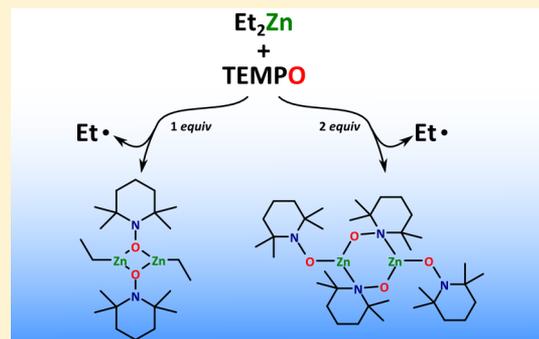


A New Look at the Reactivity of TEMPO toward Diethylzinc

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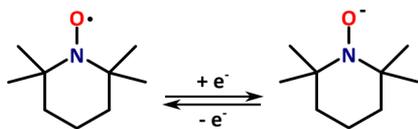
Supporting Information

ABSTRACT: Reactions of diethylzinc with TEMPO were investigated. Dropwise addition of 1 equiv of TEMPO to Et₂Zn at -10 °C leads to the nitroxide complex EtZn(TEMPO) in high yield, whereas upon addition of 2 equiv of TEMPO the corresponding homoleptic nitroxide compound Zn(TEMPO)₂ is formed. Diffusion ordered NMR spectroscopy experiments revealed that both zinc nitroxide compounds exist in monomeric forms in solution, while single-crystal X-ray diffraction confirmed their dimeric structure in the solid state.



The stable nitroxyl radical TEMPO (2,2,6,6-tetramethylpiperidinyl oxide) was first synthesized in 1959¹ and since that time has attracted widespread interest. It has been widely used in polymer synthesis and catalytic organic reactions.² Much attention has also been paid to its application as a ligand or radical trapping agent in reactions with metal complexes.^{3,4} The latter studies have demonstrated that TEMPO is a very versatile molecule and can retain its radical character, acting as a neutral two-electron donor, or can be reduced to an anionic unit (Scheme 1). The behavior of TEMPO as a ligand is a topic of significant interest, as its bonding and reactivity provide mechanistic insights into various chemical transformations.

Scheme 1. Radical and Anionic Forms of TEMPO



The first group 2 complex of the TEMPO anion, $[\{\text{Mg}(\text{HMDS})(\mu\text{-TEMPO})\}_2]$, was reported by Mulvey and co-workers in 2001.^{4d} Afterward Power and co-workers isolated the monomeric moiety $(4\text{-Me}_3\text{Si-Ar}^*)\text{Zn}(\text{TEMPO})$, resulting from a reaction of the zinc hydride $(4\text{-Me}_3\text{Si-Ar}^*)\text{Zn}(\mu\text{-H})_2\text{Zn}(\text{Ar}^*-4\text{-SiMe}_3)$ and TEMPO.^{4f} In the course of the revision of our paper, Stephan demonstrated that $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Zn}$ reacts with TEMPO to yield the homoleptic nitroxide compound $[\text{Zn}(\text{TEMPO})_2]_2$ with simultaneous coupling of two $\text{C}_5\text{Me}_5^\bullet$ radicals.⁵ The highly efficient formation of $[\text{Zn}(\text{TEMPO})_2]_2$ was surprising, in light of earlier work by Carmona and co-workers.⁶ In the latter report the authors used TEMPO to inhibit the formation of dizincocene $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Zn}_2$ in the reaction of Et₂Zn and $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Zn}$

to confirm the radical mechanism of this process. Incidentally, the formation of a small amount of the isolable dimeric complex $[\text{EtZn}(\mu_2\text{-TEMPO})]_2$ was observed. The authors also noted that the reaction of TEMPO with Et₂Zn does not occur unless $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Zn}$ is present in the reaction system.⁶ Recently, TEMPO has also been used as a reagent in various other transformations involving group 2 organometallics. For example, it was demonstrated that oxidative homocoupling of Grignard reagents in the presence of TEMPO and O₂ is possible in high yields.^{4e} The nitroxyl radical was also used to ascertain whether alkali-metal zincates can function as single electron transfer reagents, and the study provided the heterometallic aggregate $(\text{TMEDA})\text{Na}(\mu\text{-TMP})(\mu\text{-TEMPO})\text{-Zn}(t\text{Bu})$.^{4g}

