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Development of zinc alkyl/air systems as radical initiators for organic reactions†

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This paper reports a series of comparative experiments on the activity of carbon- and oxygen-centred radical species in a model reaction of the radical addition of THF to imines mediated by a series of zinc alkyl/air reaction systems. The study strongly contradicts the notion that generally $R^{\bullet}$ radicals are the initiating species in organic reactions mediated by R_nM/air systems, and simultaneously demonstrates that oxygen-centred radical species are the key intermediates responsible for the initiation process. In addition, a new efficient RZn(L)/air initiating system for radical organic reactions exampled by a model reaction of radical addition of THF to imines is developed. Moreover, the isolation and structural characterization of the first zinc alkylperoxide supported by a carboxylate ligand, $[Zn_4(\mu_3\text{-OO}t\text{Bu})_3(\mu_4\text{-O})(O_2CEt)_3]_2$, as well as the novel octanuclear zinc oxo(alkoxide) aggregate with entrapped O–THF species, $[Zn_4(\mu_4\text{-O})(\mu_3\text{-2-O–THF})(O_2CEt)_5]_2$, provide clear mechanistic signatures for the mode of function of the $RZn(O_2CR')$/air system.

Introduction

In the last two decades remarkable advances have been made in the area of organic radical chemistry, which have been largely driven by the development of new radical precursors.[1] In this regard homoleptic boron[2a,b] and zinc alkyls[2c,d] in combination with dry air have attracted much attention as they provide a source of radical initiators for various organic reactions.[3] For these R_nM/air systems it is commonly assumed that $R^{\bullet}$ radicals are formed in the initial step (*cf.* eqn (1)),[4] and are thus considered as the initiating species in radical organic reactions.[2]

$$R_2Zn + O_2 \rightarrow RZnOO^{\bullet} + R^{\bullet} \qquad (1)$$

While the nature of the radical species mediating the organic reactions mentioned above[3] has not been clearly elucidated, the postulated formation of $R^{\bullet}$ radicals as in eqn (1) is not in line with some of the recent fundamental studies which have shown that reactions between R_2Zn and O_2 can be conducted in a highly controllable manner without any evidence for the liberation of free alkyl radicals.[4c,5,6] For example, the controlled oxygenation of lower alkyl R_2Zn compounds (R = Me, Et, *i*Pr) leads selectively to alkylzinc alkoxides[5b,6a] save special cases such as $t\text{Bu}_2\text{Zn}$ which gives *t*BuZnOO*t*Bu species.[5c] Only oxygenation of R_2Zn compounds taking place at ambient temperature leads to a complex mixture of products resulting from secondary transformations, likely involving radical species.[5c] Strikingly, when a Me_2Zn/*t*BuDAB adduct (*t*BuDAB = di-*tert*-butyl diazabutadiene) is exposed to O_2 both zinc methylperoxide and the products of its decomposition are observed, *i.e.* a zinc oxo-alkylperoxide, an oxo-alkoxide and a product of $MeO^{\bullet}$ radical entrapment.[5d] This and further discoveries[5d–h,7] convincingly prove the pathway of decomposition of zinc alkylperoxides affording $ZnO^{\bullet}$ and $RO^{\bullet}$ radicals as primary radical species; strikingly this pathway had been overlooked for a long time in the course of investigations on oxygenation of alkylzincs. While all of the mentioned reactions proceed without liberation of an $R^{\bullet}$ radical in the initial step, some systems generating alkyl radicals upon oxygenation of RZn(L) complexes have also been documented recently.[5e,7]

We also note that the character of the radical species formed in the reactions of R_2Zn with O_2 has been studied by EPR using nitrones[8] and stable nitroxyl radicals such as DEPMPO,[4b] as radical traps. These stable radicals have been assumed to be inert towards R_2Zn (ref. 9) or to have no influence on the oxygenation process.[4a] However, very recently it has been convincingly shown that TEMPO reacts with Et_2Zn smoothly affording both EtZn(TEMPO) and $Zn(TEMPO)_2$ nitroxides with concomitant evolution of $Et^{\bullet}$ radicals.[10,11] Thus, the latter observations clearly indicate that for reactions involving

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† Electronic supplementary information (ESI) available: Detailed experimental procedures, a table of conversions and isolated yields of **2a** in the model reaction, characterization data for new products, crystallographic data. CCDC 746458 and 753795. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5sc00600g

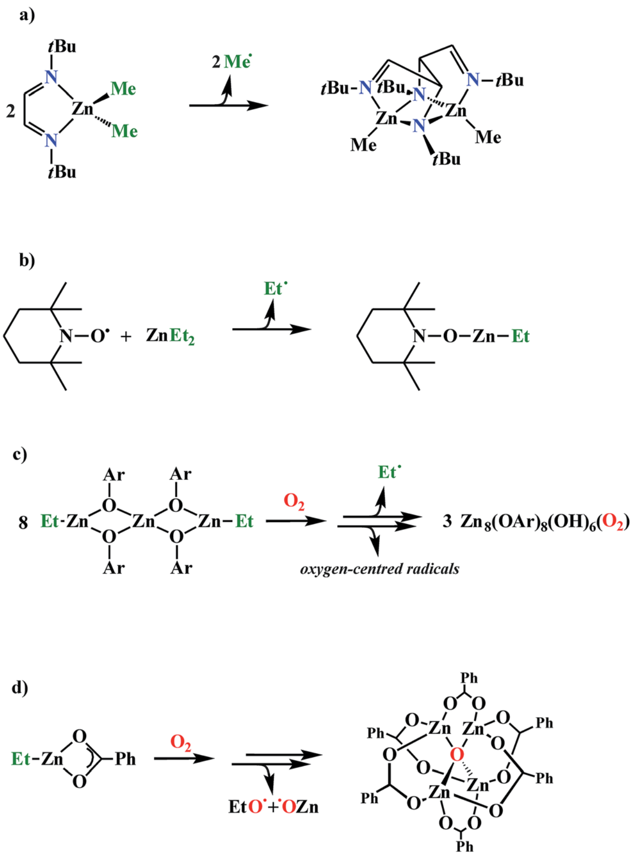
alkylzinc/O_2 systems the use of nitroxyl radicals as spin traps can lead to incorrect assignments in the determination of the character of the radicals present in the reaction mixture.

