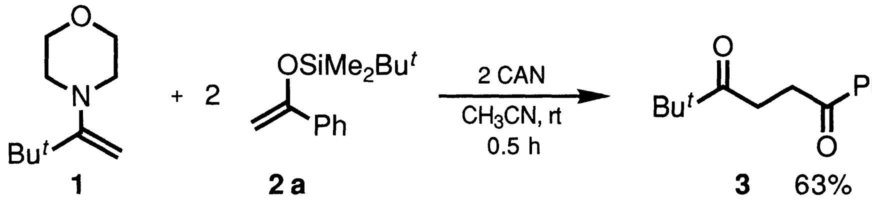
Cation radicals of enamines, generated by the oxidation with Ce^{IV} compounds, react with electron-rich olefins to give the addition products. The formal α-alkylation of formylacetate is realized by the reaction of 3-(1-pyrrolidinyl)propenoate and olefins by the use of tetrabutylammonium cerium(IV) nitrate as an oxidant.

Enamines are widely used in organic synthesis as nucleophilic reagents for the carbon-carbon bond forming reactions.1) On the other hand, cation radicals of enamines generated by electrolysis react with anions of β-keto esters as electrophiles,2) but their reactions have not been studied extensively.3) For the purpose to use nitrogen cation radicals for the construction of carbon frameworks, we investigated the generation of cation radicals of enamines and their addition reactions to olefins by the use of metallic oxidants.

The reaction of a pinacolone enamine **1** and α-(*t*-butyldimethylsiloxy)styrene (**2a**) was examined in the presence of 2 mole equivalents of various metallic oxidants such as Mn^{III}, Ag^{II}, Fe^{III}, and Ce^{IV} compounds. Among these oxidants examined, the use of ammonium cerium(IV) nitrate (CAN)4) gave the addition product **3** in 63% yield (Eq. 1).

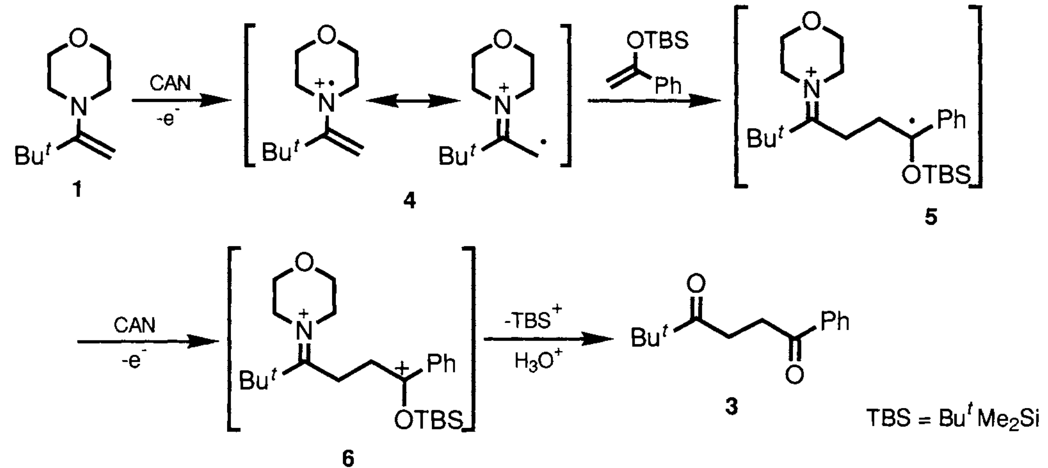


(1)

CAN = $(NH_4)_2Ce(NO_3)_6$

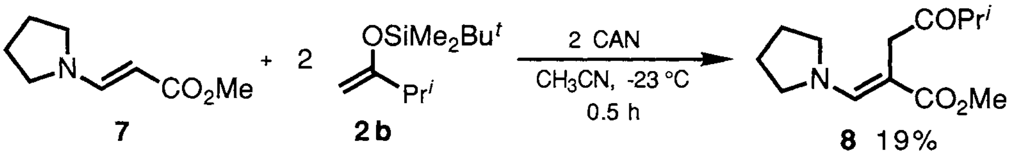
The reaction is supposed to proceed via the enamine cation radical **4**. That is, the enamine is oxidized to the cation radical **4** with CAN, which adds to the silyl enol ether **2a**. The resulting α-siloxy radical **5** is further oxidized with CAN to the cation **6**, and the 1,4-diketone **3** is formed eventually with the elimination of the silyl cation (Scheme 1).

