

# Recent Advances in Synthetic Transformations Mediated by Cerium(IV) Ammonium Nitrate

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Received May 14, 2003

## ABSTRACT

Cerium(IV) ammonium nitrate (CAN) has recently emerged as a versatile reagent for oxidative electron transfer; the overwhelming number of reports serve as a testimony to the unparalleled utility of CAN in a variety of transformations of synthetic importance. Our recent work has uncovered novel carbon–carbon bond-forming reactions leading to the one-pot synthesis of dihydrofurans, tetrahydrofurans, and aminotetralins. In addition, we have developed a number of facile carbon–heteroatom bond-forming reactions by the CAN-mediated oxidative addition of soft anions to alkenes. A mechanistic rationale has been provided for the reactions explored. As might be expected of very powerful one-electron oxidants, the chemistry of cerium(IV) oxidation of organic molecules is dominated by radical and radical cation chemistry.

## Introduction

Gomberg's epoch-making discovery of the existence of the stable triphenyl methyl radical in 1900 marked the genesis of a new domain, radical chemistry, in the vast realm of organic chemistry.<sup>1</sup> Almost four decades later, significant contributions to the development of this area were made by Hey and Waters<sup>2</sup> and Kharasch,<sup>3</sup> who carried out elaborate studies on the mechanisms of radical reactions. In spite of a clear understanding of the mechanistic background, radical reactions found little application in

synthesis, largely due to the erroneous notion that they are prone to give intractable mixtures. A dramatic change in this outlook which triggered an upsurge of interest in this approach, particularly over the past two decades, can be attributed to the conceptualization and demonstration by Stork that the controlled generation and addition of vinyl radicals to olefins constitutes a unique and powerful method for complex carbocyclic construction.<sup>4</sup> It is noteworthy that the investigations by Julia,<sup>5a,b</sup> Beckwith,<sup>5c</sup> Ingold,<sup>5d</sup> and Giese<sup>5e</sup> have contributed to a deeper understanding of the structure and reactivity of radicals. A number of others, most notably Curran<sup>6c,f</sup> and Pattenden,<sup>6h</sup> have made significant contributions to the application of radical methodology in organic synthesis. Today, radical methodology has evolved as a prominent tool in the arsenal of the synthetic organic chemist.<sup>6</sup>

Of the principal methods developed for the generation of radicals, redox processes based on electron-transfer deserve special mention. Chemical methods for electron-transfer oxidation involve the use of salts of high-valent metals such as Mn(III), Ce(IV), Cu(II), Ag(I), Co(III), V(V), and Fe(III). Among these, Mn(III) has received the most attention.<sup>7</sup> In spite of the well-established and frequent use of this reagent for the generation of electrophilic carbon-centered radicals from enolic substrates, particularly in intramolecular processes, procedural problems associated with it have prompted the development of other oxidants of choice. The availability of Ce(IV) reagents as suitable one-electron oxidants assumes importance in this context.

The earliest report on the use of Ce(IV) salts for the generation of carbon-centered radicals dates back to the pioneering work of Heiba and Dessau in 1971, as illustrated by the addition of acetone to 1-octene mediated by cerium(IV) acetate (Scheme 1).<sup>8</sup>

In a related reaction,  $\gamma$ -lactones were synthesized by Ce(IV)-mediated oxidative addition of carboxylic acids to olefins (Scheme 2).<sup>9</sup>

Most of the initial experiments relied on the use of cerium(IV) acetate in acetic acid. Subsequently, investigations in a number of laboratories, including our own, have shown that cerium(IV) ammonium nitrate (CAN) is a convenient and excellent reagent for effecting a wide array of synthetic transformations.<sup>10</sup> Inter alia, its solubility in

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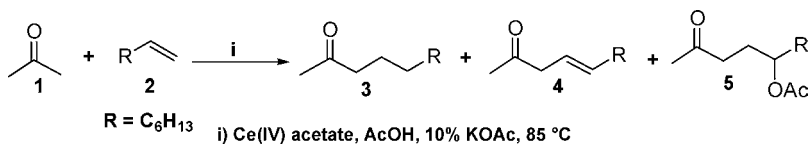
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Jessy Mathew obtained her M.Sc and M.Phil. degrees in chemistry from Mahatma Gandhi University. She carried out research under the supervision of Dr. Vijay Nair and obtained her Ph.D (1996) from the University of Kerala. She was a postdoctoral fellow in the group of Professor Mike Kahn at Molecumetics (1996–99) and subsequently senior scientist (1999–2002) in the same company. Presently she is a senior scientist with Chem Codes, Inc., in Durham, North Carolina.