Building on our continuous interest and expertise in radicals' chemistry and dioxygen activation,[5,7,10,12] we herein report comparative experiments on the activity of carbon- and oxygen-centred radical species (derived from a series of zinc alkyl/air reaction systems with a clear mechanistic picture, see Scheme 1), in a model reaction of radical addition of THF to imines as a selected model reaction. The study of these model systems not only provides better understanding of how the oxygenated products participate in radical organic reactions but also assists in the development of new types of radical initiators.

Results

Control experiments on the addition of THF to imines mediated by systems generating solely $R^{\bullet}$ radicals

In order to verify the hypothesis that $R^{\bullet}$ radicals are the reactive species mediating the addition of ethers to imines,[2d] we have attempted to create an environment in which only alkyl radicals are liberated. For this purpose, two well-characterized reaction systems were selected as the control experiments: (i) the reaction of Me_2Zn with *t*BuDAB previously studied by van Koten where the initially formed adduct Me_2Zn(*t*BuDAB) decomposes slowly at ambient temperature to a C–C coupling product [MeZn(*t*BuDABC)]$_2$ with concomitant liberation of $Me^{\bullet}$ radicals (Scheme 1a),[13] and (ii) the equimolar reaction of Et_2Zn and TEMPO generating a nitroxide EtZn(TEMPO) complex along with an $Et^{\bullet}$ radical (Scheme 1b).[10,14] These two systems were employed as sources of $R^{\bullet}$ radicals in the model reaction of THF addition to *N*-(4-methoxybenzylidene)aniline (**1a**) (Scheme 2, path A; see ESI for details†). Strikingly, no reactions between THF and **1a** were observed after 48 h at room temperature in either case. These findings strongly contradict the notion that $R^{\bullet}$ radicals are the key intermediates responsible for the initiation process in organic reactions mediated by R_nM/air systems. The examples also highlight that there is much to be clarified with respect to the character of the radical initiators in the reaction systems considered. Therefore in the subsequent experiments, we turned our attention to the reaction systems capable of producing non-carbon centred radicals.

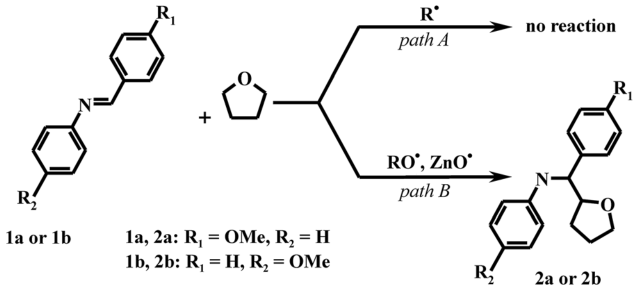


Scheme 1 Selected organozinc systems generating either alkyl radicals or oxygen-centred radicals.

Control experiments on the addition of THF to imines mediated by RZn(L)/air systems

From amongst several zinc alkyl/O_2 systems affording oxygen-centred radicals as primary radical species and described recently by our group,[5d–g,7] we have selected two reaction systems (Scheme 1c and d). The first one involves a trinuclear ethyl aryloxide $(EtZn)_2Zn(OAr)_4$ and O_2, where a range of carbon and oxygen centred radical species, including $Et^{\bullet}$, $EtO^{\bullet}$ and $HO^{\bullet}$, are generated in the course of formation of an aryloxide(hydroxide) cluster $Zn_8(OAr)_8(OH)_6(O_2)$ (ArOH = *o*-hydroxybiphenyl) with an encapsulated peroxide moiety (Scheme 1c).[7] However, this system proved to be inefficient, when used as a mediator of the model reaction, probably due to interception of the forming radicals in the inner sphere of the zinc complex.[15]

Then, building upon our experience with ZnO–OR bond homolysis,[5d–g] we turned our attention to the alkylzinc carboxylate/O_2 system. Previously, we showed that the ZnO–OR bond homolysis proceeds effectively for the ethylzinc benzoate/O_2 system generating $ZnO^{\bullet}$ and $EtO^{\bullet}$ radicals in the course of formation of an oxo complex $Zn_4(\mu_4\text{-}O)(O_2CPh)_6$ (Scheme 1d).[5g] Thus, we have anticipated that the readily prepared alkylzinc carboxylates subjected to O_2 can be interesting experimental probes for determining the character of initiating species in the model reaction. Therefore, a series of alkylzinc carboxylates, $RZn(O_2CR')$ (where R = Me, Et or *t*Bu and R′ = Ph and Et), was



Scheme 2 The model reaction of the radical addition of THF to imines.

prepared according to procedures described in the literature.[5e] It was then investigated how the character of the carboxylate ligand, and the alkyl group bonded to the metal, influence the rate of conversion of **1a** with THF (Fig. 1; for experimental details also see ESI†). To the best of our knowledge, this is the first example of a heteroleptic $R_xM(L)_y$-type complex mediating an organic radical reaction.

