# Iminoxyl Radical-Based Strategy for Intermolecular C–O Bond Formation: Cross-Dehydrogenative Coupling of 1,3-Dicarbonyl Compounds with Oximes

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Received: February 7, 2014; Published online:

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201400143.

Abstract: Cross-dehydrogenative C–O coupling of 1,3-diketones and 1,3-keto esters with oximes was realized for the first time. The reaction proceeds in the presence of the oxidants [KMnO<sub>4</sub>, Mn(OAc)<sub>2</sub>/  $Mn(OAc)_3 \cdot 2H_2O$ , KMnO<sub>4</sub>,  $MnO_2$ ,  $Mn(acac)_3$ ,  $Fe(ClO_4)_3$ ,  $Cu(ClO_4)_2 \cdot 6H_2O$ ,  $Cu(NO_3)_2 \cdot 2.5H_2O$ , and  $(NH_4)_2Ce(NO_3)_6$ ]. Twenty cross-coupling products were synthesized using potassium permanganate  $(KMnO_4)$ . manganese(II) acetate dihydrate  $[Mn(OAc)_3 \cdot 2H_2O]$ , or the manganese(II) acetate/potassium permanganate [Mn(OAc)<sub>2</sub>/KMnO<sub>4</sub>] system; yields are 27–92%. The synthesis can be easily scaled up to gram quantities of the target products. Appa-

# Introduction

Cross-dehydrogenative coupling, as a rule, is a reaction in which two different starting molecules are connected by a new bond with the elimination of one hydrogen atom from each of the molecules. In the last decade, these reactions have attracted great attention<sup>[1-11]</sup> because they can be used to form a new bond with almost the maximum possible atom economy and do not require additional synthetic steps for the introduction of functional groups (Hal, OTf, BR<sub>2</sub>, SiR<sub>3</sub>, SnR<sub>3</sub>, ZnHal, etc.) that are necessary in other approaches to the cross-coupling.

The cross-dehydrogenative C-C coupling has been studied in most detail;<sup>[1-11]</sup> the C-N,<sup>[9-42]</sup> C-P,<sup>[7,8,10,43-55]</sup> and C-O<sup>[10-12,56-97]</sup> cross-coupling reactions are less well developed. It is difficult to achieve high selectivity in the cross-dehydrogenative C-O coupling berently, the reaction proceeds *via* a radical mechanism in which the oxidizing agent serves to generate radicals from oximes and perform the one-electron oxidation of 1,3-dicarbonyl compounds. The formation of oxime radicals was confirmed quantitatively by electron spin resonance (ESR) spectroscopy. The coupling described in the present study is the first example of the selective intermolecular reaction involving unstable iminoxyl radicals generated *in situ*.

**Keywords:** cross-coupling; 1,3-dicarbonyl compounds; iminoxyl radicals; oxidation; oximes

cause the starting compounds are prone to side oxidation and fragmentation reactions giving, for example, alcohols and carbonyl compounds. This gives rise to a problem of searching for oxidizing agents and reaction conditions suitable for the cross-coupling of different types of substrates.

The literature data were thoroughly analyzed to determine the scope of the C–O cross-dehydrogenative coupling reactions. Aldehydes,<sup>[12,56,57]</sup> formamides,<sup>[58]</sup> alkylarenes,<sup>[56,59–63]</sup> isochromanes,<sup>[64a]</sup> alcohols,<sup>[57,65,66]</sup> compounds containing the allyl moiety,<sup>[59,64b,67–83]</sup> 1,3-dicarbonyl compounds,<sup>[84–90]</sup> malononitriles and cyanoacetic esters,<sup>[88,91]</sup> monocarbonyl compounds<sup>[66,92–96]</sup> and pyrrolidines<sup>[97]</sup> were used as C–H reagents for the C–O coupling. Alcohols,<sup>[12,65,84–86,97]</sup> *N*-hydroxy imides,<sup>[12,57,59,63,88]</sup> hydroxamic acids,<sup>[88,90]</sup> oximes,<sup>[64]</sup> sulfonic acids,<sup>[66,84,85,92–95]</sup> carboxylic acids,<sup>[60–62,67–83,85,87,96]</sup>

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phosphonic acids,<sup>[85]</sup> *t*-BuOOH,<sup>[89,91]</sup> phenols,<sup>[58]</sup> and 1,3-keto esters<sup>[58]</sup> were used as O–H reagents.

Depending on the nature of C–H and O–H reagents for the cross-dehydrogenative C–O coupling, various catalysts, oxidants, oxidizing systems and conditions were used:  $(n-Bu)_4NBr/t-BuOOH$ ,<sup>[12]</sup>  $(n-Bu)_4NI/t-BuOOH$ ,<sup>[12,61,67,87,96]</sup> NH<sub>4</sub>I/MCPBA,<sup>[92]</sup> I<sub>2</sub>/MCPBA,<sup>[93]</sup> DDQ,<sup>[64]</sup> iodine(III) and iodine(IV) compounds,<sup>[57,84–86]</sup> iodoarene/peroxide,<sup>[66,93–95]</sup> CuCl/PhI(OAc)<sub>2</sub>,<sup>[59]</sup> Cu<sup>2+</sup>/t-BuOOH,<sup>[56,58,89,91]</sup> CuCl<sub>2</sub>/LiCl,<sup>[69]</sup> Cu(OTf)<sub>2</sub>/ligand/MnO<sub>2</sub>,<sup>[90]</sup> ruthenium complexes,<sup>[65]</sup> Mn(OAc)<sub>3</sub>,<sup>[88]</sup> Co<sup>2+</sup>/KMnO<sub>4</sub>,<sup>[88]</sup> NaBrO<sub>3</sub>/NaHSO<sub>3</sub>,<sup>[60]</sup> (NH<sub>4</sub>)<sub>2</sub>Ce(NO<sub>3</sub>)<sub>6</sub>,<sup>[63]</sup> Pd(II)-based systems,<sup>[62,68-83]</sup> and anodic oxidation.<sup>[97]</sup>

To the best of our knowledge, the only one type of the cross-dehydrogenative C–O coupling involving oximes was described in the literature, i.e., the crosscoupling with isochromanes<sup>[64a]</sup> or 1-phenylpropene derivatives<sup>[64b]</sup> promoted by 2,3-dichloro-5,6-dicyano*para*-benzoquinone (DDQ). It was suggested that the C–O bond is formed *via* the nucleophilic attack of oxime on the carbocation generated from the C–H reagent.<sup>[64]</sup>

In the present work, the cross-dehydrogenative C– O coupling of 1,3-dicarbonyl compounds with oximes was performed for the first time. In previous studies, we found a series of unusual cross-dehydrogenative C–O coupling reactions in which the C–O bond is formed by a homolytic mechanism involving O radicals.<sup>[63,88,89,91]</sup> The oximes used in the present study also give O radicals in the presence of oxidants.<sup>[98–103]</sup> However, only a few reactions with oxime (iminoxyl) radicals were described in the literature. The synthetic application of these radicals has long been limited to reactions of the stable di-*tert*-butyliminoxyl radical:<sup>[99,100]</sup> the oxidation of amines to imines,<sup>[104]</sup> the oxidative addition to phenols,<sup>[105]</sup> and the replacement of allylic hydrogen in cyclohexene.<sup>[106]</sup> First selective reactions involving unstable iminoxyl radicals generated *in situ* were realized only recently: the intramolecular hydrogen atom abstraction by oxime radical followed by cyclization<sup>[107]</sup> and the intramolecular addition to the C=C double bond<sup>[108]</sup> were performed. The drawback of these protocols is the use of expensive reagents such as TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, 2–3 equiv.) and/or DEAD (diethyl azodicarboxylate, 1–3 equiv.).<sup>[107,108]</sup>

Iminoxyl radicals generated by the oxidation of oximes decompose to give a complex mixture of products, in particular, these radicals can dimerize to form N–N, N–O, or O–C bonds.<sup>[102]</sup> In many cases, the oxidation of oximes affords the corresponding ketones.<sup>[109–118]</sup> In known intramolecular cyclization reactions of iminoxyl radicals, the latter act both as O radicals<sup>[108]</sup> and N radicals<sup>[101,108]</sup> to form a C–O or C–N bond, respectively.

