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Solvent-Dependent Chemoselectivities in Ce(IV)-Mediated Oxidative Coupling Reactions

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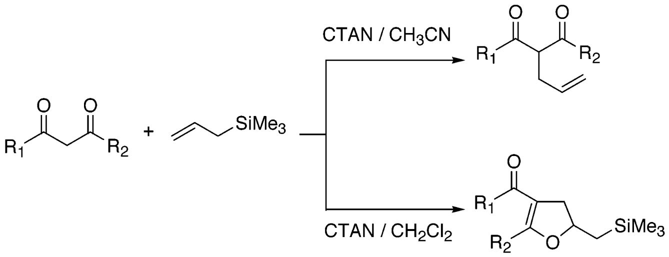
ABSTRACT



The oxidative coupling of 1,3-diketones, *β*-keto esters, and *β*-keto silyl enol ethers with allyl trimethylsilane in the presence of CTAN was investigated. In the case of acyclic diketones and esters, different chemoselectivities were observed in CH_3CN and CH_2Cl_2 leading to good yields of allylation and dihydrofuran products, respectively.

Ceric ammonium nitrate (CAN) has been utilized extensively for oxidative bond-forming reactions including the oxidative addition of carbonyls,[1−3] silyl enol ethers,[4,5] and diones[6,7] to alkenes, arenes, and dienes. While CAN is useful in the aforementioned reactions, its use is limited to polar organic and aqueous solvents. The poor solubility of Ce(IV) in less polar solvents can be circumvented by the preparation of ceric tetra-*n*-butylammonium nitrate (CTAN).[8,9] Recent work in our group has revealed that while CTAN oxidizes substrates more slowly than CAN by a factor of 2, they behave in a mechanistically analogous manner.[10]

The solubility of CTAN in a number of solvents provides an opportunity to determine the impact of solvation on both substrates and Ce-based oxidants. During our initial studies we decided to examine the influence of solvent on the reaction between allyl trimethylsilane and 1,3-dicarbonyls. This particular reaction, previously reported by Hwu and coworkers, has a number of advantages including relatively fast reaction times and the absence of competing side reactions such as internal ligand transfer.[11]

Scheme 1

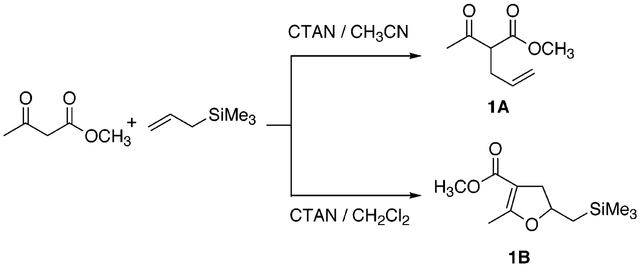


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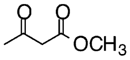
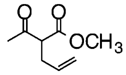
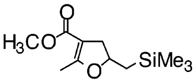
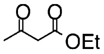
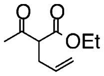
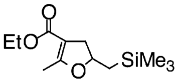
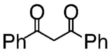
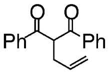
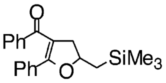
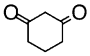
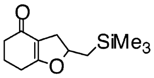
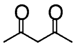
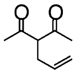
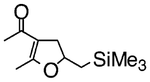
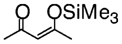
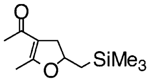
Table 1. Results of Oxidative Addition of 1,3-Dioxo Compounds with CTAN[a]

Entry	Substrate	Conditions[a]	Yield[b]	Ratio (%A:%B)[c]	Product	
1		A	81% (1A)	quantitative (1A)		1A
		B	72% (1B)	quantitative (1B)		1B
2		A	73% (2A)	quantitative (2A)		2A
		B	62% (2B)	19:81		2B
3		A	78% (3A)	88:12		3A
		B	68% (3B)	15:85		3B
4		A	72% (4B)	quantitative (4B)		4B
		B	78% (4B)	quantitative (4B)		
5		A	62% (5A)	76:24		5A
		B	66% (5B)	18:82		5B
6		A	80% (6B)	quantitative (6B)		6B
		B	74% (6B)	quantitative (6B)		

[a] Conditions: (A) 2 equiv of CTAN, 1 equiv of substrate in CH_3CN, 4 h; (B) 2 equiv of CTAN, 1 equiv of substrate in CH_2Cl_2, 4 h. [b] Isolated yield. [c] GC yields.

In an initial experiment, equimolar amounts of methylacetoacetate and allyltrimethylsilane were treated with 2 equiv of CTAN in CH_3CN and CH_2Cl_2 at room temperature. It was expected that the allylation would occur in both solvents so that the influence of solvent polarity on rate could be examined in further kinetic studies. Surprisingly, a totally different chemoselectivity was observed in both solvents (Scheme 1). The products **1A** and **1B** were generated exclusively in CH_3CN and CH_2Cl_2, respectively. To probe the generality of this finding, the investigation was extended to a number of substrates and the results are summarized in Table 1.

Examination of the results in Table 1 clearly shows that cyclized dihydrofuran products or allyl addition products are obtained as primary products in CH_2Cl_2 or CH_3CN, respectively. The β-keto silylenol ether (**6**) and 1,3-cyclohexadione (**4**) provided only the furan products under both sets of conditions.