The investigated alkylzinc carboxylate complexes were mixed with **1a** or **1b** (**1b** = *N*-benzylidene-4-methoxyaniline, the imine commonly used with the Me_2Zn/air initiating system[3a]) in a 1 : 4 molar ratio in THF (Scheme 2, path B). The reactions mediated by $EtZn(O_2CPh)$ under O_2 atmosphere were found to stop after *ca.* 15 minutes at approximately 70% conversions. When, on the other hand, pure dioxygen was replaced by dry air, the model reactions slowed down and conversions of 95% and 93% for **1a** and **1b**, respectively, were observed after 2 h (90% and 87% isolated yield of **2a** and **2b**, respectively). It seems reasonable that the observed dependence of the conversion of **1a** and **1b** on the gas phase composition (O_2 *vs.* air), *i.e.* on oxygen partial pressure, is related to the transient concentration of free radicals (in the presence of air, a lower radical concentration disfavours their nonproductive recombination). Following this reasoning, dry air was used in the subsequent experiments. When **1a** was used as the substrate in the model reaction, the $MeZn(O_2CPh)$/air and the $MeZn(O_2CEt)$/air systems both allowed us to obtain **2a** with 98% conversion after 2 h (92% and 95% isolated yield, respectively; Fig. 1, curves I and II). The observed reaction rates were slightly higher than those for the analogous ethylzinc complexes (Fig. 1, curves III and IV). The comparison of the data for the $EtZn(O_2CPh)$/air and $EtZn(O_2CEt)$/air initiating systems indicates that the identity of the carboxylic group has essentially no influence on the conversion and kinetic profile (Fig. 1, curves III and IV); the addition of THF to **1a** proceeded relatively quickly and reached full conversion after 2 h.

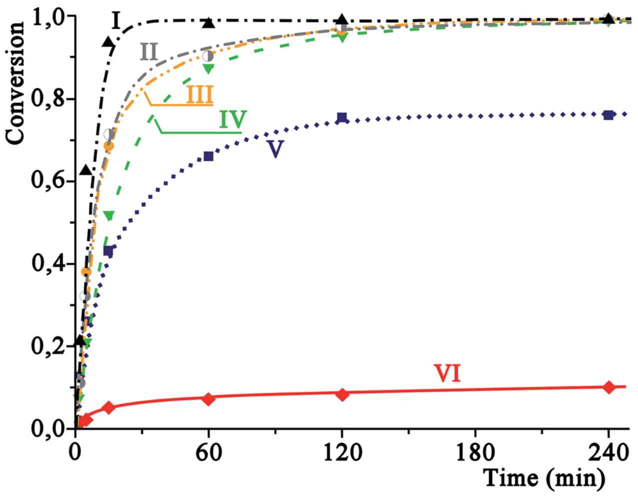


Fig. 1 Conversion *versus* time plot for the reactions of **1a** with THF conducted at 20 °C and mediated by: $MeZn(O_2CPh)$/air (I), $MeZn(O_2CEt)$/air (II), $EtZn(O_2CPh)$/air (III), $EtZn(O_2CEt)$/air (IV), Me_2Zn/air (V), and $tBuZn(O_2CEt)$/air (VI).

Strikingly, the *tert*-butyl derivative, $tBuZn(O_2CEt)$, appeared to be entirely ineffective for initiating THF radical addition (Fig. 1, curve VI). Comparison of the initiation effectiveness of the developed alkylzinc carboxylate/air system with the classic one, *i.e.* the Me_2Zn/air system, showed superiority of the carboxylate-based system. In the reaction mediated by Me_2Zn/air (4 equiv. of Me_2Zn) at 20 °C, conversion of **1a** reached only 76% after 2 h (isolated yield of **2a** was 72%) and no further reaction progress was observed (Fig. 1, curve V), while **1b** was obtained with 80% yield only after 18 hours, according to Tomioka *et al.*[3a] This result shows that the Me_2Zn/air system becomes deactivated in the course of the reaction or the radical species are produced too rapidly and undergo recombination reactions, while no such observations can be made in the case of our $RZn(O_2CR')$/air systems (R = Me, Et; R′ = Ph, Et).

The described findings convincingly demonstrate that the readily prepared alkylzinc carboxylates in combination with molecular oxygen, afford oxygen-centred radical species and can act as very efficient initiators of the radical addition of THF to imines.

Detailed investigations on the oxygenation of alkylzinc carboxylates

Isolation of zinc alkylperoxide supported by a carboxylate ligand. We anticipated that the observed ineffectiveness of the $tBuZn(O_2CEt)$/air system to promote the radical addition reaction was due to the low efficiency of the generation of radical initiating species through the ZnO–OR bond homolysis. To clarify this issue we set out to investigate the controlled oxygenation of an *in situ*-generated *tert*-butylzinc propionate with dry air at −78 °C in THF, which after a standard work-up afforded colourless crystals of a novel zinc oxo(alkylperoxide) aggregate $[Zn_4(\mu_3\text{-OO}t\text{Bu})_3(\mu_4\text{-O})(O_2CEt)_3]_2$ (**3**) (Fig. 2) stable at room temperature. The structure of **3** possesses idealized C_{3i} symmetry and exists as an octanuclear cluster with six bridging OO*t*Bu moieties, six bridging propionate ligands and two encapsulated μ_4-oxo anions.‡ The central core of **3** is composed of six five-coordinate zinc atoms bridged by six alkylperoxide