The cross-dehydrogenative coupling products, oxime ethers containing carbonyl groups near the C= N-O-C moiety, are structurally similar to compounds exhibiting neuroprotective,<sup>[119]</sup> AMPA-antagonis-tic,<sup>[119,120]</sup> anti-inflammatory,<sup>[121]</sup> fungicidal,<sup>[122]</sup> and antiviral activities.<sup>[123]</sup> The C=N-O-C moiety is also involved in the antimicrobial agents ceftazidime and roxithromycin, the insect growth regulator flucyclox-uron, and other biologically active compounds.

### **Results and Discussion**

The starting reagents used for the study were 1,3-keto esters **1a–f**, 1,3-diketones **1g–k** and diethyl etylmalonate **1l** combined with oximes **2a–i** (Scheme 1).

In the first step, we studied the cross-dehydrogenative coupling of ethyl 2-methyl-3-oxobutanoate **1a** with 3-(hydroxyimino)pentane-2,4-dione **2a** in order to find the optimal reaction conditions (Table 1). The



Scheme 1. Cross-dehydrogenative C–O coupling of 1,3-dicarbonyl compounds 1a–I with oximes 2a–i.

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Table 1. Effect of the nature of the oxidant, the solvent, the temperature, and the reaction time on the yield of cross-dehydrogenative coupling product 3.<sup>[a]</sup>



Run	Oxidant (ratio: mole per mole of 1a)	Solvent	Temperature [°C]	Time [min]	Isolated yield of <b>3</b> [%]
1	KMnO <sub>4</sub> "macrocrystalline" (0.4)	AcOH	60	20	90
2	KMnO <sub>4</sub> "macrocrystalline" (0.4)	AcOH	40	10	91
3	KMnO <sub>4</sub> "macrocrystalline" (0.4)	AcOH	40	5	90
4	KMnO <sub>4</sub> "macrocrystalline" (0.4)	AcOH	24	40	84
5	KMnO <sub>4</sub> "macrocrystalline" (0.4)	AcOH/H <sub>2</sub> O 20/1	40	10	74
6	$KMnO_4$ "powder" (0.4)	AcOH	40	10	90
7	$KMnO_4$ "fine powder" (0.4)	AcOH	40	10	64
8	$KMnO_4$ "fine powder" $(0.4)^{[b]}$	AcOH	40	10	90
9	$KMnO_4$ "fine powder" (0.4), $Mn(OAc)_2 \cdot 4H_2O$ (1.6)	AcOH	40	10	92
10	$KMnO_4$ "fine powder" $(0.4)^{[c]}$	AcOH	40	10	90
11	$MnO_2(1)$	AcOH	60	20	79
12	$Mn(\tilde{OAc})_3 \cdot 2H_2O(2)$	AcOH	60	20	92
13	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	AcOH	80	10	92
14	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	AcOH	40	20	91
15	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	AcOH	24	20	80
16	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	CHCl <sub>3</sub>	60	20	77
17	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	MeCN	80	20	74
18	$Mn(OAc)_{3} \cdot 2H_{2}O(2)$	MeOH	60	20	85
19	$Mn(acac)_3(2)$	AcOH	60	20	74
20	$Fe(C O_{4})$ , $H_{2}O_{2}(2)$	MeCN	80	20	84
21	$Fe(ClO_4)_3 \cdot nH_2O(2)$	MeCN	24	5	84
22	$Fe(NO_2) \cdot 9H_2O(2)$	MeCN	80	20	25
23	$Fe(C O_{4}) \cdot n H_{2}O(2)$	AcOH	24	5	0
24	$Fe(C O_4) \cdot n H_2O(2)$	MeOH	24	5	0
25	$Fe(ClO_4)$ , $H_2O(2)$	EtOAc	24	5	14
26	$Fe(C O_4) \cdot n H_2O(2)$	CHCl	60	20	55
27	$Cu(C O_4)_{3:6} H_2O(2.5)$	MeCN	80	20	45
28	$Cu(NO_2)_2 \cdot 2.5 H_2O(2.5)$	MeCN	80	20	49
29	$Cu(OAc)_{2}:H_{2}O(2.5)$	MeCN	80	20	0
30	$(NH_{1})_{2}Ce(NO_{2})_{2}(2)$	AcOH	60	20	55
31	$(NH_4)_2 Ce(NO_3)_6 (2)$	MeOH	60	20	17
32	$(NH_4)_2 Ce(NO_3)_6(2)$	MeCN	60	20	12
33	$Pb(OAc)_{4}(1)$	AcOH	60	20	0
34	$K_{a}(r_{a}O_{a}(0.33))$	AcOH	60	20	8
35	$M_{1}(OAc) + 4H_{2}O(0.05) + (NH_{1}) + S_{2}O_{2}(1)$	AcOH	80	20	6
36	$Fe(ClO_{1}) = H_{2}O(0,0,0); (1,114/2) = 0.000 (1)$	MeCN	80	20	15
37	$Cu(ClO_4)_3 HI_2O(0.1), t BuOOH 70% aq. (1)$	MeCN	80	20	40
38	$Cu(ClO_4)_2 \circ H_2O(0.05); t BuOOH 70% aq. (1)$	AcOH	60	20	6
39	$Cu(ClO_4)_2 \circ H_2O(0.05); H = Or 34\% ag (1)$	MeCN	80	20	10
40	$Cu(ClO_4)_2 \circ H_2O(0.05); H_2O_2 \circ H_2O(uq. (1))$	MeCN	80	20	35
40	$C_0(OA_c)$ $::$ $(0.05)$ $:$ $O_2$	AcOH	60	20	0
41 12	$C_0(OAc)_2 + H_2O(0.05); H_2O(34\% ac (1))$	AcOH	60	20	0
72 //3	$C_0(NO_1) = 6H_0 (0.05); t_B = 0.00H_70\% ag (1)$	MeCN	80	20	0
44	$C_0(NO_3)_2 OH_2O(0.05); t-DuOOH 7070 aq. (1)$	MeCN	80	20	0
44 45	PhI(OAc) (1)	AcOH	80	20 60	0
45 46	$B_{7}OOB_{7}75\%$ (1)	ACOH	80	60	0
47	DDO(1)	AcOH	80	60	0
48	DIAD(1)	AcOH	80	60	0

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Sample 1. "Macrocrystalline" KMnO<sub>4</sub>

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Catalysis

Synthesis &

Sample 2. "Powdered" KMnO<sub>4</sub>

Sample 3. "Fine powdered" KMnO<sub>4</sub>

Figure 1. Samples of KMnO<sub>4</sub> used in the study: "macrocrystalline", "powdered," and "fine powdered".

reaction was performed in CH<sub>3</sub>COOH, MeCN, MeOH, EtOAc and CHCl<sub>3</sub> using different oxidants at temperatures from 24 to 80 °C.

Compounds of Mn(III, IV, and VII), Fe(III), Cu(II), Ce(IV), Pb(IV), and Cr(VI), combinations of Mn(II), Fe(III), Cu(II), and Co(II) salts with peroxides or oxygen, and non-metal agents, such as (diacetoxyiodo)benzene [PhI(OAc)<sub>2</sub>], dibenzoyl peroxide (BzOOBz), DDQ, and diisopropyl azodicarboxylate (DIAD), were examined as oxidants.

The cross-coupling proceeds in the presence of various manganese-based oxidants [Mn(OAc)<sub>3</sub>, Mn(acac)<sub>3</sub>, KMnO<sub>4</sub>, MnO<sub>2</sub>; runs 1–19] under a wide variety of reaction conditions: at 24–80 °C in different solvents [AcOH, MeCN, MeOH, CHCl<sub>3</sub>; runs 12 and 16–18; the oxidant Mn(OAc)<sub>3</sub>]; the reaction times were 5–20 min. KMnO<sub>4</sub> and Mn(OAc)<sub>3</sub> proved to be the most efficient oxidants; the yield of **3** was up to 90–92% (runs 1–3, 6, 8–10, and 12–14).