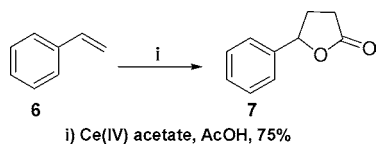
Vijay Nair has Ph.D degrees from the Banaras Hindu University (1967, with Professor R. H. Sahasrabudhey) and the University of British Columbia (1969, with Jim Kutney). Subsequently he was a postdoctoral fellow with Josef Fried at the University of Chicago, with Peter Yates in Toronto, and with Gilbert Stork at Columbia University. After a 16-year career (Senior Research Chemist and Principal Scientist, Outstanding Scientist Award 1981) with Lederle Laboratories (American Cyanamid Co.) in Pearl River, New York, he returned to his native Kerala State in India to join the Regional Research Laboratory (CSIR) in 1990 as its Deputy Director and established an Organic Synthesis Division there. During 1997–2001, he was the Director of the Institute. Presently he is continuing as a Director-Grade Scientist. In addition, he is an Honorary Professor in the Department of Environmental Sciences, Cochin University of Science and Technology. Dr. Nair's research interests are in the areas of oxidative electron-transfer-mediated C–C and C–heteroatom bond-forming reactions, multicomponent reactions, heterocyclic synthesis via dipolar cycloadditions, and medicinal chemistry. Dr. Nair has been an invited lecturer at a number of international symposia, and he has lectured extensively in Universities in Germany, Japan, the United States, and India. He is a Fellow of the Indian Academy of Sciences.

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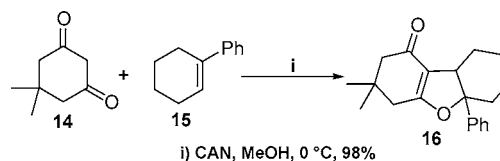
Scheme 1



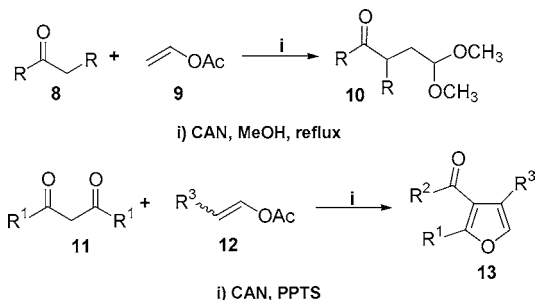
Scheme 2



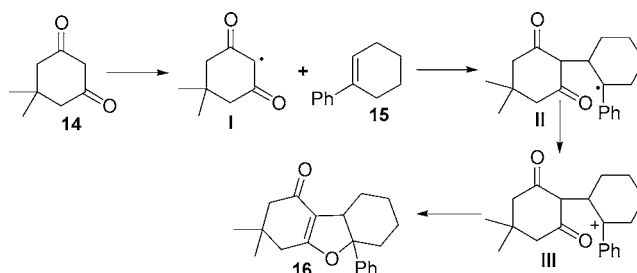
Scheme 4



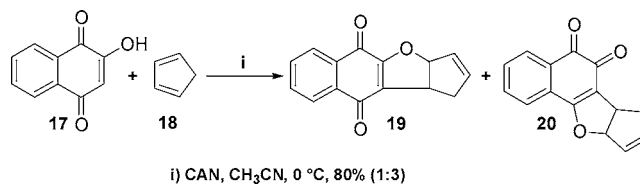
Scheme 3



Scheme 5



Scheme 6



organic solvents such as methanol and acetonitrile, low toxicity, ease of handling, and profound reactivity endowed in the reduction potential of  $\sim 1.6$  eV have contributed to the general acceptance of CAN as a reagent of choice for one-electron oxidations. It is worthy of note that there has been a flurry of activity in the area of CAN-mediated reactions since our review was published in 1997. Our group has uncovered a number of novel CAN-mediated reactions of interest from both synthetic and mechanistic standpoints. This Account is aimed at presenting a composite picture of this area, with the anticipation that it will spur further research. By design, the Account highlights our own work, but important contributions from other laboratories are included. The plethora of CAN-mediated reactions may be broadly classified under the following categories, each of which is discussed separately in what follows: reactions involving carbon–carbon bond formation, reactions involving carbon–heteroatom bond formation, and miscellaneous transformations.

## Reactions Involving Carbon–Carbon Bond Formation

Initial attempts in this direction were largely due to Baciocchi et al., who focused on the oxidative addition of simple ketones and 1,3-dicarbonyl compounds to activated alkenes such as silyl enol ethers, enol ethers, and enol acetates. Representative examples include the synthesis of 4-ketaldehyde dimethyl acetals and 3-acyl furans by the CAN-mediated addition of carbonyl and dicarbonyl compounds, respectively, to enol acetates (Scheme 3).<sup>11</sup>

About a decade ago, we embarked on a systematic and in-depth investigation of CAN-mediated addition of active methylene compounds to a range of  $\pi$ -systems including

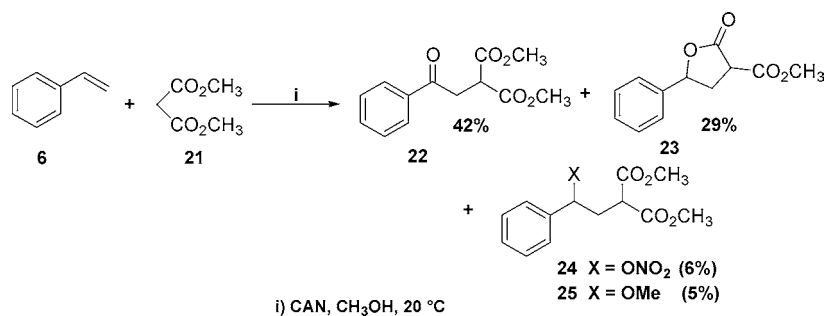
unactivated alkenes, cyclic as well as acyclic. Our studies were initiated with the addition of dimerone to phenylcyclohexene in the presence of CAN in methanol. The reaction afforded the corresponding dihydrofuran derivative in nearly quantitative yield (Scheme 4).<sup>12</sup>

The reaction proceeds by the regioselective addition of electrophilic carbon-centered radical **I** to the alkene to generate the stable benzylic radical **II**, which is oxidized by a second equivalent of CAN to the corresponding cation. The cationic species undergoes intramolecular ring closure with the carbonyl oxygen, affording the dihydrofuran (Scheme 5).