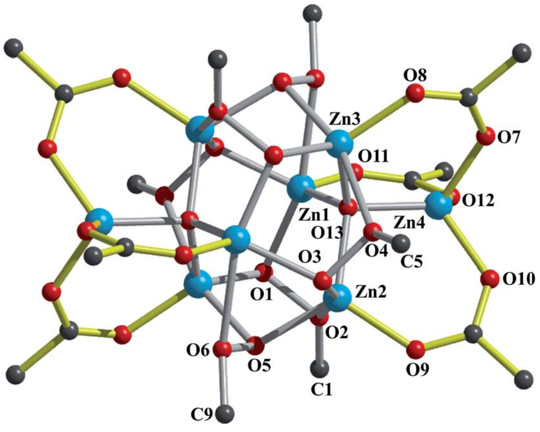
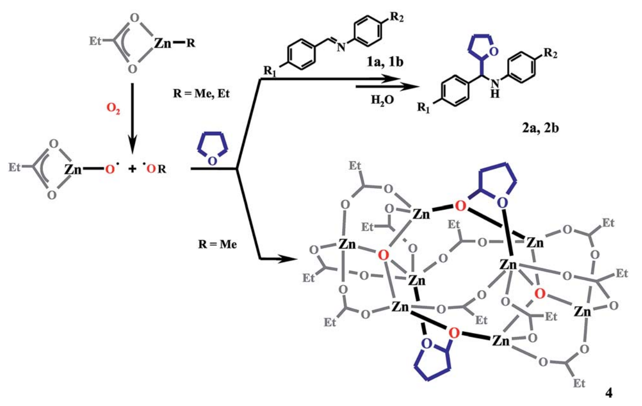


Fig. 2 Molecular structure of **3**; hydrogen atoms, Me groups of the *t*Bu groups and of the carboxylate ligand were omitted for clarity.

moieties which form a hexagonal cage $(\text{ZnOO}t\text{Bu})_6$ with faces made of five-membered rings and capped by two O^{2-} ions on both brims of the cage. Analysis of the spatial conformation of the peroxide moiety in **3** indicates a unique μ_3-η^2:η^1-OO*t*Bu coordination mode not observed for zinc alkylperoxide complexes reported previously.[5a–d,5f,5i] The isolation of the zinc *tert*-butylperoxide **3** supports the assumption that the apparent stability of the alkylperoxide species inhibits the initiation step of the tested radical organic reaction because the concentration of the oxygen-centred radical species, normally resulting from the homolysis of the ZnO–O*t*Bu bond, is very low in this case.

THF radical entrapment mediated by the $\text{MeZn(O}_2\text{CEt)}$/air system. To confirm our assumptions about the nature of the active species mediating the model radical reaction, we performed a more detailed investigation on the interaction of O_2 with methylzinc propionate (Scheme 3). Interestingly, when a solution of $\text{MeZn(O}_2\text{CEt)}$ in THF at 0 °C was treated with an excess of dry air, colourless crystals of the novel octanuclear zinc oxo(alkoxide) aggregate $[\text{Zn}_4(\mu_4\text{-O})(\mu_3\text{-2-O–THF})(\text{O}_2\text{CEt})_5]_2$ (**4**) deposited after four days. The structure of **4** possesses C_i symmetry with six bridging propionate ligands, two bridging μ_3-2-O–THF moieties and two encapsulated μ_4-oxo ligands, and features Zn–O bond distances typical for both zinc oxo(carboxylate)[5b] and zinc alkoxide[5e] complexes (Fig. 3, Table 3S†). The presence of both the oxidized THF moieties and O^{2-} ions is the most striking feature of **4**. We note that THF oxidation to 2-hydroxytetrahydrofuran has been observed previously for transition metal/O_2 systems,[16] but a M–O–THF intermediate has never been structurally characterized (Fig. 3).

The composition of **4** provides strong evidence that homolysis of the incipient alkylperoxide O–O bond is likely responsible for the formation of oxo ions[5e–h] and is the source of the O–THF species. The peroxide undergoing homolytic cleavage of the O–O bond produces zinc oxyl $\text{ZnO}^\bullet$ and alkoxy $\text{RO}^\bullet$ radicals, *i.e.* the intermediates responsible for the initiation of further transformations. These oxygen centred radicals are able to abstract an α-hydrogen atom from THF and the resulting tetrahydrofuran-2-yl radical can react further with **1a** or **1b** to form **2a** or **2b**, respectively. Otherwise the forming radicals can recombine with the $\text{ZnO}^\bullet$ radical leading to the alkoxide **4**, which is outlined in Scheme 3.



Scheme 3 Reaction pathways in the radical addition of THF to the imines **1a** or **1b** mediated by the $\text{RZn(O}_2\text{CEt)}$/air system (R = Me, Et).

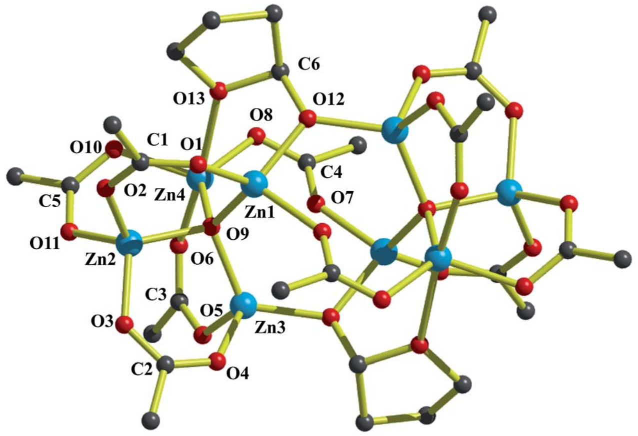


Fig. 3 Molecular structure of **4**; hydrogen atoms and Me groups of the carboxylate ligand were omitted for clarity.