The yield of **3** depends on the particle size of  $KMnO_4$  (runs 2, 6 and 7). Photomicrographs of three manganese permanganate samples are shown in Figure 1. "Powdered" and "fine powdered"  $KMnO_4$  samples were prepared by grinding "macrocrystalline"  $KMnO_4$  in a mortar.

Despite a large difference in the KMnO<sub>4</sub> particle size of samples 1 and 2, the reactions with their use give product **3** in the same yield (runs 2 and 6, yield 90–91%). The reaction with the use of sample 3 (run 7) affords cross-coupling product **3** in substantially lower yield (64% *versus* 90–91%). After the standard treatment, the mixture of reaction products obtained in run 7 contained unconsumed keto ester **1a** (approximately 29% based on the <sup>1</sup>H NMR data, see the Experimental Section). An increase in the addition time of "fine powdered"  $KMnO_4$  from 5–10 s to 8 min (run 8) leads to an increase in the yield of **3** from 64% to 90%. Apparently, the effect of the slow addition of "fine powdered"  $KMnO_4$  is similar to the effect of the slow dissolution of larger  $KMnO_4$  particles in runs 6 and 2.

The ESR study showed that KMnO<sub>4</sub> oxidizes oxime 2a to form iminoxyl O-centered radicals (see below). Since manganese forms stable compounds in all oxidation states from +2 to +7, the oxidation of **2a** with potassium permanganate can be accompanied by the formation of different manganese compounds in the reaction mixture, the composition of which obviously depends on the rate of supply of KMnO<sub>4</sub> to the reaction zone. Thus, the slow dissolution of large particles or the slow addition of small particles (runs 2, 6, and 8) corresponds to an excess of the reducing agent (2a and 1a) in the reaction zone over the oxidant  $(KMnO_4)$  and facilitates the formation of manganese compounds in lower oxidation states than in the case of the fast addition of small particles (run 7). Based on our previous experience in the study of the crossdehydrogenative coupling involving 1,3-dicarbonyl compounds and O radicals,<sup>[88]</sup> we suggested that, for the coupling to proceed, the reaction mixture should contain a one-electron oxidant for the oxidation of the dicarbonyl compound. An Mn(III) compound, for example, manganese triacetate, can be such oxidant.<sup>[124-128]</sup> The conditions of the following experiments are favorable for the formation of Mn(III) compounds: run 2 (the use of large KMnO<sub>4</sub> particles), run 8 (the slow addition of "fine powdered"  $KMnO_4$ ), run 9 [*in situ* generation of  $Mn(OAc)_3$  by the addition

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<sup>&</sup>lt;sup>[a]</sup> General reaction conditions: an oxidant [in runs 9 and 35–44, the salt  $Mn(OAc)_2 \cdot 4H_2O$ ,  $Fe(ClO_4)_3 \cdot nH_2O$ ,

Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Co(OAc)<sub>2</sub>·4H<sub>2</sub>O, or Co(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O was added one minute prior to the addition of the oxidant] was added to a stirred mixture of ethyl 2-methyl-3-oxobutanoate **1a** (200 mg, 1.39 mmol), 3-(hydroxyimino)pentane-2,4-dione **2a** (179 mg, 1.39 mmol), and a solvent (5 mL) at a specified temperature for 5–10 s, and then the reaction mixture was stirred at the same temperature for a specified time.

<sup>&</sup>lt;sup>[b]</sup> KMnO<sub>4</sub> was added for 8 min, and then the reaction mixture was stirred for 2 min.

<sup>&</sup>lt;sup>[c]</sup> The amount of oxime **2a** was doubled (358 mg, 2.78 mmol)

of the extra reducing agent  $Mn(OAc)_2$  to the reaction mixture, the reaction conditions are similar to those used for the synthesis of  $Mn(OAc)_3$  from  $Mn(OAc)_2$ and  $\text{KMnO}_4^{[124]}$ ], and run 10 (the use of the double amount of oxime 2a, which reduces KMnO<sub>4</sub>). In these experiments, cross-coupling product 3 was obtained in high yields, and the complete conversion of keto ester **1a** was observed. On the contrary, the conditions of run 7 facilitate a higher concentration of  $KMnO_4$  in the reaction zone and, correspondingly, the formation of products of the reduction of manganese in higher oxidation states, resulting in a decrease in the efficiency of the reaction. The suggestion about the involvement of Mn(III) compounds in the cross-dehydrogenative coupling of 1a with 2a in the presence of  $KMnO_4$  is confirmed also by the results of run 5. Thus, the addition of small amounts of water to the reaction mixture leads to a decrease in the yield of **3** by 17% compared to run 2 and to the incomplete conversion of keto ester **1a** (run 5, about 16% of **1a** were present in the mixture of reaction products according to the <sup>1</sup>H NMR data). It is known that in water Mn(III) tends to disproportionate into Mn(II) and Mn(IV).<sup>[129]</sup> Therefore, the results of runs 2 and 5–10 can be attributed to the fact that Mn(III) formed in the course of the reaction between 1a, 2a and KMnO<sub>4</sub> plays an important role in the cross-coupling of 1a with 2a.

Since substantially different results can be obtained in the reactions with the use of powdered  $KMnO_4$ samples, depending on the particle size, we used "macrocrystalline"  $KMnO_4$  in subsequent experiments for the cross-dehydrogenative coupling of 1,3dicarbonyl compounds with oximes.

Iron(III) perchlorate in acetonitrile proved to be the iron salt of choice (runs 20 and 21, yield 84%). The reactions with the use of iron nitrate (run 22) instead of  $Fe(CIO_4)_3$  or with the use of acetic acid, methanol, ethyl acetate, or chloroform (runs 23–26, respectively) instead of acetonitrile afford the target product in substantially lower yields.  $Fe(CIO_4)_3 \cdot n H_2O$ is a slightly less effective reagent for the coupling than manganese-based oxidants, the other drawbacks of this reagent are high molecular weight and hygroscopicity.

The reactions with the use of copper(II) salts or cerium(IV) ammonium nitrate as oxidants give **3** in yields of no higher than 55% (runs 27–32); lead tetraacetate and ammonium dichromate are inefficient in this reaction (runs 33 and 34). The cross-dehydrogenative coupling with the use of metal/peroxide or metal/oxygen oxidizing systems (runs 35–44) affords the target products in yields of at most 40%. The target product is not formed in the presence of the non-metal oxidants used in our experiments (runs 45–48).

The cross-dehydrogenative coupling reactions of 1,3-dicarbonyl compounds **1a–l** with oximes **2a–i** were carried out under conditions similar to those used in runs 2 (oxidant KMnO<sub>4</sub>, method A), 12 [oxidant Mn(OAc)<sub>3</sub>, method B], and 9 [oxidant Mn(OAc)<sub>2</sub>/KMnO<sub>4</sub>, method C] presented in Table 1. The results are summarized in Table 2.

1,3-Diketones and keto esters with different structures, including compounds containing easily oxidizable allyl and benzyl moieties, are involved in the cross-dehydrogenative coupling reactions with oximes. Diethyl ethylmalonate **11** does not react with oxime **1a** (Methods A–C, reaction temperature 80 °C).

The cross-coupling of a wide range of 1,3-dicarbonyl compounds with 3-(hydroxyimino)pentane-2,4dione **2a** proceeds efficiently. The cross-coupling of oxime **2b** containing only one electron-withdrawing carbonyl group with keto ester **1a** gives lower yields compared to the cross-coupling of oxime **2a** containing two electron-withdrawing groups (runs 2 and 1, respectively). The cross-coupling reactions of oximes **2c-e** and **2h** and **2i** containing no electron-withdrawing groups also take place. The yield of the cross-coupling product increases with increasing bulkiness of the substituents at the C=NOH moiety (runs 14–16).

Except for the cross-coupling reactions with oxime **2a**, the efficiency of the oxidants  $Mn(OAc)_3$  and  $Mn(OAc)_2/KMnO_4$  is higher compared to  $KMnO_4$  (runs 2, 3, 4, 9, and 14–16).