With regard to group 2 organometallic chemistry, it is pertinent to note that TEMPO and related nitroxyl radicals have been particularly used as inhibitors or radical traps in the R₂Zn/O₂ system. In 1968 Davies and Roberts in a seminal work on the mechanism of autoxidation of metal alkyls, including Et₂Zn, probed the involvement of radicals in these reactions using galvinoxyl.⁷ After a series of experiments the authors concluded that “galvinoxyl apparently reacts with Et₂Zn (in the presence of oxygen) to give a product which has little effect on the rate of oxidation of the first ethyl-zinc bond, but strongly inhibits the oxidation of the second”.⁷ Nevertheless, as we noted in our first paper from the series devoted to the oxygenation of zinc alkyls,⁸ a significant source of inconsistency in such studies may result from the fact that radical scavengers can act as donor ligands and simply affect the oxygenation reaction by complex formation with alkylzinc compounds. In recent years, various nitroxyl radicals, including TEMPO, have

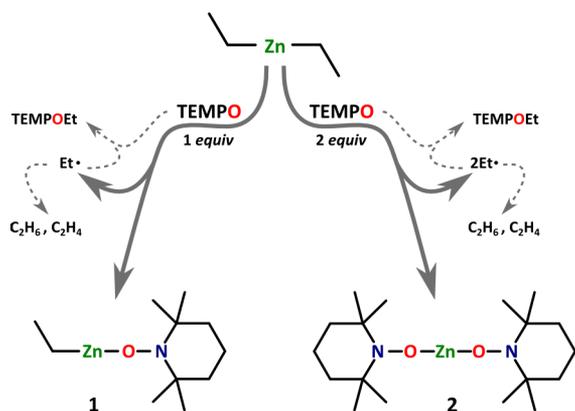
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been continually used to confirm the presence of alkyl radicals in the R_2Zn/O_2 system.⁹ The latter reaction system has been able to initiate various dialkylzinc-mediated radical additions.¹⁰ However, while it is commonly assumed that a R^\bullet radical generated through the reaction of R_2Zn with O_2 acts as the initiator, up to now there has been no clear answer to the question of how the oxygenated products participate in radical reactions. Spin-trapping experiments designed to get a more in-depth understanding of these systems are apparently complicated by the fact that R^\bullet radical is liberated upon homolytic substitution at the zinc atom with TEMPO in the absence of oxygen, as was evidenced by EPR experiments very recently.^{9b}

In the course of our systematic studies on reactions of alkylzinc complexes with dioxygen,^{8,11} we turned our attention to other noninnocent reagents such as 1,2-diketones¹² and TEMPO. Herein we unequivocally dispose of an old problem of the reactivity of TEMPO toward R_2Zn compounds, showing that it reacts smoothly with Et_2Zn to form two types of nitroxide moieties, $EtZn(TEMPO)$ and $Zn(TEMPO)_2$ (Scheme 2). In addition, the developed synthetic protocol

Scheme 2. Reactions of TEMPO with Et_2Zn



provides a very efficient route to zinc nitroxides, which in light of the seminal work by Stephan appear to be very intriguing reagents for the activation of small molecules.⁵