The observed high yield of the radical addition of THF to imines indicates that this reaction is favoured over the recombination of $\text{ZnO}^\bullet$ and tetrahydrofuran-2-yl radicals. Also, comparison of the inefficiency of the $\text{R}^\bullet$ yielding radical initiating systems (Scheme 1a–c) with our well defined, potent alkylzinc carboxylate-based system producing $\text{RO}^\bullet$ and $\text{ZnO}^\bullet$ radical species leads to another conclusion – namely that alkyl radicals are rather unlikely to be involved in mediating the type of radical organic reactions we studied.

Conclusions

In conclusion, a new and efficient RZn(L)/air-type initiating system for the radical addition of THF to imines was developed that provides a new strategy to expand the scope of organozinc initiators for organic synthesis. The mode of its function was evidenced by the isolation and structural characterization of the novel zinc oxo aggregate with the entrapped oxidized THF moieties from the $\text{RZn(O}_2\text{CR}')$/air systems. Moreover the latter result along with additional control experiments demonstrate that the oxygen-centred radicals are the key initiating species in radical organic reactions mediated by R_nM/air systems and strongly contradict the notion that $\text{R}^\bullet$ radicals are the initiating species. Undoubtedly, further in-depth understanding of the various modes of reactivity of the metal alkyl complexes with O_2 will be the key to developing effective systems promoting organic radical reactions.

Experimental

Ethylzinc benzoate,[5e] $[(\text{EtZn})_2\text{Zn}(\text{OAr})_4]$,[7] *N*-(4-methoxy-benzylidene)aniline (**1a**), *N*-benzylidene-4-methoxyaniline (**1b**)[17] and $t\text{Bu}_2\text{Zn}$,[18] were prepared according to the literature procedures under a nitrogen atmosphere using standard Schlenk techniques. All other reagents were of commercial grade obtained from Sigma-Aldrich Co. The solvents and propionic acid used for preparation of the initiators were carefully dried and distilled under a nitrogen atmosphere prior to use. TEMPO was sublimated and stored under a nitrogen atmosphere. Oxygenation reactions were carried out using atmospheric air dried by passing it through a tube filled with anhydrous $CaCl_2$/KOH. NMR spectra were acquired on a Varian Mercury 400 Spectrometer, and IR spectra were recorded on a Perkin-Elmer System 2000 FT-IR spectrophotometer. GC-MS analysis was performed on an Agilent 6890N chromatograph coupled with an Agilent 5973N MS detector.

General procedure for synthesis of alkylzinc carboxylates

R_2Zn (2 mmol) was added dropwise to the solution of the appropriate carboxylic acid (2 mmol) at −78 °C. The reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The resulting alkylzinc carboxylates were used in the model radical reaction without further purification.

General procedure for addition of the THF to imines mediated by the RZn(L)/air and R_2Zn/air systems

An excess of dry air was introduced to a stirred THF (14 mL) solution of an appropriate initiator (4.00 mmol) and **1a** (0.220 g, 1.00 mmol) at 20 °C. The samples (2 mL) for measuring the conversion rates were subsequently taken *via* septum after 1.5 min, 5 min, 15 min, 1 h, 2 h, 4 h, 24 h, followed by hydrolysis with a saturated solution of $NaHCO_3$. 5 mL of ethyl acetate was added and the white precipitate was filtered off and the water phase was extracted with ethyl acetate (2 × 10 mL). Combined organic phases were dried over anhydrous $MgSO_4$ and the solvents were removed under vacuum. The product obtained after 24 h was purified by column chromatography (AcOEt/*n*-hexane 9/1). **2a** was obtained as a mixture of diastereomers in various yields, depending on the time of sample collection and the reaction conditions (relevant conversion ratios in these samples calculated according to ^1H NMR analyses are summarized in Table 1S† together with the final % yields). Product **2a** is a dark-orange oily mixture of diastereomers. δ_H(400 MHz, $CDCl_3$) ppm: 1.70–1.86 (m, 4H, $-CH_2-$), 3.72–3.83 (m, 1.1H, $-OCH_2-$, major diastereomer), 3.78 (s, 3H, $-OCH_3$), 3.88–3.96 (m, 0.9H, $-OCH_2-$, minor diastereomer), 4.01 (q, 0.55H, –OC*H*–, major diastereomer), 4.16 (d, 0.55H, –NC*H*–, major diastereomer), 4.23 (q, 0.45H, –OC*H*–, minor diastereomer), 4.37 (d, 0.45H, –NC*H*–, minor diastereomer), 4.44–4.96 (br s, 1H, –N*H*), 6.52 (m, 2H, $CH_{(Ar)}$), 6.62 (m, 1H, $CH_{(Ar)}$), 6.85 (m, 2H, $CH_{(Ar)}$), 7.06 (m, 2H, $CH_{(Ar)}$), 7.27–7.36 (m, 2H, $CH_{(Ar)}$). δ_C (100 MHz, $CDCl_3$) ppm: 25.7 ($-CHCH_2CH_2-_{(THF)}$), 29.7 ($-CH_2CH_2CH_2-_{(THF)}$), 55.1 ($-OCH_3$), 60.1 ($-OCH_2-_{(THF)}$), 68.7 ($-NCH-$), 83.0 ($-OCH-_{(THF)}$), 113.6 ($C_{(Ar)}$), 113.8 ($C_{(Ar)}$), 117.3 ($C_{(Ar)}$), 128.1 ($C_{(Ar)}$), 128.7 ($C_{(Ar)}$), 131.9 ($CCH_{(Ar)}$), 147.8 ($CN_{(Ar)}$), 158.7 ($CO_{(Ar)}$). The isolation method and analytical data for the product **2b** was identical to the literature report.[3a]