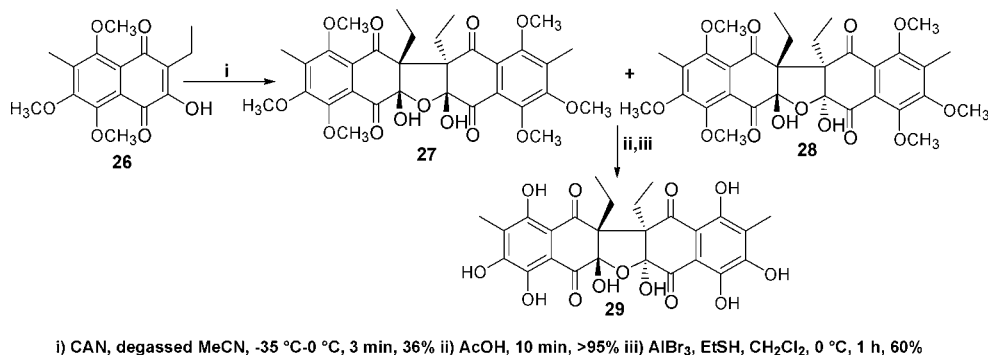
This protocol was found to be applicable to a variety of dicarbonyl compounds and alkenes, including exocyclic alkenes, the latter affording the corresponding spirodihydrofurans.<sup>13</sup> In an interesting extension of this reaction, we have demonstrated that CAN-mediated addition of active methylene compounds to dienes in methanol also constitutes an easy route for the synthesis of dihydrofuran derivatives.<sup>14</sup>

The analogous addition of 2-hydroxy-1,4-naphthoquinone to various dienes, promoted by CAN, led to the corresponding furanonaphthoquinone derivatives in moderate to good yields (Scheme 6). In all cases, both linear and angular adducts were formed.<sup>15</sup> It is noteworthy that there are a number of biologically active natural products which contain both linear and angular furanoquinone frameworks.

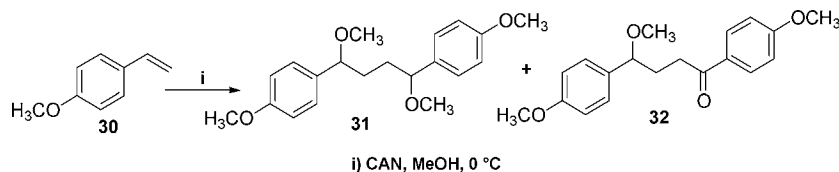
Scheme 7



Scheme 8



Scheme 9



The addition of dimethyl malonate to styrene occurred via a mechanistically intriguing reaction, resulting in the formation of the ketone **22** and the lactone **23** as the major products along with smaller amounts of **24** and **25** (Scheme 7).<sup>16</sup>

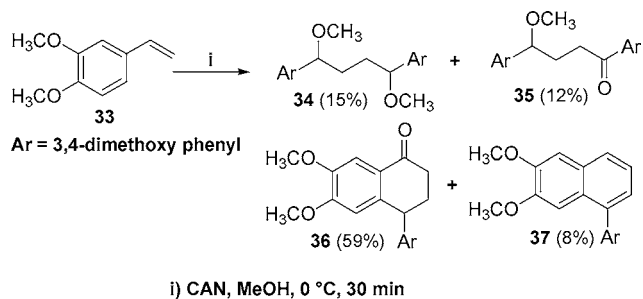
Subsequently, Linker developed an expeditious synthesis of C-2 branched sugars by the CAN-mediated addition of malonates to glycals.<sup>17</sup>

The results of our comparative studies on the oxidative additions of 1,3-dicarbonyl compounds to alkenes, mediated by CAN and manganese(III) acetate, clearly indicate that the former offers a number of advantages with respect to overall yields, mild reaction conditions, and experimental simplicity.<sup>18</sup>

All the reactions discussed so far are based on the CAN-mediated generation of electrophilic carbon-centered radicals and their trapping with electron-rich substrates. In addition, these radicals are also susceptible to dimerizations, and such processes have been investigated. For instance, Nicolaou has reported the synthesis of racemic hybocarpones **29** by CAN-mediated dimerization of naphthazirin **26** (Scheme 8).<sup>19</sup>

In the course of our investigations on CAN-mediated addition of dimethyl malonate to different ring-substituted styrenes, the reaction of 4-methoxystyrene presented an unprecedented outcome. Instead of the expected adducts,