Apparently, the reaction proceeds through the formation of iminoxyl O radicals from oximes, and the stability of these radicals has a key effect on the yield of the cross-coupling product. It is known that 2-iminoxy-1,3-dicarbonyl radicals, particularly diacetyliminoxyl radical **A**, which is formed by the oxidation of 3-(hydroxyimino)pentane-2,4-dione **2a**, are relatively stable compared to the iminoxyl radicals generated from oximes containing alkyl and aryl substituents.<sup>[103,130]</sup>

The hypothesized pathway of the cross-dehydrogenative coupling of 1,3-dicarbonyl compounds with oximes is depicted in Scheme 2 for the cross-coupling of 1a with 2a.

In the presence of an oxidant, iminoxyl radicals **A** are generated from oxime **2a**. The reaction of radical **A** with metal complex **B** or radical **C** affords crosscoupling product **3**. The metal ion is necessary for the one-electron oxidation of the dicarbonyl compound **1a**. The probability of the one-electron oxidation of 1,3-dicarbonyl compounds with Mn(OAc)<sub>3</sub>,<sup>[124-128]</sup> Fe(ClO<sub>4</sub>)<sub>3</sub>,<sup>[131,132]</sup> (NH<sub>4</sub>)<sub>2</sub>Ce(NO<sub>3</sub>)<sub>6</sub>,<sup>[133,134]</sup> and Cu(ClO<sub>4</sub>)<sub>2</sub><sup>[135]</sup> is supported by the published data. The generation of iminoxyl radicals **A** under the conditions similar to the reaction conditions was confirmed by ESR spectroscopy.

Most of the iminoxyl radicals with alkyl and aryl substituents at the carbon atom, except for the di-tert-

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<b>Fable 2.</b> Products 3–22 of the cross-del	ydrogenative coupl	ing of 1,3-dicarbonyl o	compounds <b>1a–l</b> with oximes <b>2a–i</b>
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- [a] Method A (oxidant KMnO<sub>4</sub>): macrocrystalline KMnO<sub>4</sub> (0.8 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (2 mmol), oxime (2 mmol), and acetic acid (7 mL) at 40 °C for 5–10 s, and then the mixture was stirred at 40 °C for 10 min.
- <sup>[b]</sup> Method B [oxidant Mn(OAc)<sub>3</sub>]: Mn(OAc)<sub>3</sub>·2H<sub>2</sub>O (4 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (2 mmol), oxime (2 mmol), and acetic acid (7 mL) at 60 °C for 5–10 s, and then the mixture was stirred at 60 °C for 5 min.
- [c] Method C [oxidant Mn(OAc)<sub>2</sub>/KMnO<sub>4</sub>]: "fine powdered" KMnO<sub>4</sub> (0.8 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (2 mmol), oxime (2 mmol), Mn(OAc)<sub>2</sub>·4H<sub>2</sub>O (3.2 mmol), and acetic acid (7 mL) at 40 °C for 5–10 s, and then the mixture was stirred at 40 °C for 5 min.
- <sup>[d]</sup> The synthesis was performed (method A) was scaled up to 1.00 g of ethyl 2-methyl-3-oxobutanoate **1a**, see the Experimeental Section.

butyliminoxyl radical,<sup>[99,100,104–106]</sup> are unstable at room temperature even in solutions.<sup>[98,102,106]</sup> It is necessary to use flow techniques<sup>[98]</sup> or generate radicals by irradiation of the sample in the cavity of the spectrometer<sup>[102]</sup> in order to detect these radicals by ESR spectroscopy. The iminoxyl radicals R<sup>1</sup>COC(=NO<sup>•</sup>)COR<sup>2</sup>, particularly the 2,4-pentanedione-3-iminoxyl radical **A**,<sup>[103,130]</sup> are substantially more stable.

Hence, in ESR experiments, the latter radical was generated from model oxime 2a. 3-(Hydroxyimino)pentane-2,4-dione oxidized 2a was with  $Mn(OAc)_2 \cdot 4H_2O/KMnO_4$  $Mn(OAc)_3 \cdot 2H_2O_1$ the system, KMnO<sub>4</sub>,  $Fe(ClO_4)_3$ ,  $Cu(ClO_4)_2 \cdot 6H_2O$ ,  $(NH_4)_2Ce(NO_3)_6$ , Pb(OAc)<sub>4</sub>, and PhI(OAc)<sub>2</sub> in AcOH or MeCN at room temperature (Table 3). In all cases, the ESR spectrum corresponding to the diacetylimin-

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**Scheme 2.** Plausible pathway of the cross-dehydrogenative coupling of 1,3-dicarbonyl compounds with oximes.

oxyl radical  $\mathbf{A}^{[103,130]}$  was recorded. The conversion of the oxime into the radical was estimated from the intensity of the ESR signal using solutions of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a concentration standard. An example of the ESR spectrum of radical  $\mathbf{A}$  is shown in Figure 2. The values of the g factor and <sup>14</sup>N hyperfine coupling constant (g= 2.0047;  $\mathbf{a}_N$ =28.5 G) are in agreement with literature data.<sup>[103,130]</sup>

As can be seen from runs 1–7, the oxidants, which were active in the cross-dehydrogenative coupling of oxime 2a with keto ester 1a, generate considerable amounts of iminoxyl radicals A from oxime 2a even at room temperature. The only exception is



**Figure 2.** ESR spectrum of diacetyliminoxyl radical **A** generated by the oxidation of 3-(hydroxyimino)-2,4-pentanedione **2a** with potassium permanganate in AcOH (Table 3, run 3, 2–3 min after the mixing).

 $(NH_4)_2Ce(NO_3)_6$ ; in the presense of this oxidant radical **A** is generated, but decomposes rapidly (run 5). Lead(IV) acetate and (diacetoxyiodo)benzene (runs 8 and 9) also generate radicals **A** from oxime **2a**; however, the cross-coupling of **2a** with **1a** does not take place in the presence of these oxidants (Table 1, runs 33, 45). This observation is in agreement with the assumption that the oxidant not only generates iminoxyl radicals **A** but is also involved in the one-electron oxidation of dicarbonyl compounds.

To the best of our knowledge, all cross-dehydrogenative coupling products **3–22** are new. The products

oxidant AcOH or MeCN OН 0 2a Α Yield<sup>[a]</sup> of A [%] Run Oxidant (oxidant/oxime molar ratio) Solvent 2-5 min<sup>[b]</sup> 10 min<sup>[b</sup> 20 min<sup>[b]</sup> 40 39 1  $Mn(OAc)_3 \cdot 2H_2O(1)$ AcOH 34 2 Mn(OAc)<sub>2</sub>·4H<sub>2</sub>O (0.8)/KMnO<sub>4</sub> (0.2) AcOH 49 52 52 72 3 KMnO<sub>4</sub> (0.2) AcOH 55 77 AcOH 96 4 KMnO<sub>4</sub> (0.4) 86 5  $(NH_4)_2Ce(NO_3)_6(1)$ AcOH 3 2 81 81 6  $Fe(ClO_4)_3 \cdot n H_2O(1)$ MeCN

Table 3. Generation of iminoxyl radical A from oxime 2a under conditions similar to the conditions of the cross-dehydrogenative coupling of 2a with keto ester 1a. Estimation of the yield of radical A by ESR spectroscopy of reaction solution.

[a] Calculated as follows: [concentration of A estimated by ESR spectroscopy]/[starting concentration of 2a]×100%.
 [b] Time elapsed after mixing of 2a with oxidant

 $Cu(ClO_4)_2 \cdot 6H_2O(1)$ 

Pb(OAc)<sub>4</sub> (0.5)

 $PhI(OAc)_{2}(0.5)$ 

7

8

9

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MeCN

AcOH

AcOH

19

20

2

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8

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22

5

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were characterized by <sup>1</sup>H and <sup>13</sup>C NMR, IR spectroscopy, elemental analysis, EI mass spectrometry, and HR-MS. The configurations of the double bond in the cross-coupling products **4**, **5**, **7**, **14**, and **15** and their structures were determined by 2D NOESY, HMBC, editing-HSQC and DOSY NMR.