Previous work of Hwu described the reaction of 1,3-dicarbonyls and allyl trimethylsilane with CAN and $Mn(OAc)_3$.[11] Allylation products were obtained when the reaction was carried out with CAN in CH_3OH at room temperature

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(11) Hwu, J. R.; Chen, C. N.; Shiao, S.-S. *J. Org. Chem.* **1995**, 60, 856.

whereas dihydrofuran products were obtained with $Mn(OAc)_3$ in acetic acid at 80 °C. While Hwu and co-workers examined a number of variables in these reactions one point in their discussion proposed that the diversity of the reactions came from the reactivity difference between CAN and $Mn(OAc)_3$, where the latter is a weaker oxidant.

The redox potentials of lanthanides are known to be sensitive to the solvent milieu.[12−14] Cyclic voltammetry (CV) was utilized to determine the redox potential of CTAN in CH_3CN and CH_2Cl_2 to establish whether the chemoselectivity was possibly due to different redox potentials of CTAN in those two solvents. Figure 1 shows the CV data for CTAN in CH_2Cl_2 and CH_3CN. The potentials (vs $Ag/AgNO_3$) are 510 ±20 and 540 ±10 mV, respectively. While the CV of CTAN in acetonitrile is nearly ideal (ΔE of 67 mV), inspection of the voltammogram for CTAN in CH_2Cl_2 is clearly quasireversible with a ΔE of 180 mV. While the low polarity of CH_2Cl_2 made the experiment somewhat more difficult, the results of numerous determinations were consistent and repeatable. The redox potential of CTAN in CH_2Cl_2 was indeed lower by 30 mV (0.7 kcal/mol), but it is unlikely that this small difference is responsible for the change in chemoselectivity.

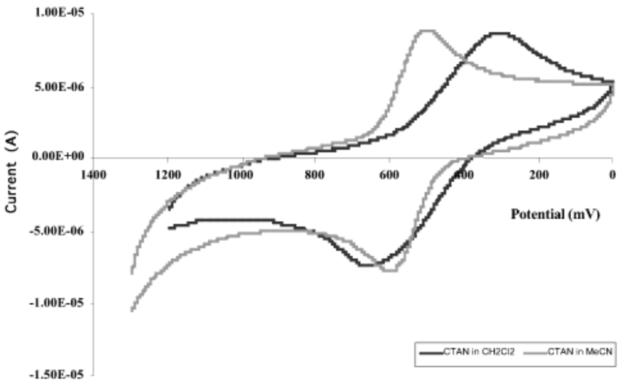
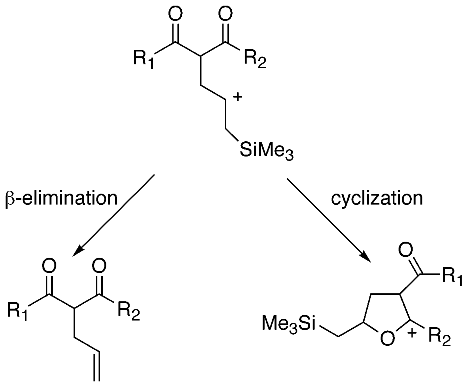


Figure 1. Cyclic voltammograms of CTAN at a glassy carbon electrode in acetonitrile and CH_2Cl_2 vs $Ag/AgNO_3$ reference electrode.

Since the oxidizing power of Ce(IV) is nearly the same in CH_3CN and CH_2Cl_2, the chemoselectivity does not arise from solvent-induced changes in the thermodynamic redox potential of the oxidant. Nonetheless, solvent must play a role in determining the product distribution. During the course of the reaction, the dicarbonyl substrate is oxidized to produce a radical cation, which attacks the allyl trimethylsilane forming a β-silyl radical. Further oxidation of the β-silyl radical produces a carbocation (Scheme 2). It is our supposition that the more polar CH_3CN stabilizes the β-silyl cation through solvation providing a pathway to elimination. Upon oxidation of the radical in the less polar CH_2Cl_2, cyclization is favored through the proximity of a carbonyl (in the absence of solvent stabilization) producing an oxo stabilized cation.

Scheme 2



The discussion in the preceding paragraphs focuses on the effect of solvent on allylation vs addition−cyclization in acyclic substrates **1**−**3** and **5** but does not address the absence of this phenomenon in substrates **4** and **6**. In the case of substrate **4**, addition of the allyltrimethylsilane and subsequent oxidation places the β-silyl cation in close proximity to the carbonyls due to the restricted conformational flexibility of the cyclic system. In this more ordered system it is reasonable to expect less solvent dependence on the product distribution. On the other hand, dihydrofuran formation after addition of allyltrimethylsilane to oxidized **6** in both solvents is somewhat more surprising. Initial rate studies on the CTAN-mediated oxidative addition to **6** indicate an ordered transition state, consistent with recent reported work,[10] but further studies are necessary to determine the underlying mechanistic nuances of this reaction.

In conclusion, we have unraveled some interesting solvent-dependent chemoselectivities of the CTAN-mediated oxidative coupling of 1,3-dicarbonyl compounds and allyltrimethylsilane. Further work on the discreet mechanistic details of the oxidation process in various solvents and the general synthetic utility of this approach is currently being explored.

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Supporting Information Available: General methods, electrochemical data, experimental protocols, and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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