$[Zn_4(\mu_3\text{-OO}t\text{Bu})_3(\mu_4\text{-O})(O_2CEt)_3]_2$ (3). Dry air was introduced to a stirred solution of *t*BuZn(O_2CEt) (0.196 g, 1.00 mmol), in 5 mL of a solvent mixture of THF and hexane (1 : 1) at −78 °C, for 5 min. The reaction mixture was then deoxygenated and stored at −20 °C. After 6 h, colourless crystals of **3** were deposited from this solution (57 mg, 30%). δ_H(400 MHz, C_6D_6) ppm: 1.03 (t, 3H, CH_3CH_2-), 1.43 (s, 9H, $(CH_3)_3COO-Zn$), 2.27 (q, 2H, CH_3CH_2-). Elemental analysis (%) found: C 32.95, H 5.46, calcd for $C_{21}H_{42}O_{13}Zn_4$: C 33.01, H 5.54.

$[Zn_4(\mu_4\text{-O})(\mu_3\text{-2-OTHF})(O_2CEt)_5]_2$ (4). Dry air was introduced to a stirred solution of $[MeZn(O_2CEt)]_n$ (0.153 g, 1.00 mmol), in 5 mL of THF at 0 °C, for 30 min. The reaction mixture was then deoxygenated and stored at −20 °C. After 4 days colourless crystals of **4** were deposited from this solution (44 mg, 24%). δ_H(C_6D_6, 400 MHz) ppm: 0.90 (br t, 3H, CH_3CH_2-), 1.00 (br t, 6H, CH_3CH_2-), 1.08 (br t, 3H, CH_3CH_2-), 1.22 (br t, 3H, CH_3CH_2-), 1.37 (m, 1H, $-CH_{2(THF)}-$), 1.84 (m, 1H, $-CH_{2(THF)}-$), 2.06 (q, 2H, CH_3CH_2-), 2.15 (q, 4H, CH_3CH_2-), 2.23 (q, 2H, CH_3CH_2-), 2.33 (q, 2H, CH_3CH_2-), 2.44 (m, 1H, $-CH_{(THF)}$), 2.55 (m, 1H, $-CH_{(THF)}$), 3.56 (m, 1H, $-OCH_{(THF)}$), 4.00 (m, 1H, $-OCH_{(THF)}$), 5.91 (dd, 1H, $-OCHO_{(THF)}$). Elemental analysis (%) found: C 31.35, H 4.47 calcd for $C_{19}H_{32}O_{13}Zn_4$: C 31.26, H 4.43.

Crystal data for **3**: $C_{42}H_{84}O_{26}Zn_8$: M = 1528.05, crystal dimensions 0.42 × 0.28 × 0.22 mm^3, monoclinic, space group $C2/c$ (no. 15), $a = 22.502(2)$ Å, $b = 12.8820(12)$ Å, $c = 21.7730(14)$ Å, $\beta = 98.995(5)°$, $U = 6233.7(9)$ Å^3, $Z = 4$, $F(000) = 3136$, $D_c = 1.628$ g cm^{-3}, $T = 100(2)$ K, μ(Mo-Kα) = 3.097 mm^{-1}, $\theta_{max} = 21.97°$, $R_1 = 0.0956$, w$R_2 = 0.1910$ for 2200 reflections with $I_o > 2\sigma(I_o)$. The residual electron density = +1.01/−0.93 eÅ^{-3}. Crystal data for **4**, $C_{38}H_{64}O_{26}Zn_8$: M = 1460.01, crystal dimensions 0.52 × 0.45 × 0.38 mm^3, triclinic, space group $P\bar{1}$ (no. 2), $a = 9.5731(4)$ Å, $b = 10.8542(6)$ Å, $c = 13.0771(7)$ Å, $\alpha = 77.371(2)°$, $\beta = 83.044(3)°$, $\gamma = 80.914(3)°$, $U = 1304.01(12)$ Å^3, $Z = 1$, $F(000) = 740$, $D_c = 1.859$ g cm^{-3}, $T = 100(2)$ K, μ(Mo-Kα) = 3.696 mm^{-1}, $\theta_{max} = 24.71°$, $R_1 = 0.0535$, w$R_2 = 0.0831$ $R_1 = 0.0391$, w$R_2 = 0.0774$ for 3685 reflections with $I_o > 2\sigma(I_o)$. The residual electron density = +0.51/−0.56 eÅ^{-3}. The structures were solved by direct methods using the SHELXS97 (ref. 19) program and refined by full matrix least-squares on F^2 using the program SHELXL97.[20] H-atoms were included in idealized positions and refined with a fixed isotropic displacement parameter equal to 1.2 (**3**) or isotropically (**4**). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 746458 (**3**) and CCDC 753795 (**4**).

Acknowledgements

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Notes and references

‡ Due to a poor quality of crystals of **3** for single-crystal X-ray diffraction, it was not possible to get a fully satisfactory refinement of the molecular structure (the final R = 9.56%), this precludes also a detailed discussion of the metrical parameters.