Initially, a toluene solution of Et_2Zn was treated at $-78\text{ }^\circ\text{C}$ with a deep orange toluene solution of TEMPO (1 equiv). The reaction mixture was then slowly heated and remained orange until it reached $-40\text{ }^\circ\text{C}$, when it slowly turned yellow, and full decoloration of the solution occurred at room temperature. In this case compound $[EtZn(TEMPO)]$ (**1**) was obtained in moderate yield by crystallization from a hexane solution (isolated yield 52%). We were wondering if the concentration of TEMPO in the reaction mixture would influence the yield of **1**. Therefore, in order to optimize the synthetic protocol, 1 equiv of TEMPO in toluene was added dropwise to a toluene solution of Et_2Zn at $-10\text{ }^\circ\text{C}$. In this way **1** was obtained in ca. 80% yield on the basis of the ^1H NMR spectrum of the postreaction mixture (isolated yield 74% upon crystallization from hexane). The ^1H and ^{13}C NMR spectra of the reaction mixtures in benzene- d_6 contain the patterns characteristic for **1** and TEMPOEt (for detailed NMR data see the Supporting Information). This observation indicates that TEMPO is consumed by both Et_2Zn and the Et^\bullet radical being formed during the reaction. The synthetic approach in which TEMPO is added dropwise to a Et_2Zn solution disfavors the coupling

between TEMPO and Et^\bullet radicals. To estimate the molecular mass of the species present in solution, a diffusion ordered NMR spectroscopy (DOSY) experiment was performed. The data show that **1** most likely exists as a monomer in solution (for details, see Table S1 in the Supporting Information).

To investigate the effect of excessive amounts of TEMPO on the reaction course, 1 equiv of Et_2Zn was added dropwise to the stirred orange solution of TEMPO (2 equiv) at $25\text{ }^\circ\text{C}$. During the addition of Et_2Zn the solution turned yellow. Crystallization of the crude product from hexane at $-26\text{ }^\circ\text{C}$ afforded colorless crystals of a homoleptic dimeric complex $[Zn(TEMPO)_2]_2$ (**2**) in a high isolated yield (71%) as the only zinc-containing product. The ^1H NMR spectrum of **2** in benzene- d_6 (Figure S4, Supporting Information) is consistent with that presented by Stephan.⁵ The ^1H NMR (toluene- d_8) spectrum of the oily residue obtained by evaporation of volatiles from the mother liquor remaining after crystallization of **2** contains signals characteristic for TEMPOEt (the signals at 1.3–1.8 ppm are broadened due to overlapping with the signals of traces of **2** (Figure S5, Supporting Information)), and no signals characteristic of **1** were observed. A DOSY experiment revealed that **2** exists as a monomer in solution (for details, see Table S1 in the Supporting Information).

To obtain a deeper understanding of the reactions involving the formation of **1**, *in situ* ^1H NMR variable-temperature experiments were conducted (Figure S3, Supporting Information). Toluene- d_8 solutions of TEMPO and Et_2Zn were mixed in an NMR tube at $-78\text{ }^\circ\text{C}$ and transferred to the precooled spectrometer. The spectra acquired at the -78 to $-55\text{ }^\circ\text{C}$ temperature range were stationary in time, and each revealed a set of signals with all resonances strongly broadened due to paramagnetic relaxation induced by unpaired electrons within the reaction system (a number of smaller resonances characteristic for ethane (s, 0.81 ppm), ethylene (s, 5.25 ppm), and TEMPOEt are present in the spectrum from the beginning of the experiment).^{13,14} At the fixed temperature of $-40\text{ }^\circ\text{C}$ the observed signals narrowed to the natural line width of about 1 Hz within around 10 minutes. Upon gradual heating of the sample to $25\text{ }^\circ\text{C}$ (in which temperature the reaction was completed), the signals of Et_2Zn decreased with a simultaneous increase of the signals corresponding to TEMPOEt. At the same time the blurred signals of **1** appeared in the spectra (Figure S3). In the described NMR tube experiment we observed a relatively higher conversion of TEMPO to TEMPOEt (ca. 40%) and lower conversion of Et_2Zn and as a consequence a yield of **1** lower than that in the corresponding Schlenk vessel experiment (*vide supra*).