Scheme 10



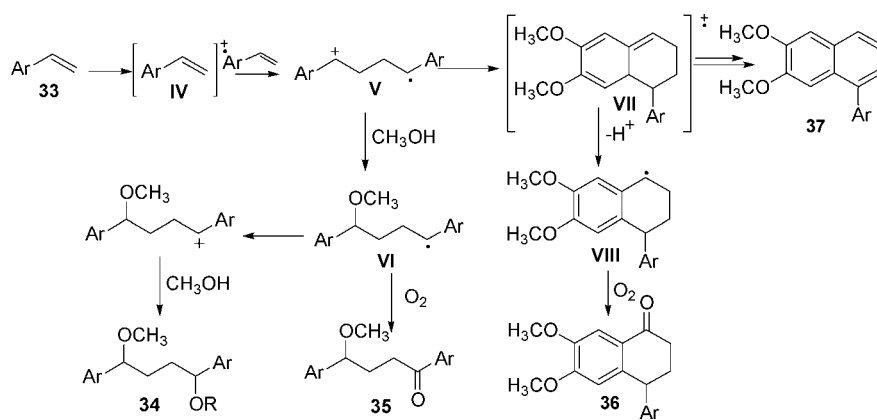
products resulting from the dimerization of the styrene were isolated (Scheme 9).<sup>20</sup>

When 3,4-dimethoxystyrene was subjected to the reaction under identical conditions, the tetralone derivative **36** and the naphthalene derivative **37** were formed in addition to the linear products **34** and **35** (Scheme 10).

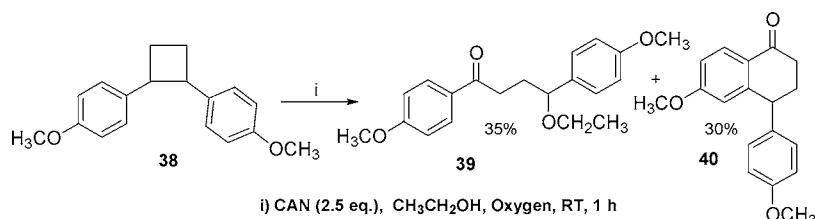
The exact mechanistic details of these reactions are not known. However, a rationalization along the following lines can be invoked, with 3,4-dimethoxystyrene as a representative example (Scheme 11).

The initial event involves the oxidative electron transfer from styrene to Ce(IV) to afford the radical cation **IV**. This would, in turn, add to another molecule of styrene to generate a distonic radical cation **V**. The cationic center of **V** will be quenched by nucleophilic solvents such as

Scheme 11



Scheme 12



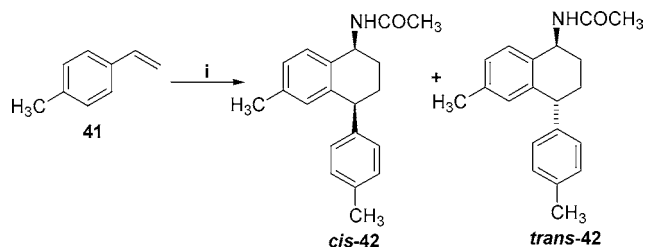
methanol, whereas the radical center can react with oxygen from the atmosphere, affording the ketomethoxy product **35**. Alternatively, further oxidation of this radical by Ce(IV) to a cation, followed by the addition of nucleophilic solvents, can afford the dimethoxy product **34**. The 1,4-radical cation **V** can also undergo 1,6-cyclization to give a substituted hexatriene radical cation **VII**, which can eventually lose a proton to yield a radical intermediate **VIII** that gets converted to the tetralone **36**. Alternatively, the hexatriene radical cation undergoes aromatization to afford the naphthalene derivative **37**.

It is noteworthy that the CAN-mediated protocol for the synthesis of aryltetralins from alkoxy-styrenes is far superior to the photochemical method in terms of experimental simplicity as well as yields of products.<sup>21</sup>

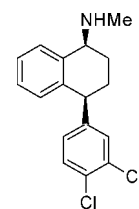
In addition to the synthetic potential of the reaction, vested in the close relationship of the aryltetralins to naturally occurring bioactive lignans, we were intrigued by the mechanistic implications of the cyclodimerization. We reasoned that, if the formation of the long-bond cyclobutane radical cation was involved, then the corresponding reaction of alkoxyarylcyclobutanes with CAN should afford products similar to those obtained in the CAN-mediated dimerization of alkoxy-styrenes. Gratifyingly, the reaction of cyclobutane **38**, prepared by the photochemical [2 + 2] cycloaddition of 4-methoxystyrene, with an ethanolic solution of CAN under an atmosphere of oxygen furnished the keto-ethoxybutane derivative **39** in 35% yield and the tetralone derivative **40** in 30% yield, thus validating our assumption (Scheme 12).<sup>22</sup>

Our studies also revealed that the choice of solvent plays a crucial role in determining the outcome of these reactions.<sup>20</sup> Hence, we reasoned that the use of acetonitrile as the solvent would result in the termination of cyclodimerization of styrenes by the trapping of the cationic