1 *Radicals in Organic Synthesis*, ed. P. Renaud and M. P. Sibi, Wiley-VCH Verlag GmbH, Weinheim, 2001, vol. 1 and 2; *Radicals in Synthesis I and II*, ed. A. Gansäuer, *Top. Curr.*

Chem., Springer-Verlag, Berlin, Heidelberg, 2006, vol. 263 and 264.

2 For reviews, see: (*a*) C. Ollivier and P. Renaud, *Chem. Rev.*, 2001, **101**, 3415–3434; (*b*) V. Darmency and P. Renaud, *Radicals in Synthesis I*, Springer-Verlag, Berlin/Heidelberg, 2006, vol. 263; (*c*) S. Bazin, L. Feray and M. P. Bertrand, *Chimia*, 2006, **60**, 260–265; (*d*) T. Akindele, K. Yamada and K. Tomioka, *Acc. Chem. Res.*, 2009, **42**, 345–355.

3 For selected examples, see: (*a*) Radical addition of ethers to imines: K. Yamada, H. Fujihara, Y. Yamamoto, Y. Miwa, T. Taga and K. Tomioka, *Org. Lett.*, 2002, **4**, 3509–3511; (*b*) K. Yamada, Y. Yamamoto, M. Maekawa and K. Tomioka, *J. Org. Chem.*, 2004, **69**, 3581–3584; (*c*) Radical addition of ethers to aldehydes: K.-I. Yamada, Y. Yamamoto and K. Tomioka, *Org. Lett.*, 2003, **5**, 1797–1799; (*d*) Radical addition of cycloalkanes to imines: K. Yamada, Y. Yamamoto, M. Maekawa, J. Chen and K. Tomioka, *Tetrahedron Lett.*, 2004, **45**, 6595–6597; (*e*) Radical addition of ethers to arylamines, alkoxyamines, dialkylhydrazines: Y. Yamamoto, M. Maekawa, T. Akindele, K. Yamada and K. Tomioka, *Tetrahedron*, 2005, **61**, 379–384; (*f*) Radical addition of primary alkyls to imines: K. Yamada, Y. Yamamoto, M. Maekawa, T. Akindele, H. Umeki and K. Tomioka, *Org. Lett.*, 2006, **8**, 87–89; (*g*) Radical addition of iodomethylesters to imines: K. Yamada, M. Nakano, M. Maekawa, T. Akindele and K. Tomioka, *Org. Lett.*, 2008, **10**, 3805–3808; (*h*) Radical addition of terminal alkynes to imines: Z. Chen, Y.-X. Zhang, Y. An, X.-L. Song, Y.-H. Wang, L.-L. Zhu and L. Guo, *Eur. J. Org. Chem.*, 2009, 5146–5152; (*i*) Aminomethylation of Michael acceptors: J. Maury, D. Mouysset, L. Feray, S. R. a. Marque, D. Siri and M. P. Bertrand, *Chem.–Eur. J.*, 2012, **18**, 3241–3247; (*j*) Domino reactions involving 1,4-addition of alkyl radical to β-(propargyloxy)enoates followed by carbocyclization: A. Pérez-Luna, C. Botuha, F. Ferreira and F. Chemla, *Chem.–Eur. J.*, 2008, **14**, 8784–8788; (*k*) Radical addition of alkyls to imines and enones: M. P. Bertrand, L. Feray, R. Nouguier and P. Perfetti, *J. Org. Chem.*, 1999, **64**, 9189–9193; (*l*) Radical Reformatsky reaction: P. G. Cozzi, *Adv. Synth. Catal.*, 2006, **348**, 2075–2079; (*m*) P. G. Cozzi, F. Benfatti, M. G. Capdevila and A. Mignogna, *Chem. Commun.*, 2008, 3317–3318; (*n*) Silylzincation of ynamides: E. Romain, C. Fopp, F. Chemla, F. Ferreira, O. Jackowski, M. Oestreich and A. Perez-Luna, *Angew. Chem., Int. Ed.*, 2014, **53**, 11333–11337.

4 For selected examples, see: (*a*) A. G. Davies and B. P. Roberts, *J. Chem. Soc. B*, 1968, 1074–1078; (*b*) J. Maury, L. Feray, S. Bazin, J.-L. Clément, S. R. A. Marque, D. Siri and M. P. Bertrand, *Chem.–Eur. J.*, 2011, **17**, 1586–1595; (*c*) D. Mukherjee, A. Ellern and A. D. Sadow, *J. Am. Chem. Soc.*, 2012, **134**, 13018–13026; (*d*) J. M. Grevy, in *Encyclopedia of Inorganic Chemistry*, ed. R. B. King, Wiley-VCH Verlag GmbH, Chichester, 2005, p. 5953.