Single-crystal X-ray diffraction analysis demonstrated that **1** and **2** have dimeric structures in the solid state. The crystallographic data for **1**₂ differs from that obtained by Carmona and co-workers,⁶ in both the space group determination and the smaller structural distortions observed (see the Supporting Information for more detailed data). In the molecular structure of **1** two three-coordinated zinc atoms are bridged by a μ_2 -TEMPO anion, thus forming a planar Zn_2O_2 ring ($Zn1-O1 = 1.921(4)\text{ \AA}$, $Zn1-O1' = 1.986(4)\text{ \AA}$; Figure 1). The crystallographic data of **2**₂ (for details, see the Supporting Information) is consistent with that reported by Stephan.⁵ Compound **2** crystallizes as the dimer **2**₂ with two chemically equivalent trigonal zinc centers bridged by monoanionic μ_2 - η^1 : η^1 -TEMPO ligands and two remaining TEMPO anions acting as external ligands with η^1 hapticity.

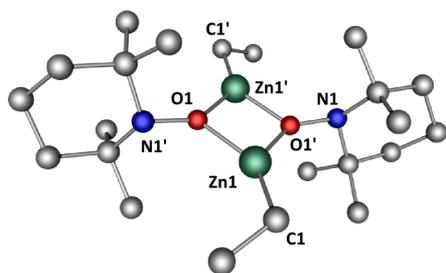
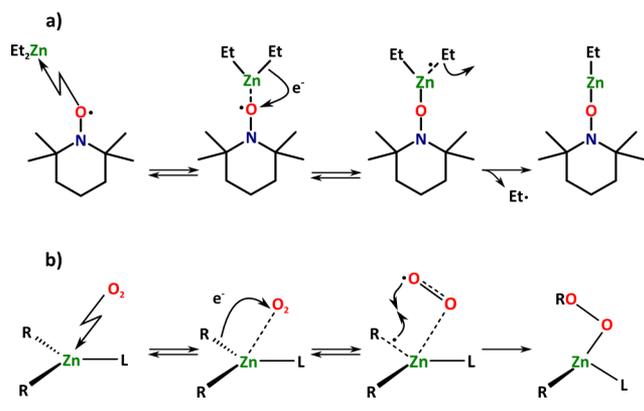


Figure 1. Molecular structure of I_2 . Hydrogen atoms are omitted for clarity.

The key features of the studied reaction between Et_2Zn and TEMPO are the evolution of Et^\bullet radical and the conversion of a TEMPO radical to a TEMPO anion with concomitant formation of zinc nitroxide species (Scheme 2). On the basis of the preliminary results, it is reasonable to propose a plausible pathway for the reaction of Et_2Zn and TEMPO (Scheme 3a).

Scheme 3. Proposed Mechanisms for the Reactions of (a) Et_2Zn with TEMPO and (b) R_2Zn Compounds with O_2 ^{11b}



The primary step of the reaction is an attack of TEMPO radical on the electrophilic zinc. The coordination of TEMPO to the metal center is followed by electron transfer from the Zn–C bond to TEMPO to afford a solvent-caged radical pair. Diffusion of the Et^\bullet radical (which was substantiated by the observed formation of ethane, ethylene, and TEMPOEt; vide supra) away from the cage leads to the formation of the ethylzinc nitroxide moiety. This mechanism nicely resembles the newly proposed mechanism for reactions of alkylzinc complexes with O_2 (Scheme 3b).^{11b} In the latter reaction system the initial step involves attack of an O_2 molecule on a three-coordinate zinc alkyl species, which results in an electron transfer from the Zn–C bond to dioxygen, yielding a radical pair. This transition state can either give an alkylperoxide complex or become a source of alkyl radicals.¹¹

In conclusion, we have convincingly demonstrated that TEMPO is highly reactive toward Et_2Zn , affording both $EtZn(TEMPO)$ and $Zn(TEMPO)_2$ nitroxides. The provided simple and selective method for accessing this important class of compounds opens new opportunities to probe their chemistry. Further studies on the interaction of metal alkyl complexes with TEMPO and the related nitroxyl radicals and the reactivity of metal nitroxides are in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Text giving synthetic procedures, figures, a table, a CIF file, spectroscopic and crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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