Scheme 13



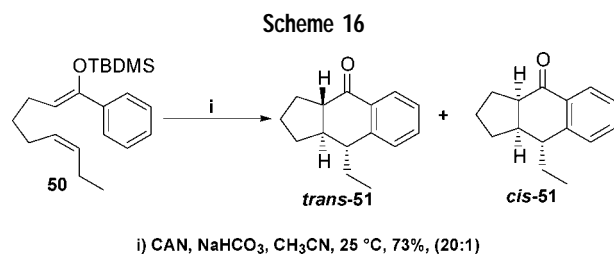
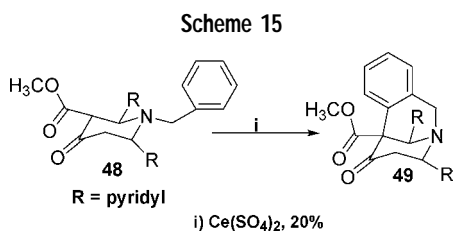
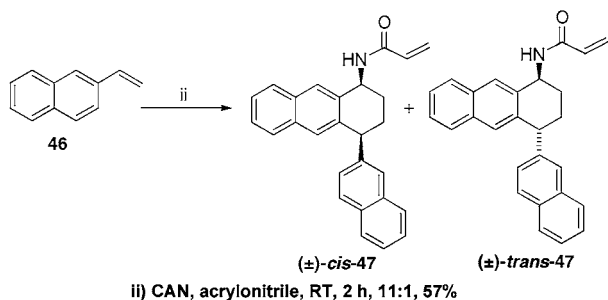
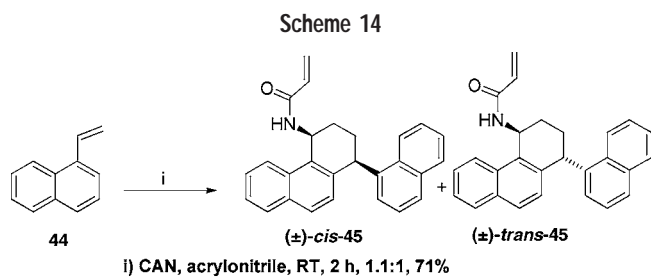
i) CAN, dry MeCN, argon, 2 h, RT, 62% (*cis*: *trans*, 1.3:1)

FIGURE 1. Sertraline (**43**).

intermediate in a Ritter-type reaction. Our assumptions were validated by the reaction of 4-methylstyrene with CAN in acetonitrile, which afforded the  $\alpha$ -acetamidotetralins *cis*-**42** and *trans*-**42** in good yields (Scheme 13).<sup>23</sup>

The acetamidotetralins are formed by the oxidation of the radical intermediate analogous to **VIII** to the cation, which is trapped by the solvent acetonitrile in a Ritter fashion. It is noteworthy that  $\alpha$ -aminotetralin derivatives manifest a number of important and therapeutically useful biological activities; some of them are potent central nervous system (CNS) stimulants and others are antibiotics, immunomodulators, and antitumor agents. Special mention may be made of the top-selling antidepressant, Sertraline (Figure 1).

The reaction was found to be general with a variety of styrenes and vinyl naphthalenes.  $\alpha$ -Acrylamidotetralins



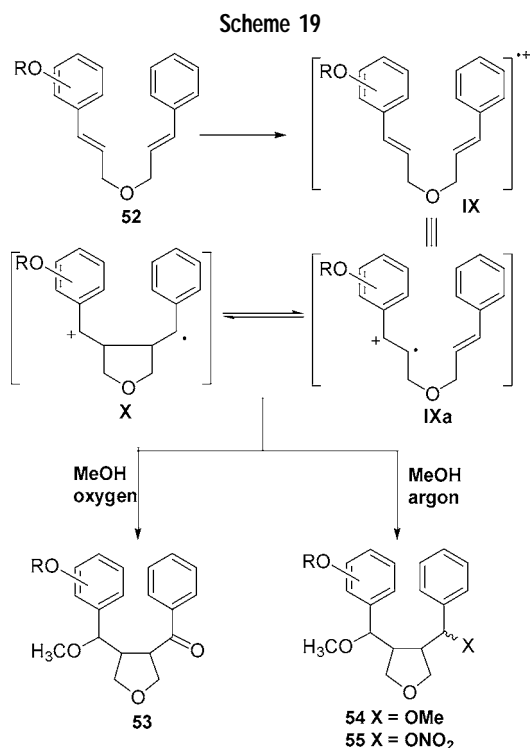
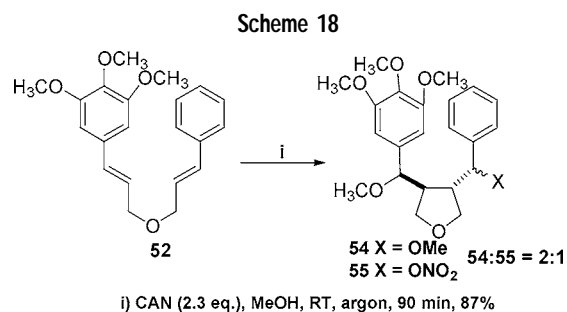
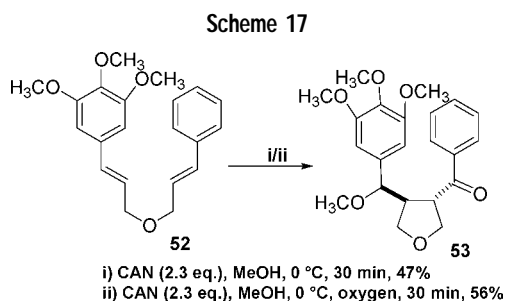
were obtained when acrylonitrile was used as the solvent (Scheme 14).

The importance of this method, which allows the one-pot assembly of the complex structural framework from readily available starting materials under very mild conditions in high yields, may be underscored.