## Conclusions

Cross-dehydrogenative C–O coupling of 1,3-diketones and 1,3-keto esters with oximes is reported for the first time. The best results were obtained with the use of the widely available manganese-based oxidants KMnO<sub>4</sub>, Mn(OAc)<sub>2</sub>·4H<sub>2</sub>O/KMnO<sub>4</sub>, and Mn(OAc)<sub>3</sub>·2H<sub>2</sub>O. The method is applicable for the cross-coupling of a wide range of oximes with  $\beta$ -dicarbonyl compounds; the yields are up to 92%.

The results are unusual because of the fact that Mn-containing oxidants, including  $Mn(OAc)_3 \cdot 2H_2O$  and permanganates, were previously used for the deeper oxidation of oximes with selective formation of carbonyl compounds.<sup>[110–118]</sup>

Apparently, the oxidant serves two functions in the cross-dehydrogenative coupling reaction: the generation of iminoxyl radicals from oximes and the oneelectron oxidation of 1,3-dicarbonyl compounds. This reaction is the first example of the selective intermolecular transformation of unstable iminoxyl radicals.

# **Experimental Section**

#### **General Methods and Materials**

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker AMX-III 400 (400.1 and 100.6 MHz, respectively) and Bruker AVANCE II 300 (300.1 and 75.5 MHz, respectively) spectrometers in CDCl<sub>3</sub> and DMSO- $d_6$ . Assignments of <sup>1</sup>H and <sup>13</sup>C signals and determinations of the structures and their stereochemistry were made with the aid of 2D NOESY, HMBC, editing-HSQC, and DOSY spectra where necessary.

High resolution mass spectra were recorded on a Bruker maXis instrument equipped with electrospray ionization (ESI) ion source.<sup>[136,137]</sup> All measurements were performed in a positive (MS<sup>+</sup>) ion mode (interface capillary voltage: 4500 V) with scan range m/z: 50–3000. External calibration of the mass spectrometer was performed with Electrospray Calibrant Solution (Fluka). A direct syringe injection was used for the all analyzed solutions in MeCN (flow rate:  $3 \,\mu \text{Lmin}^{-1}$ ). Nitrogen was used as nebulizer gas (0.4 bar) and dry gas (4.0 Lmin<sup>-1</sup>); interface temperature was set at 180°C. MeCN (HPLC grade) for ESI-HR-MS experiments was ordered from Merck and used as supplied. All samples for ESI-HR-MS experiments were prepared in 1.5 mL Eppendorf tubes. All plastic disposables (Eppendorf tubes and tips) used in sample preparation were washed with MeCN before use. All spectra were processed by using Bruker DataAnalysis 4.0 software package.

IR spectra were recorded on a Bruker ALPHA FT-IR spectrometer.

The scanning electron microscopy of the KMnO<sub>4</sub> samples (see Figure 1 and the Supporting Information) was carried out using a Hitachi SU8000 field-emission scanning electron microscope (FE-SEM).<sup>[137]</sup> Before measurements the samples were mounted on a 25 mm aluminum specimen stub and fixed by conductive carbon tape. Sample morphology was studied under native conditions to exclude metal coating surface effects.<sup>[138]</sup> Images were acquired in secondary electron mode at 2 kV accelerating voltage and at working distance 8–10 mm.

For ESR experiments,  $100 \,\mu\text{L}$  glass micropipettes equipped with a stopper at the bottom were used as ESR tubes (inner diameter 1.2 mm). Spectra were recorded on an X-band ESR instrument (Varian-E104 A) using the following adjustments: HF (100 kHz) field modulation amplitude 1 G; microwave power 5 mW; scan range 200 G; scan time 15 s; time constant 8 ms, temperature 23–24 °C.

Column chromatography was performed on silica gel (0.060–0.200 mm, 60 A, Acros). CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, ethyl acetate, MeOH, and acetic acid of high purity grade were used as obtained from commercial sources. MeCN was distilled over  $P_2O_5$ .

 $KMnO_4$  99%,  $MnO_2$  99%,  $Mn(OAc)_3 \cdot 2H_2O$  95%, Fe(ClO<sub>4</sub>)<sub>3</sub> hydrate (10.0–12.5% Fe), Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O 99%, 98%,  $Cu(ClO_4)_2 \cdot 6H_2O$ 98%.  $Cu(NO_3)_2 \cdot 2.5 H_2O$ Cu(OAc)<sub>2</sub>·H<sub>2</sub>O 99%, (NH<sub>4</sub>)<sub>2</sub>Ce(NO<sub>3</sub>)<sub>6</sub> 99%, Pb(OAc)<sub>4</sub> 95%,  $K_2Cr_2O_7$  99%,  $Mn(OAc)_2 \cdot 4H_2O$  99%,  $(NH_4)_2S_2O_8$  98%, Co(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O 99%, Co(OAc)<sub>2</sub>·4H<sub>2</sub>O 98%, t-BuOOH (70% aqueous solution)  $H_2O_2$  (34% aqueous solution), PhI(OAc)<sub>2</sub> 98%, dibenzoyl peroxide (BzOOBz, 75%, remainder water), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) 98%, diisopropyl azodicarboxylate (DIAD) 94%, ethyl 2-methyl-3-oxobutanoate 1a 95%, diethyl acetylsuccinate 1c 99%, ethyl 2-oxocyclohexane-1-carboxylate 1f 95%, 2-acetylcyclopentanone 1j 99%, 2-methyl-1,3-cyclohexanedione 1k 98%, and diethyl ethylmalonate 99% 1l were commercial reagents.

Mn(acac)<sub>3</sub><sup>[139]</sup> 2-substituted 1,3-dicarbonyl compounds  $\mathbf{h}_{1}^{[140]}$  1d,<sup>[141]</sup> 1e,<sup>[142]</sup> 1g,<sup>[143]</sup> 1h,<sup>[144]</sup> 1i,<sup>[145]</sup> oximes 2a<sup>[146]</sup> and 2f<sup>[147]</sup> were synthesized according to the literature. Oximes 2c-e, 2h and 2i were synthesized from corresponding carbonyl compounds, NH<sub>2</sub>OH·HCl and NaHCO<sub>3</sub>, 2b was synthesized from ethyl pyruvate and NH<sub>2</sub>OH·HCl; oxime 2g was synthesized from propanal in 3 steps (oxime formation, chlorination and substitution of chlorine with cyanide anion). For experimental details of the synthesis of oximes 2b-e, 2g-i see the Supporting Information.

The composition of  $Fe(ClO_4)_3$  hydrate  $[Fe(ClO_4)_3 \cdot n H_2O]$ was taken as  $Fe(ClO_4)_3 \cdot 8 H_2O$  (MW = 498.4 gmol<sup>-1</sup>) to calculate the weight of this reagent, which corresponds to the specified Fe(III) content (10.0–12.5%, titration by Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>).

#### **Experiments for Table 1**

The oxidant (87.7–1520 mg, 0.555–3.47 mmol, 0.4–2.5 mol/ mol **1a**) was added to a stirred mixture of ethyl 2-methyl-3-oxobutanoate **1a** (200 mg, 1.39 mmol), 3-(hydroxyimino)-pentane-2,4-dione **2a** (179 mg, 1.39 mmol), and the solvent (5 mL) at a specified temperature for 5–10 s. Then the mixture was stirred at the same temperature for a specified

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time. In runs 9 and 35–44, the salts  $Mn(OAc)_2 \cdot 4H_2O$ ,  $Fe(CIO_4)_3 \cdot nH_2O$ ,  $Cu(CIO_4)_2 \cdot 6H_2O$ ,  $Co(OAc)_2 \cdot 4H_2O$ , and  $Co(NO_3)_2 \cdot 6H_2O$  (17.0–544 mg, 0.0693–2.22 mmol, 0.05–1.6 mol/mol **1a**) were added one minute prior to the addition of the oxidant. In runs 40, 41, and 44, a stream of oxygen (0.3 mL s<sup>-1</sup>) was passed through the mixture for 20 min.

The reaction mixture was cooled to room temperature, CHCl<sub>3</sub> (10 mL) and a solution of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> (200 mg) in H<sub>2</sub>O (30 mL) were added, the mixture was shaken, the organic layer was separated, and the aqueous layer was extracted with CHCl<sub>3</sub> (2×10 mL). All organic extracts were combined and washed with H<sub>2</sub>O (3×20 mL). The mixture was dried with MgSO<sub>4</sub>, and the solvent was removed on a rotary evaporator. An oily mixture of products was obtained. Product **3** was isolated by silica gel column chromatography using gradient elution with 0% to 20% (v/v) of ethyl acetate in CH<sub>2</sub>Cl<sub>2</sub>.