Then, this method was applied for the formal α-alkylation of 3-oxopropanoate (formylacetate). Although formylacetate seems to be an interesting synthetic reagent, this has been scarcely used in organic synthesis because formylacetate is unstable and the alkylation gives an *O*-alkylated product.5) The enamine of formylacetate, 3-aminopropenoate, is easily prepared and stable enough to be purified by chromatographic separation



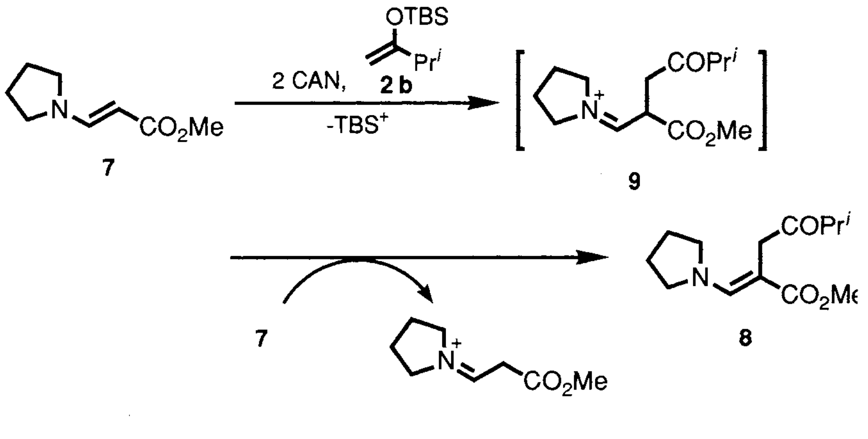
Scheme 1.

with alumina gel.[6] The cation radical of 3-aminopropenoate was expected to react with olefinic compounds to give *C*-alkylated products. In fact, treatment of a mixture of methyl 3-(1-pyrrolidinyl)propenoate (**7**) and a silyl enol ether **2b** with CAN gave the corresponding addition product **8** but in only 19% yield (Eq. 2).



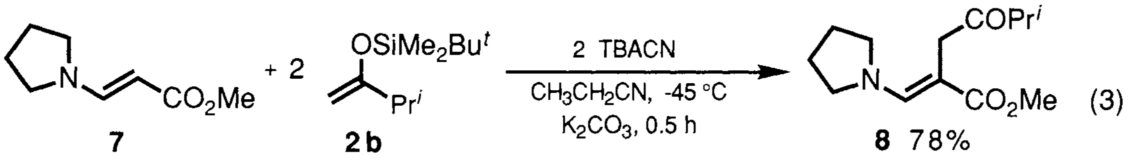
(2)

It was considered that the enamine-type adduct **8** is formed by deprotonation of the rather acidic proton of the intermediate iminium salt **9** with the aid of the enamine **7**. Since the enamine ester **7** was thus consumed as a proton acceptor, the product **8** was yielded in such a low yield (Scheme 2).



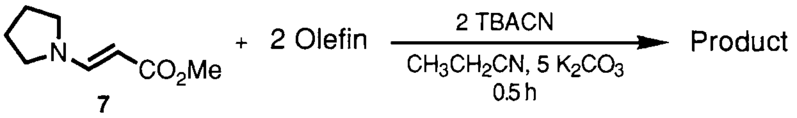
Scheme 2.

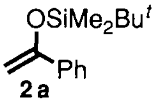
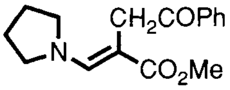
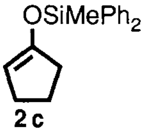
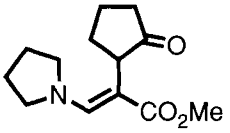
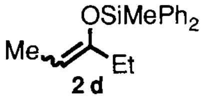
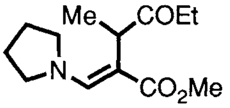
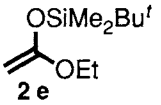
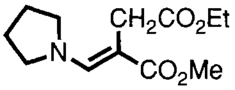
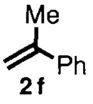
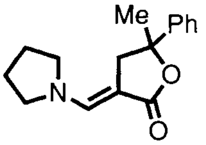
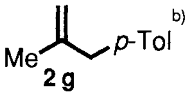
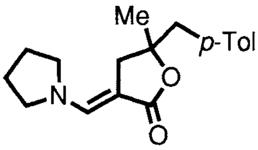
To prevent the loss of the enamine ester **7**, the reaction was examined in the presence of various bases and Ce^{IV} compounds. When a mixture of **7** and **2b** was treated with 2 mole equivalents of tetrabutylammonium cerium(IV) nitrate (TBACN)[7] in the presence of K_2CO_3 at -45 °C, the corresponding addition product **8**[8] was obtained in 78% yield (Eq. 3).[9] The use of CAN or triethylammonium cerium(IV) nitrate (CTAN)[10] in place of TBACN afforded **8** in lower yield, probably because CAN and CTAN were partially consumed for the oxidation of amines which are generated from CAN and CTAN by the neutralization with K_2CO_3.