In contrast to the successful use of CAN in intermolecular reactions, the reagent has found practically little use in oxidative intramolecular annulations. In an early report, it was shown that the attempted debenzoylation of 1-benzyl-2,6-bis(2'-pyridyl)-4-piperdone-3-carboxylic acid methyl ester (**48**) using cerium(IV) sulfate led inadvertently to intramolecular cyclization, albeit in very low yield (Scheme 15).<sup>24</sup>

Later, Snider demonstrated the striking utility of CAN in intramolecular annulations by his work on oxidative cyclization of  $\delta,\epsilon$ - and  $\epsilon,\phi$ -unsaturated silyl enol ethers. The reaction afforded the corresponding tricyclic ketones in high yields and with excellent diastereocontrol (Scheme 16).<sup>25</sup>

The encouraging results from CAN-mediated dimerizations of alkoxy-styrenes (vide supra) prompted us to attempt an intramolecular version of this reaction using



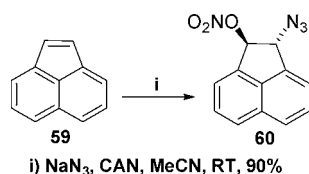
suitably substituted dicinnamyl ethers. Thus, the reaction of trimethoxycinnamyl cinnamyl ether with CAN in methanol resulted in the stereoselective formation of the corresponding 3,4-*trans*-disubstituted tetrahydrofuran derivative in moderate yield. A marginal increase in the yield was noticed when the reaction was done under an oxygen atmosphere (Scheme 17).<sup>26</sup>

Under an argon atmosphere, the reaction afforded the corresponding tetrahydrofuran derivatives as a mixture of methoxy and nitrate derivatives in the ratio 2:1 in high yields (Scheme 18).

Mechanistically, the reaction may be considered to involve the oxidation of a methoxystyrene unit of ether **52** to afford a radical cation **IX**, which can presumably



Scheme 20



exist in equilibrium with its distonic cyclic version **X**. Arguably, formation of the stable benzylic radical is the major driving force for this 5-exo-cyclization process. The cationic center of **X** gets quenched by the solvent, whereas the radical center is prone to two different transformations. Under an oxygen atmosphere, it is intercepted by molecular oxygen, affording the keto-product. Under an argon atmosphere, it may be oxidized by another equivalent of CAN to the benzylic cation, with subsequent addition of methanol to afford the dimethoxy product. Alternatively, ligand transfer from CAN would lead to the nitrate derivative (Scheme 19).

It is conceivable that this methodology for the stereospecific construction of disubstituted tetrahydrofuran derivatives will find application in the synthesis of bio-active lignans and related natural products.

## Carbon–Heteroatom Bond-Forming Reactions Mediated by CAN

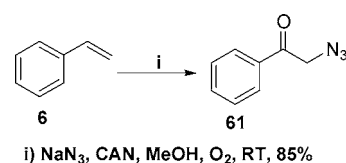
Carbon–heteroatom bond formation assumes much significance, especially from the vantage point of heterocyclic construction. Recently, there has been a flurry of activity toward developing novel methods for attaining this goal. The utility of CAN in carbon–heteroatom bond formation, particularly C–S, C–N, C–Se, C–Br, and C–I bonds, is noteworthy in this connection. Mostly, these reactions involve the oxidative addition of heteroatom-centered radicals, formed by the oxidation of anions by CAN, to alkenes or alkynes. Since we have recently reviewed this topic, only selected literature is covered here, with the emphasis being given to our contributions to this area.<sup>27</sup>

In his seminal work, which marks the beginning of the use of CAN for the construction of carbon–heteroatom bonds, Trahanovsky demonstrated that CAN promotes a facile addition of azide radicals to olefins such as stilbene and acenaphthalene, to afford *trans*- $\alpha$ -azido- $\beta$ -nitroalkanes (Scheme 20).<sup>28</sup> Lemieux exploited this protocol in the synthesis of azido sugars, which serve as convenient precursors of the corresponding amino sugars.<sup>29</sup>

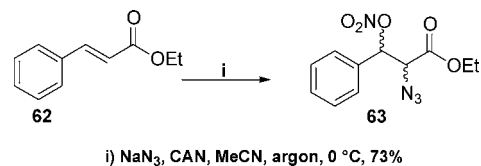
Most of the initial work of Trahanovsky and Lemieux involved the use of acetonitrile as the solvent to afford  $\alpha$ -azido- $\beta$ -nitroalkanes. Interestingly, we have observed a different reactivity in methanol. For example, the reaction of styrene with sodium azide and CAN in methanol under oxygenated conditions provided the azidoketone as the major product (Scheme 21).<sup>30</sup>

In contrast to the earlier reports, we have accomplished an efficient CAN-mediated addition of azide to  $\alpha,\beta$ -unsaturated carbonyl compounds under completely deoxygenated conditions in dry acetonitrile as the solvent. In