In runs 1–15, a part of the mixture of products was analyzed by <sup>1</sup>H NMR spectroscopy with the addition of 1,4-dinitrobenzene as a standard for the determination of the amount of unconsumed ethyl 2-methyl-3-oxobutanoate **1a** based on the signal of the CH fragment ( $\delta$ =3.49, q, J=7.1 Hz, the <sup>1</sup>H NMR spectrum of **1a** is given in the Supporting Information). Unconsumed **1a** was detected only in runs 5 (16%) and 7 (29%).

**Ethyl 2-methyl-3-oxobutanoate (1a):** commercial reagent, 95%; slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.19 (q, *J*=7.1 Hz, 2H, OCH<sub>2</sub>), 3.49 (q, *J*=7.1 Hz, 1H, CHMe), 2.23 (s, 3H, CH<sub>3</sub>C=O), 1.33 (d, *J*=7.1 Hz, 3H, CH<sub>3</sub>), 1.27 (t, *J*=7.1 Hz, 3H, CH<sub>3</sub>).

#### **Experiments for Table 2**

**Method A (oxidant KMnO<sub>4</sub>):** "Macrocrystalline" KMnO<sub>4</sub> (126.4 mg, 0.8 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (228–441 mg, 2 mmol), oxime (196–378.4 mg, 2 mmol), and acetic acid (7 mL) at 40 °C for 5–10 s. The reaction mixture was stirred at 40 °C for 10 min.

Method B [oxidant Mn(OAc)<sub>3</sub>]:  $Mn(OAc)_3$ :  $H_2O$  95% (1.13 g, 4.0 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (228–441 mg, 2 mmol), oxime (196– 428 mg, 2 mmol), and acetic acid (7 mL) at 60 °C for 5–10 s. The reaction mixture was stirred at 60 °C for 5 min.

**Method C [oxidant Mn(OAc)<sub>2</sub>/KMnO<sub>4</sub>]:** "Fine powdered" KMnO<sub>4</sub> (126.4 mg, 0.8 mmol) was added to a stirred mixture of a 1,3-dicarbonyl compound (288–441 mg, 2 mmol), oxime (230–378 mg, 2 mmol), Mn(OAc)<sub>2</sub>·4 H<sub>2</sub>O (784 mg, 3.2 mmol), and acetic acid (7 mL) at 40 °C for 5–10 s, The reaction mixture was stirred at 40 °C for 5 min.

**Product isolation for methods A–C:** The reaction mixture was cooled to room temperature,  $CHCl_3$  (10 mL) and a solution of  $Na_2S_2O_4$  (200 mg) in  $H_2O$  (30 mL) were added, the mixture was shaken, the organic layer was separated, and the aqueous layer was extracted with  $CHCl_3$  (2×10 mL). All organic extracts were combined and washed with a saturated aqueous NaHCO<sub>3</sub> solution (15 mL) and then with  $H_2O$  (20 mL). The mixture was dried with MgSO<sub>4</sub>, and the solvent was removed on a rotary evaporator. Products **3–22** were purified by silica gel column chromatography using gradient elution with 0% to 20% (v/v) of ethyl acetate in  $CH_2Cl_2$ .

### Ethyl 2-(2,4-Dioxopentan-3-ylideneaminooxy)-2methyl-3-oxobutanoate 3 (Experiment with an Increase in the Amounts of the Reagents, Table 2, run 1, note [d])

Macrocrystalline KMnO<sub>4</sub> (438 mg, 2.77 mmol, 0.4 mol/mol of **1a**) was added to a mixture of ethyl 2-methyl-3-oxobutanoate **1a** (1.00 g, 6.93 mmol), 3-(hydroxyimino)pentane-2,4dione **2a** (895 mg, 6.93 mmol), and CH<sub>3</sub>COOH (10 mL) at 40 °C for 10 s. Then the mixture was stirred at the same temperature for 10 min.

The reaction mixture was cooled to room temperature, CHCl<sub>3</sub> (15 mL) and a solution of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> (200 mg) in H<sub>2</sub>O (30 mL) were added, the mixture was shaken, the organic layer was separated, and the aqueous layer was extracted with  $CHCl_3$  (2×10 mL). All organic extracts were combined and washed with a saturated aqueous NaHCO3 solution (15 mL) and then with H<sub>2</sub>O (20 mL). The mixture was dried with MgSO<sub>4</sub>, and the solvent was removed on a rotary evaporator. Ethyl 2-(2,4-dioxopentan-3-ylideneaminooxy)-2methyl-3-oxobutanoate 3 was obtained as a slightly orange oil; yield: 1.74 g (92%) (see <sup>1</sup>H NMR spectrum in the Supporting information); elemental analysis: calcd. (%) for C<sub>12</sub>H<sub>17</sub>NO<sub>6</sub>: C 53.13, H 6.32, N 5.16; found: C 53.09, H 6.17, N 5.40.

Ethyl 2-(2,4-dioxopentan-3-ylideneaminooxy)-2-methyl-3oxobutanoate (3): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$ =4.29–4.13 (m, 2H, OCH<sub>2</sub>), 2.36 (s, 3H, CH<sub>3</sub>), 2.30 (s, 3H, CH<sub>3</sub>), 2.20 (s, 3H, CH<sub>3</sub>), 1.68 (s, 3H, CH<sub>3</sub>), 1.24 (t, *J*=7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$ = 201.1, 197.2, 193.6 (C=O), 167.4 (COO), 157.3 (C=N), 91.5 (CON), 62.4 (CH<sub>2</sub>O), 30.4, 25.8, 25.6, 19.3, 14.1 (CH<sub>3</sub>); IR (thin layer): v<sub>max</sub>=2988, 2943 (CH<sub>2</sub>, CH<sub>3</sub>), 1753, 1728, 1695 (C=O), 1362, 1297, 1270, 1130, 1109, 978, 959 cm<sup>-1</sup>; MS (70 eV) *m*/*z* (%)=271 [M<sup>+</sup>] (47), 159 (100), 117 (95), 112 (60), 89 (53), 55 (95); HR-MS (ESI): *m*/*z*=294.0949, calcd. for C<sub>12</sub>H<sub>17</sub>NO<sub>6</sub>+Na<sup>+</sup>: 294.0948; elemental analysis: calcd. (%) for C<sub>12</sub>H<sub>17</sub>NO<sub>6</sub>: C 53.13, H 6.32, N 5.16; found: C 53.05, H 6.08, N 5.18.

Ethyl 2-{[(1-ethoxy-1-oxopropan-2-ylidene)amino]oxy}-2methyl-3-oxobutanoate (mixture of *E* and *Z* isomers 10:1) (4): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$ =4.38– 4.12 (m, 4H, OCH<sub>2</sub>), 2.25 (s, 2.73 H, CH<sub>3</sub>), 2.22 (s, 0.27 H, CH<sub>3</sub>), 2.15 (s, 2.73 H, CH<sub>3</sub>), 2.05 (s, 0.27 H, CH<sub>3</sub>), 1.68 (s, 2.73 H, CH<sub>3</sub>), 1.61 (s, 0.27 H, CH<sub>3</sub>), 1.40–1.18 (m, 6H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$ =202.8 (C=O), 168.2, 163.5 (COO), 151.4 (C=N), 90.8 (CON), 62.1, 61.9 (OCH<sub>2</sub>), 25.9, 19.7, 14.2, 14.1, 11.9 (CH<sub>2</sub>, CH<sub>3</sub>); IR (CHCl<sub>3</sub>):  $v_{max}$ =1728 (C=O), 1135 cm<sup>-1</sup>; MS (70 eV): *m/z* (%)=228 (72), 159 (86), 117 (100), 87 (94), 84 (95); HR-MS (ESI): *m/z*= 296.1108, calcd. for C<sub>12</sub>H<sub>19</sub>NO<sub>6</sub>+Na<sup>+</sup>: 296.1105; elemental analysis: calcd. (%) for C<sub>12</sub>H<sub>19</sub>NO<sub>6</sub>: C 52.74, H 7.01, N 5.13; found: C 52.65, H 7.13, N 5.21.

