

# Radical cyclization of $\alpha$ -iodo enones by photoinduced electron transfer reaction

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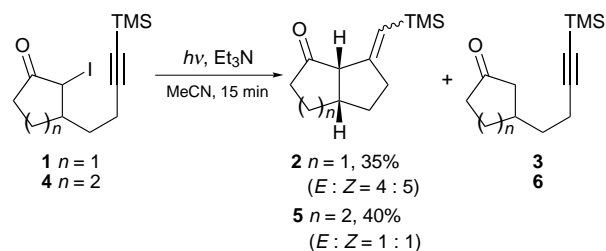
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A facile intramolecular radical cyclization of  $\alpha$ -iodo enones effected by triethylamine-mediated photoinduced electron transfer (PET) reactions is described.

Photoinduced electron transfer (PET) reactions have been widely used for one electron reduction and cyclization reactions.<sup>1</sup> Recently, Cossy has employed a triethylamine-promoted PET reaction for the generation of alkyl radicals<sup>2</sup> and for various cyclization reactions.<sup>3</sup> Mattay has described the radical cyclization reactions of cyclopropyl and epoxy ketones effected by triethylamine-mediated PET reactions.<sup>4</sup> Triethylamine-induced carbocyclization of  $\beta$ -bromoprop-2-ynyl ethers in pyrimidenedione has also been reported.<sup>5</sup> As part of our investigation directed toward the total synthesis of natural products based on  $\alpha$ -ketone<sup>6</sup> and  $\alpha$ -enone<sup>7</sup> radical cyclizations, we were in search of an efficient and mild alternative route to the tributyltin hydride method. In this context we examined the triethylamine-mediated PET reactions of  $\alpha$ -iodo ketones,  $\alpha$ -iodo enones and vinyl iodides. Herein we report the preliminary results of our investigation.

We initiated our study with  $\alpha$ -iodo ketones.<sup>1</sup>  $\alpha$ -Iodo ketone **1** or **4** with triethylamine (10 equiv.) in MeCN (0.02 M) was irradiated in a Rayonet photoreactor with low pressure mercury lamp for 15 min (Scheme 1). The reaction mixture was purified by silica-gel column chromatography to afford the cyclized product **2** or **5** in low yield (35 and 40%, respectively). The other compounds isolated were the reduction products **3** and **6**. Attempts to improve the yields of this reaction under various conditions were futile. We then examined the PET radical cyclization of  $\alpha$ -iodo enones. The  $\alpha$ -iodo enones were synthesized from the corresponding enones<sup>8</sup> via a literature procedure.<sup>9</sup> A solution of  $\alpha$ -iodo enone **8** or **11** in MeCN (0.02 M) with triethylamine (10 equiv.) was irradiated for 45 min. Upon workup, we obtained the cyclized product **9** ( $E:Z = 3:1$ ) or **12** ( $E:Z = 1:1$ ) in 74 and 61% yield, respectively. The generality of this PET radical cyclization of  $\alpha$ -iodo enones was then investigated. The results are summarized in Table 1.

$\alpha$ -Iodo vinylogous esters **14** and **20** with a terminal acetylenic moiety and **17** and **23** with trimethylsilyl acetylenic groups underwent cyclization readily. While  $\alpha$ -iodo enones and  $\alpha$ -iodo vinylogous esters underwent smooth cyclization, the corresponding unprotected  $\alpha$ -iodo vinylogous amide **26** failed to cyclize under these photolysis conditions. However,  $N$ -protected  $\alpha$ -iodo vinylogous amide **29** underwent clean cyclization and afforded the double bond isomerized compound **30** upon silica-gel column chromatography. In order to test the limitations of this method, we also tried a similar procedure



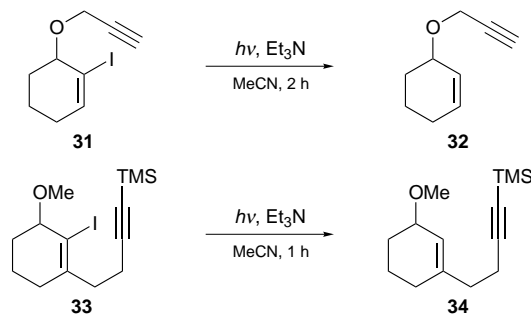
Scheme 1

Table 1 Irradiation of iodo enones, vinylogous esters and amides in the presence of triethylamine

Entry	Enones	$\alpha$ -Iodo enones	Cyclized products	Yield (%) <sup>a,b</sup> $E:Z$
1				74 3:1 <sup>c</sup>
				61 1:1 <sup>c</sup>
2				72 —
				68 5:3 <sup>c</sup>
3				64 —
				64 3:1 <sup>c</sup>
4				— —
				51 <sup>d</sup> —

<sup>a</sup> Isolated yield. <sup>b</sup> The uncyclized reduction products were 10–25% for entries 1–3. <sup>c</sup> The  $Z$  and  $E$  isomers were characterized by NOE experiments. <sup>d</sup> The exocyclic double bond was isomerized to form the pyrrole ring during silica-gel column chromatography.

with vinyl iodides. The required iodo compounds **31** and **33** were prepared by standard procedures.<sup>10</sup> Compound **31** was photolyzed with triethylamine for 2 h, but the expected cyclization did not occur. Instead **31** underwent simple reduction to give compound **32**. Similarly, iodo compound **33** failed to cyclize upon irradiation and led only to the formation of reduction product **34** (Scheme 2).



Scheme 2

In conclusion, we have achieved the efficient radical cyclization of  $\alpha$ -iodo enones *via* triethylamine-mediated PET reactions, whereas the radical cyclization of  $\alpha$ -iodo ketones using PET conditions afforded the cyclized product only in moderate yield. Presumably  $\alpha$ -enone radicals, having the radical orbital orthogonal to the  $\pi$ -system of the enone, is more reactive and hence undergoes cyclization more effectively. Mild reaction conditions and easy product isolation make this route an attractive alternative to the tributyltin hydride method. This method eliminates the tedious separation of the tin compounds and would permit large scale preparations. The application of this method toward the total synthesis of natural products is being investigated in our laboratories.

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## Notes and References

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- 10 Compound **31** was prepared from 2-iodocyclohex-2-enone by reduction with sodium borohydride–cerium chloride followed by treatment with sodium hydride and prop-2-ynyl bromide. Compound **33** was obtained by reduction of **8** using sodium borohydride–cerium chloride followed by treatment with sodium hydride and iodomethane.

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