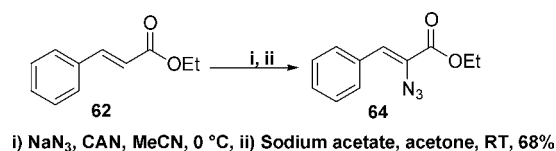
Scheme 21



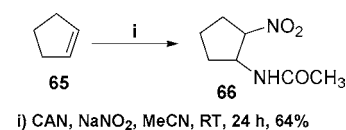
Scheme 22



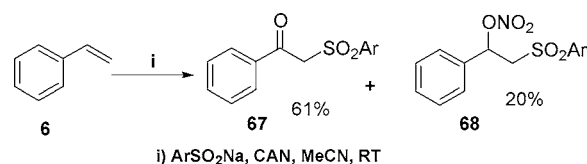
Scheme 23



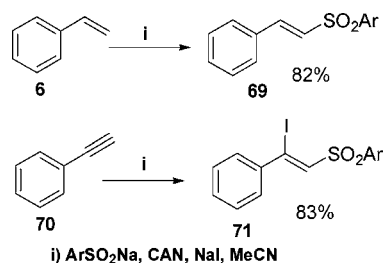
Scheme 24



Scheme 25



Scheme 26



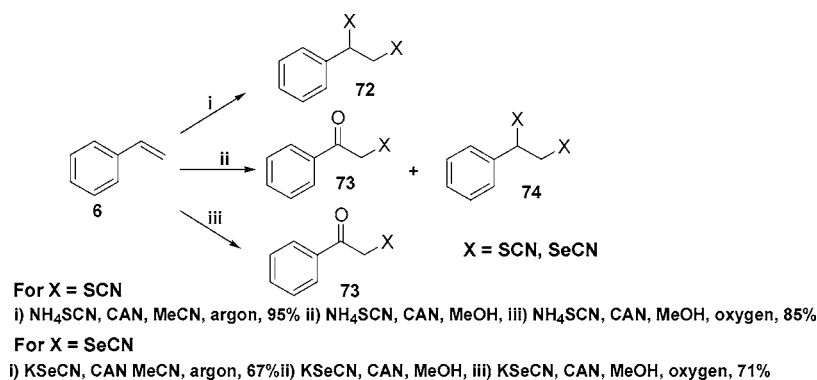
all cases, the products were isolated as a diastereomeric mixture of *syn* and *anti* isomers (Scheme 22).<sup>31</sup>

Further studies have shown that a one-pot synthesis of  $\alpha$ -azidocinnamates and  $\alpha$ -azidoketones in high yields can be accomplished by treatment of the unsaturated compounds with sodium azide and CAN in acetonitrile, followed by elimination of nitric acid using sodium acetate in dry acetone. Under similar conditions, cinnamic acids can be converted to  $\beta$ -azidostyrenes (Scheme 23).<sup>32</sup>

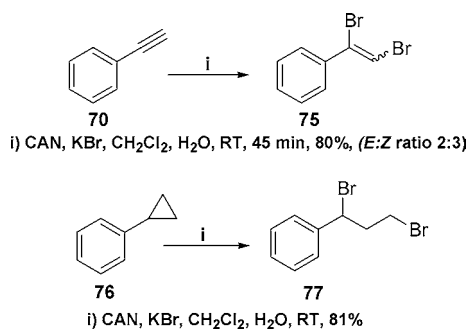
Nitroacetamidation of olefins using CAN in the presence  $NaNO_2$  in acetonitrile has been reported (Scheme 24).<sup>30</sup> Hwu et al. used the same reagent combination to obtain  $\alpha,\beta$ -unsaturated nitro olefins from simple olefins.<sup>33</sup>

Investigations in our laboratory have shown that CAN-mediated oxidative addition of sulfonates to styrenes

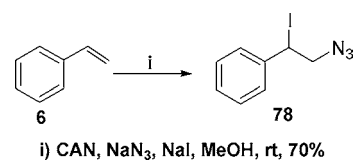
Scheme 27



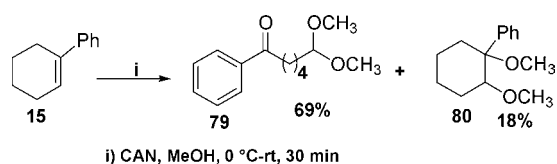
Scheme 28



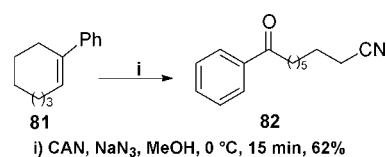
Scheme 29



Scheme 30



Scheme 31



proceeds efficiently to afford both keto and nitro sulfones (Scheme 25).<sup>34</sup> Earlier, Narasaka had reported the CAN-mediated addition of sulfinates to electron-rich olefins such as silyl enol ethers.<sup>35</sup>

Analogous CAN-mediated addition of sulfinates to alkenes in the presence of sodium iodide provided a one-pot synthesis of vinyl sulfones. Under similar conditions, alkynes afforded the corresponding iodovinyl sulfones (Scheme 26).<sup>36</sup>

We have also devised a facile CAN-mediated protocol for the thiocyanation and selenocyanation of olefins, which led to different products, depending on the reaction conditions employed (Scheme 27).<sup>37,38</sup> This method was subsequently extended to the thiocyanation of electron-rich aromatic systems and dienes.<sup>39a,b</sup>

A rapid and efficient conversion of styrenes, cycloalkenes, and  $\alpha,\beta$ -unsaturated carbonyl compounds to dibromides in good yields, using KBr and CAN in a biphasic system of water–dichloromethane, has been reported by us. The major advantage of this transformation is that it offers a convenient alternative to the direct use of bromine.<sup>40</sup> Interestingly, acetylenes and arylcyclopropanes afforded the corresponding vicinal dibromoalkenes and 1,3-dibromides, respectively (Scheme 28).<sup>40, 41</sup>

Recently, we have disclosed an interesting one-pot conversion of alkenes to azidoiodides using CAN, NaI, and  $\text{NaN}_3$ . This method for the bifunctionalization of double bonds is noteworthy for its experimental simplicity and synthetic utility (Scheme 29).<sup>42</sup>

## Miscellaneous Reactions

The serendipitous discovery of some novel and interesting processes turned out to be one of the exciting aspects of

our pursuit of Ce(IV) chemistry. Such reactions also provided additional insight into the mechanistic details of several CAN-mediated transformations. A few examples are cited in this section.