Ethyl 2-{[(3,3-dimethylbutan-2-ylidene)amino]oxy}-2methyl-3-oxobutanoate (mixture of *E* and *Z* isomers 12:1) (5): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.28– 4.12 (m, 2H, OCH<sub>2</sub>), 2.22 (s, 3H, CH<sub>3</sub>), 1.90 (s, 3H, CH<sub>3</sub>), 1.59 (s, 3H, CH<sub>3</sub>), 1.24 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>), 1.07 (s, 9H, *t*-Bu); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$  = 204.7 (C=O), 169.2, 165.9 (COO, C=N), 89.3 (CON), 61.6 (OCH<sub>2</sub>), 37.7 (CH<sub>3</sub>), 27.7 (3CH<sub>3</sub>), 25.8, 19.7, 14.2, 10.8 (CH<sub>3</sub>); IR (thin layer): v<sub>max</sub> = 2971, 2940, 2909, 2873 (CH<sub>3</sub>, CH<sub>2</sub>), 1754, 1733

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(C=O), 1368, 1264, 1170, 1133, 1108, 907 cm<sup>-1</sup>; MS (70 eV): m/z (%)=117 (34), 98 (56), 84 (100), 59 (51), 55 (56), 45 (69), 43 (47); HR-MS (ESI): m/z = 280.1524, calcd. for  $C_{13}H_{23}NO_4 + Na^+: 280.1519.$ 

2-{[(2,4-dimethylpentan-3-ylidene)amino]oxy}-2-Ethvl methyl-3-oxobutanoate (6): Slightly yellow oil; <sup>1</sup>H NMR  $(300.13 \text{ MHz}, \text{ CDCl}_3): \delta = 4.27 - 4.11 \text{ (m, 2H, OCH}_2), 3.10$ (heptet, J = 7.0 Hz, 1H, CHMe<sub>2</sub>), 2.58–2.42 (m, 1H, CHMe<sub>2</sub>), 2.22 (s, 3H, CH<sub>3</sub>), 1.58 (s, 3H, CH<sub>3</sub>), 1.24 (t, J =7.1 Hz, 3H, CH<sub>3</sub>), 1.17 (d, J=7.0 Hz, 6H, CH<sub>3</sub>), 1.10–0.96 (m, 6H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 204.8$  (C= O), 170.4, 169.2 (COO, C=N), 89.3 (CON), 61.6 (OCH<sub>2</sub>), 31.4, 28.6, 25.9, 21.30, 21.28, 19.5, 19.0, 18.9, 14.2 (CH<sub>3</sub>, CH); IR (thin layer):  $v_{max}$ =2969, 2938, 2875 (CH, CH<sub>2</sub>, CH<sub>3</sub>), 1754, 1733 (C=O), 1366, 1265, 1132, 1105, 910 cm<sup>-1</sup>; MS  $(70 \text{ eV}): m/z \ (\%) = 271 \ (2) \ [M^+], 155 \ (25), 112 \ (35), 89 \ (33),$ 85 (30), 71 (38), 70 (100); HR-MS (ESI): m/z = 294.1672, calcd. for  $C_{14}H_{25}NO_4 + Na^+$ : 294.1676; elemental analysis: calcd. (%) for C<sub>14</sub>H<sub>25</sub>NO<sub>4</sub>: C 61.97, H 9.29, N 5.16; found: C 61.71, H 9.10, N 5.16.

Ethyl (E)-2-{[(1-(4-bromophenyl)ethylidene)amino]oxy}-2-methyl-3-oxobutanoate (7): Slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 7.48$  (m, 4H, ArH), 4.32–4.18 (m, 2H, OCH<sub>2</sub>), 2.33 (s, 3H, CH<sub>3</sub>), 2.28 (s, 3H, CH<sub>3</sub>), 1.70 (s, 3H, CH<sub>3</sub>), 1.26 (t, J=7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 203.8$  (C=O), 168.8, 156.0 (COO, C=N), 134.7, 131.8, 127.8, 124.2 (C<sub>Ar</sub>), 90.1 (CON), 61.9  $(OCH_2)$ , 25.8, 19.8, 14.2, 12.8  $(CH_3)$ ; IR (thin layer):  $v_{max} =$ 2984, 2939 (CH<sub>2</sub>, CH<sub>3</sub>), 1751, 1731 (C=O), 1368, 1266, 1132, 1105, 1009, 999, 916, 827 cm<sup>-1</sup>; HR-MS (ESI): m/z =378.0306, calcd. for  $C_{15}H_{18}BrNO_4 + Na^+$ : 378.0311.

Ethyl 2-acetyl-2-{[(2,4-dioxopentan-3-ylidene)amino]oxy}hexanoate (8): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 4.25$  (q, J = 7.0 Hz, 2H, OCH<sub>2</sub>), 2.42 (s, 3H, CH<sub>3</sub>), 2.33 (s, 3H, CH<sub>3</sub>), 2.27–2.13 (m, 2H, CH<sub>2</sub>), 2.22 (s, 3H, CH<sub>3</sub>), 1.42–1.11 (m, 7H, CH<sub>2</sub>, CH<sub>3</sub>), 0.88 (t, J=7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 201.3$ , 197.4, 193.8 (C=O), 167.1 (COO), 157.4 (C=N), 94.4 (CON), 62.4 (OCH<sub>2</sub>), 32.8, 30.5, 26.6, 25.9, 25.2, 22.7, 14.2, 13.8 (CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer):  $v_{max} = 2963$ , 2936, 2854 (CH<sub>2</sub>, CH<sub>3</sub>), 1754, 1729, 1695 (C=O), 1363 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 313 (12) [M<sup>+</sup>], 201 (62), 159 (71), 85 (100), 42 (66); HR-MS (ESI): m/z = 336.1409, calcd. for C<sub>15</sub>H<sub>23</sub>NO<sub>6</sub>+Na<sup>+</sup>: 336.1418; elemental analysis: calcd. (%) for C<sub>15</sub>H<sub>23</sub>NO<sub>6</sub>: C 57.50, H 7.40, N 4.47; found: C 57.48, H 7.51, N 4.37.

Diethyl 2-acetyl-2-{[(2,4-dioxopentan-3-ylidene)amino]oxy}succinate (9): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 4.25$  (q, J = 7.1 Hz, 2H, OCH<sub>2</sub>), 4.10 (q, J =7.2 Hz, 2H, OCH<sub>2</sub>), 3.47 (d, J = 17.2 Hz, 1H, CH<sub>2</sub>), 3.32 (d,  $J = 17.2 \text{ Hz}, 1 \text{ H}, \text{ CH}_2$ , 2.39 (s, 3 H, CH<sub>3</sub>), 2.33 (s, 3 H, CH<sub>3</sub>), 2.32 (s, 3H, CH<sub>3</sub>), 1.34–1.18 (m, 6H, CH<sub>3</sub>);  $^{13}C$  NMR  $(75.47 \text{ MHz}, \text{ CDCl}_3): \delta = 200.8, 196.8, 193.4 \text{ (C=O)}, 168.7,$ 165.7 (COO), 157.8 (C=N), 91.7 (CON), 62.9, 61.4 (OCH<sub>2</sub>), 38.6, 30.4, 26.4, 25.9, 14.14, 14.09 (CH<sub>3</sub>, CH<sub>2</sub>); IR (thin layer): v<sub>max</sub>=2986, 2942, 2911, 2876 (CH<sub>2</sub>, CH<sub>3</sub>), 1731, 1696 (C=O), 1366, 1358, 1297, 1276, 1232, 1214, 1194, 1055, 1022, 965, 943 cm<sup>-1</sup>; MS (70 eV): m/z (%)=189 (100), 143 (84), 115 (92), 86 (70), 69 (62); HR-MS (ESI): m/z = 366.1147, calcd. for  $C_{15}H_{21}NO_8 + Na^+$ : 366.1159; elemental analysis: calcd. (%) for C<sub>15</sub>H<sub>21</sub>NO<sub>8</sub>: C 52.47, H 6.17, N 4.08; found: C 52.51, H 6.15, N 4.20.