5 (*a*) J. Lewiński, Z. Ochal, E. Bojarski, E. Tratkiewicz, I. Justyniak and J. Lipkowski, *Angew. Chem., Int. Ed.*, 2003, **42**, 4643–4646; (*b*) J. Lewiński, W. Marciniak, J. Lipkowski and I. Justyniak, *J. Am. Chem. Soc.*, 2003, **125**, 12698–12699; (*c*) J. Lewiński, W. Śliwiński, M. Dranka, I. Justyniak and J. Lipkowski, *Angew. Chem., Int. Ed.*, 2006, **45**, 4826–4829; (*d*) J. Lewiński, K. Suwała, M. Kubisiak, Z. Ochal, I. Justyniak and J. Lipkowski, *Angew. Chem., Int. Ed.*, 2008, **47**, 7888–7891; (*e*) J. Lewiński, W. Bury, M. Dutkiewicz, M. Maurin, I. Justyniak and J. Lipkowski, *Angew. Chem., Int. Ed.*, 2008, **47**, 573–576; (*f*) J. Lewiński, K. Suwała, T. Kaczorowski, M. Gałęzowski, D. T. Gryko, I. Justyniak and J. Lipkowski, *Chem. Commun.*, 2009, 215–217; (*g*) J. Lewiński, M. Kościelski, K. Suwała and I. Justyniak, *Angew. Chem., Int. Ed.*, 2009, **48**, 7017–7020; (*h*) K. Zelga, M. Leszczyński, I. Justyniak, A. Kornowicz, M. Cabaj, A. E. H. Wheatley and J. Lewiński, *Dalton Trans.*, 2012, **41**, 5934–5938; (*i*) M. Kubisiak, K. Zelga, I. Justyniak, E. Tratkiewicz, T. Pietrzak, A. R. Keeri, Z. Ochal, L. Hartenstein, P. W. Roesky and J. Lewiński, *Organometallics*, 2013, **32**, 5263–5265.

6 For the related studies, see: (*a*) S. Jana, R. J. F. Berger, R. Fröhlich, T. Pape and N. W. Mitzel, *Inorg. Chem.*, 2007, **46**, 4293–4297; (*b*) N. Hollingsworth, A. L. Johnson, A. Kingsley, G. Kociok-Köhn and K. C. Molloy, *Organometallics*, 2010, **29**, 3318–3326; (*c*) S. Xu, W. C. Everett, A. Ellern, T. L. Windus and A. D. Sadow, *Dalton Trans.*, 2014, **43**, 14368–14376.

7 (*a*) P. Sobota, R. Petrus, K. Zelga, L. Mąkolski, D. Kubicki and J. Lewiński, *Chem. Commun.*, 2013, **49**, 10477–10479; (*b*) Ł. Mąkolski, K. Zelga, R. Petrus, D. Kubicki, P. Zarzycki, P. Sobota and J. Lewiński, *Chem.–Eur. J.*, 2014, **20**, 14790–14799.

8 E. Mileo, F. Benfatti, P. G. Cozzi and M. Lucarini, *Chem. Commun.*, 2009, 469–470.

9 A. Grirrane, I. Resa, A. Rodriguez, E. Carmona, E. Alvarez, E. Gutierrez-Puebla, A. Monge, A. Galindo, D. del Río and R. A. Andersen, *J. Am. Chem. Soc.*, 2007, **129**, 693–703.

10 K. Budny-Godlewski, D. Kubicki, I. Justyniak and J. Lewiński, *Organometallics*, 2014, **33**, 5093–5096.

11 For a qualitative EPR study suggesting that TEMPO reacts smoothly with Et_2Zn, see ref. 4b herein.

12 I. Dranka, M. Kubisiak, I. Justyniak, M. Lesiuk, D. Kubicki and J. Lewiński, *Chem.–Eur. J.*, 2011, **17**, 12713–12721.

13 C. Van Koten and K. Vrieze, *Adv. Organomet. Chem.*, 1982, **21**, 151–239.

14 In the reaction of TEMPO with Et_2Zn the $Et^{\bullet}$ radicals being formed are trapped by unreacted TEMPO. This process is most prominent when TEMPO is present in high concentration. When, however, it is added dropwise to the solution containing Et_2Zn the radical entrapment is minimized and free $Et^{\bullet}$ radicals are present in higher concentrations (see ref. 10 herein). Employment of the latter procedure in the model reaction did not however lead to formation of any product of reaction of **1a**.

15 Since products of reactions of reactive oxygen species with the ligand are observed in the reaction mixture after oxygenation of $(EtZn)_2Zn(OAr)_4$ (see ref. 7.) and there is no product in the model reaction, it is reasonable to conclude that the forming radical species are trapped within a solvent cage.

16 (*a*) T. Matsumoto, K. Ohkubo, K. Honda, A. Yazawa, H. Furutachi, S. Fujinami, S. Fukuzumi and M. Suzuki, *J. Am. Chem. Soc.*, 2009, **131**, 9258–9267; (*b*) R. F. Moreira, E. Y. Tshuva and S. J. Lippard, *Inorg. Chem.*, 2004, **43**, 4427–4434; (*c*) C. X. Zhang, H.-C. Liang, E.-I. Kim, J. Shearer, M. E. Helton, E. Kim, S. Kaderli, C. D. Incarvito, A. D. Zuberbühler, A. L. Rheingold and K. D. Karlin, *J. Am. Chem. Soc.*, 2003, **125**, 634–635; (*d*) H. Kelm and H.-J. Krűger, *Angew. Chem., Int. Ed.*, 2001, **40**, 2344–2348; (*e*) M. T. Reetz and K. Töllner, *Tetrahedron Lett.*, 1995, **36**, 9461–9464; (*f*) F. M. MacDonnell, N. L. P. Fackler, C. Stern and T. V. O'Halloran, *J. Am. Chem. Soc.*, 1994, **116**, 7431–7432.

17 L. Casarrubios, J. A. Perez, M. Brookhart and J. L. Templeton, *J. Org. Chem.*, 1996, **61**, 8358–8359.

18 J. Lewiński, M. Dranka, W. Bury, W. Śliwiński, I. Justyniak and J. Lipkowski, *J. Am. Chem. Soc.*, 2007, **129**, 3096–3098.

19 SHELXS-97, Program for Structure Solution: G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 1990, **46**, 467–473.

20 G. M. Sheldrick, *SHELXL-97, Program for Structure Refinement*, Universität Göttingen, 1997.