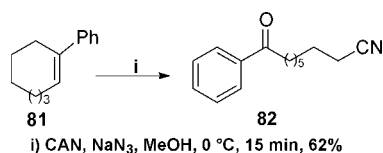
Our attempts at the oxidative addition of malononitrile to phenylcyclohexene did not furnish the expected product. On the other hand, phenylcyclohexene underwent a facile fragmentation to afford the monoacetal of 5-benzoylpentanal (**79**), along with smaller amounts of 1,2-dimethoxyphenylcyclohexane (**80**). The reaction was found to be general with other cycloalkenes, thus constituting a convenient synthesis of monoacetals of 1,*n*-dicarbonyl compounds (Scheme 30).<sup>43</sup>

Under similar conditions, treatment of styrenes with CAN in methanol afforded methoxyacetophenones in moderate yields.<sup>44</sup> Interestingly, the reaction of phenylcycloalkenes in the presence of sodium azide afforded the corresponding ketonitrile in good yields (Scheme 31).<sup>45</sup>

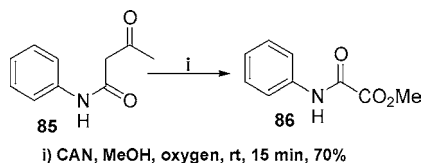
The enormous number of reports on hand attest to the widespread use of CAN as an efficient deprotecting agent. An exceedingly mild and efficient CAN-mediated deprotection of acetals has been developed in our laboratory<sup>46a</sup> and elsewhere<sup>46b</sup> (Scheme 32).

Treatment of acetoacetanilide **85** with CAN in methanol, in anticipation of an intramolecular reaction to derive

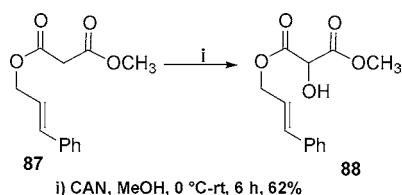
Scheme 32



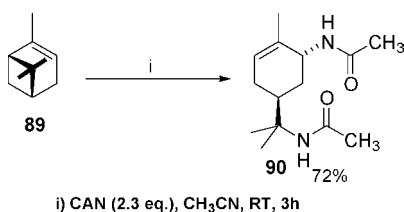
Scheme 33



Scheme 34



Scheme 35



the oxindole, nevertheless afforded the corresponding oxamate **86** in good yield. Substantial enhancement of the overall yield occurred in an atmosphere of oxygen (Scheme 33).<sup>47</sup>

A similar effort toward CAN-mediated intramolecular reaction of alkenyl malonates resulted in the formation of tartonic acid derivatives (Scheme 34).<sup>48</sup>

The reaction of monoterpenes such as (+)- $\alpha$ -pinene with CAN in acetonitrile afforded the bisamide **90** in good yield (Scheme 35).<sup>49</sup>

## Conclusions

In summary, this Account has outlined several useful organic transformations that bring to light the diverse reactivity and versatility of cerium(IV) ammonium nitrate as a one-electron oxidant. In the area of carbon-carbon bond-forming reactions, the reaction of 1,3-dicarbonyl compounds with a variety of alkenes offers a facile route to various dihydrofuran derivatives. The dimerization of various styrenes to afford tetralin derivatives in a single step is indeed remarkable. Especially noteworthy in this area is the one-pot assembly of Sertraline analogues by a Ritter trapping strategy. Although oxidative intramolecular cyclizations mediated by Mn(OAc)<sub>3</sub> have invoked enormous interest, CAN-mediated intramolecular reactions have remained virtually unexplored. Our preliminary efforts in this direction have delivered a stereoselective synthesis of 3,4-trans-disubstituted tetrahydrofuran de-

rivatives by the CAN-mediated intramolecular cyclization of disubstituted cinnamyl ethers. As of now, the studies on CAN-mediated intramolecular cyclizations are still in their early stages, and it seems to be an area worthy of exploration. The use of CAN in carbon-heteroatom bond-forming reactions ultimately has a bearing on the synthesis of building blocks such as heterocycles, amino acids, and deoxysugars. Experimental simplicity and mild reaction conditions are among the most attractive features of CAN-mediated reactions. Although much fascinating chemistry of CAN has been unraveled, further investigations are sure to uncover even more interesting reactions. It is obligatory that future work should be mainly focused on two specific issues: (i) to make CAN catalytic in its reactions and (ii) to devise asymmetric transformations using CAN or related species. It is quite remarkable that, even in stoichiometric use, CAN is finding general acceptance for the laboratory-scale synthesis of a variety of organic compounds, and it is anticipated that CAN will continue to find increasing application in synthesis.

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AR030002Z