TBACN = $(Bu^n{}_4N)_2Ce(NO_3)_6$

Table 1. The Reactions of 3-(1-Pyrrolidinyl)propenoate (**7**) with Various Olefins



Olefin	Temp/°C	Product	Yield/%[a)]
	-78		91
	-45		84
	-45		72
	-45		53
	-45		45
	-45		34

a) Based on **7**. b) *p*-Tol = *p*-MeC_6H_4

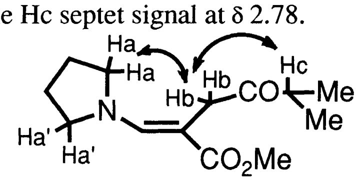
The reactions of the enamine **7** and various electron-rich olefins **2a** and **2c-g** were illustrated in Table 1. In addition to β-unsubstituted silyl enol ethers **2a** and **2b**, β-substituted silyl enol ethers **2c** and **2d** and a ketene silyl acetal **2e** reacted with **7** and the corresponding addition products were obtained in good yields. The reactions of **7** with conjugated and non-conjugated olefins **2f** and **2g** also proceeded, giving the lactones in moderate yield.

The alkylation of β-amino propenoate with alkyl bromide is known to give the *C*-alkylated product in only low to modest yield, because *N*- and *O*-alkylations and double alkylation occurred simultaneously.[11] On the other hand, by the present radical reaction, various substituents are successfully introduced formally into 3-aminopropenoate.

The typical experimental procedure is as follows: To a propionitrile (12.0 ml) solution of TBACN (4.20 g, 4.21 mmol) and K_2CO_3 (1.50 g, 10.9 mmol) was added a propionitrile (12.0 ml) solution of **2b** (0.866 g, 4.33 mmol) and **7** (0.311 g, 2.00 mmol) at -45 °C under an argon atmosphere. After stirring for 0.5 h, triethylamine (1.0 ml) was added to quench the reaction mixture. Usual work-up and purification by column chromatography (basic alumina) gave the corresponding product **8** (0.372 g, 78%).

References

1) For example: G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrel, *J. Am. Chem. Soc.*, **85**, 207 (1963); M. E. Kuehne, *Synthesis*, **1970**, 510; J. K. Whitesell and M. A. Whitesell, *ibid.*, **1983**, 517.
2) T. Chiba, M. Okimoto, H. Nagai, and Y. Takata, *J. Org. Chem.*, **44**, 3519 (1979).
3) T. Shono, Y. Matsumura, H. Hamaguchi, T. Imanishi, and K. Yoshida, *Bull. Chem. Soc. Jpn.*, **51**, 2179 (1978); S. Torii, T. Yamada, and H. Tanaka, *J. Org. Chem.*, **43**, 2882 (1978).
4) CAN was dried under reduced pressure (0.1 Torr) at 80 °C for 10 h before use.
5) R. Gompper and H. -H. Vogt, *Chem. Ber.*, **114**, 2866 (1981); B. Föhlisch and W. Giering, *Synthesis*, **1980**, 231.
6) R. Huisgen, K. Herbig, A. Siegl, and H. Huber, *Chem. Ber.*, **99**, 2526 (1966).
7) H. A. Muathen, *Indian J. Chem.*, **30B**, 522 (1991).
8) The geometry of **8** was determined as *Z* configuration by the observation of NOEs as indicated below. Irradiation of the Hb singlet at δ 3.55 gave a 1.3% increase of the Ha and Ha' multiplet signals at δ 3.37-3.43 as well as to a 5.9% increase of the Hc septet signal at δ 2.78.



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9) When an equimolar amount of **2b** was employed, **8** was obtained in 65% yield.
10) H. Firouzabadi and N. Iranpoor, *Synth. Commun.*, **13**, 1143 (1983).
11) C. B. Kanner and U. K. Pandit, *Tetrahedron*, **38**, 3597 (1982).

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