Ethyl 2-acetyl-2-{[(2,4-dioxopentan-3-ylidene)amino]oxy}pent-4-enoate (10): Slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 5.73 - 5.51$  (m, 1H, C=CH), 5.21-5.04 (m, 2H, C=CH<sub>2</sub>), 4.24 (q, J=7.1 Hz, 2H OCH<sub>2</sub>), 2.96 (d, J = 7.0 Hz, 2H, CH<sub>2</sub>), 2.39 (s, 3H, CH<sub>3</sub>), 2.33 (s, 3H,  $CH_3$ ), 2.20 (s, 3H,  $CH_3$ ), 1.26 (t, J=7.1 Hz, 3H,  $CH_3$ ); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 200.7$ , 197.2, 193.6 (C= O), 166.5 (COO), 157.5 (C=N), 130.1, 120.5 (C=C), 93.6 (CON), 62.5 (OCH<sub>2</sub>), 37.6, 30.4, 26.7, 25.9, 14.2 (CH<sub>2</sub>, CH<sub>3</sub>); IR (CHCl<sub>3</sub>):  $v_{max} = 1752$ , 1728, 1695 (C=O) cm<sup>-1</sup>; MS  $(70 \text{ eV}): m/z \ (\%) = 255 \ (100), \ 143 \ (95), \ 115 \ (74); \ HR-MS$ (ESI): m/z = 320.1099, calcd. for  $C_{14}H_{19}NO_6 + Na^+$ : 320.1105; elemental analysis: calcd. (%) for C14H19NO6: C 56.56, H 6.44, N 4.71; found: C 56.85, H 6.67, N 5.04.

Diethyl 2-{[(2-benzyl-1-ethoxy-1,3-dioxobutan-2-yl)oxy]imino}malonate (11): Slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 7.33-7.16$  (m, 3H, ArH), 7.16-7.03 (m, 2H, ArH), 4.47-4.08 (m, 6H, OCH<sub>2</sub>), 3.55 (s, 2H, PhCH<sub>2</sub>), 1.95 (s, 3H, CH<sub>3</sub>), 1.36 (t, J=7.1 Hz, 3H, CH<sub>3</sub>), 1.28 (t, J = 7.2 Hz, 3H, CH<sub>3</sub>), 1.22 (t, J = 7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup> NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 202.1$  (C=O), 166.2, 160.0, 159.2 (COO), 146.3 (C=N), 133.9, 130.6, 128.4, 127.2 (C<sub>Ar</sub>), 94.8 (CON), 62.9, 62.6, 62.4 (OCH<sub>2</sub>), 38.9, 27.2, 14.13, 14.05 (CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer):  $v_{max}$ =2985, 1752, 1725, 1258, 1095 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 407 (3) [M], 217 (57), 193 (59), 192 (59), 131 (76), 119 (100), 91 (86), 56 (72); HR-MS (ESI): m/z = 430.1469, calcd. for C<sub>20</sub>H<sub>25</sub>NO<sub>8</sub>+Na<sup>+</sup>: 430.1472; elemental analysis: calcd. (%) for C<sub>20</sub>H<sub>25</sub>NO<sub>8</sub>: C 58.96, H 6.19, N 3.44; found: C 58.99, H 6.27, N 3.38.

Ethyl 2-benzyl-2-{[(2,4-dimethylpentan-3-ylidene)ami**no]oxy}-3-oxobutanoate** (12): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta = 7.25 - 7.15$  (m, 3H, ArH), 7.15-7.03 (m, 2H, ArH), 4.28–4.05 (m, 2H, OCH<sub>2</sub>), 3.57 (d, J =14.1 Hz, 1H, PhCH<sub>2</sub>), 3.43 (d, J = 14.1 Hz, 1H, PhCH<sub>2</sub>), 3.15-2.96 (m, 1H, CHMe<sub>2</sub>), 2.68-2.50 (m, 1H, CHMe<sub>2</sub>), 1.99 (s, 3H, CH<sub>3</sub>C=O), 1.21 (t, J = 7.1 Hz, 3H, CH<sub>3</sub>), 1.17–1.09 (m, 12H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 204.8$ (C=O), 170.6, 168.1 (COO, C=N), 135.7, 130.6, 128.1, 126.7 (CAr), 92.5 (CON), 61.6 (OCH2), 38.5, 31.6, 28.8, 27.2, 21.4, 18.8, 18.7, 14.2 (CH, CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer):  $v_{max} = 2968$ , 2935, 2874 (CH<sub>3</sub>, CH<sub>2</sub>, CH), 1754, 1722 (C=O), 1467, 1455, 1366, 1353, 1260, 1231, 1198, 1085, 1067, 1018, 912, 702 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 219 (26), 112 (28), 91 (93), 70 (100); elemental analysis: calcd. (%) for C<sub>20</sub>H<sub>29</sub>NO<sub>4</sub>: C 69.14, H 8.41, N 4.03; found: C 69.28, H 8.44, N 4.21.

Ethyl 1-{[(2,4-dioxopentan-3-ylidene)amino]oxy}-2-oxocyclohexane-1-carboxylate (13): Colorless oil; <sup>1</sup>H NMR  $(300.13 \text{ MHz}, \text{ CDCl}_3): \delta = 4.35 - 4.18 \text{ (m, 2H, OCH}_2), 2.69 - 4.18 \text{ (m, 2H, OCH}_2)$ 2.51 (m, 2H, CH<sub>2</sub>), 2.51–2.12 (m, 2H, CH<sub>2</sub>), 2.37 (s, 3H,  $CH_3$ , 2.29 (s, 3 H,  $CH_3$ ), 2.00–1.60 (m, 4 H,  $CH_2$ ), 1.28 (t, J =7.0 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 202.6$ , 197.7, 193.9 (C=O), 168.2 (COO), 156.9 (C=N), 91.2 (CON), 62.1 (OCH<sub>2</sub>), 40.0, 34.9, 30.4, 27.2, 25.8, 20.8, 14.2 (CH<sub>3</sub>, CH<sub>2</sub>); IR (thin layer):  $v_{max}$ =2945, 2871 (CH<sub>2</sub>, CH<sub>3</sub>), 1749, 1728, 1693 (C=O), 1365, 1298, 1282, 1249, 1096, 1052, 998, 962, 943 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 185 (84), 111 (100), 83 (72), 55 (95); HR-MS (ESI): m/z = 320.1105, calcd. for  $C_{14}H_{19}NO_6 + Na^+$ : 320.1105; elemental analysis: calcd. (%) for C<sub>14</sub>H<sub>19</sub>NO<sub>6</sub>: C 56.56, H 6.44, N 4.71; found: C 56.59, H 6.55, N 4.86.

Ethyl 2-{[(3-methyl-2,4-dioxopentan-3-yl)oxy]imino}propanoate (mixture of E and Z isomers 15:1) (14): Colorless

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oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  (*E*-isomer) = 4.24 (q, J = 7.1 Hz, 2H, OCH<sub>2</sub>), 2.19 (s, 6H, O = CCH<sub>3</sub>), 2.17 (s, 3H, N = CCH<sub>3</sub>), 1.61 (s, 3H, CH<sub>3</sub>), 1.28 (t, J = 7.1 Hz, 3H, CH<sub>3</sub>);  $\delta$  (*Z*-isomer, minor) = 4.33 (q, J = 7.1 Hz, 2H, OCH<sub>2</sub>), 2.23 (s, 3H, CH<sub>3</sub>), 1.34 (t, J = 7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$  = 203.3 (C=O), 163.3 (COO), 151.8 (C=N), 95.8 (CON), 62.0 (OCH<sub>2</sub>), 26.2, 19.4, 14.1, 12.0 (CH<sub>3</sub>); IR (thin layer):  $v_{max}$  = 2988, 2940 (CH2, CH3), 1739, 1720 (C=O), 1367, 1359, 1322, 1178, 1155, 1132, 1120, 1000 cm<sup>-1</sup>; MS (70 eV): *m/z* (%) = 243 (1) [M+], 199 (36), 159 (32), 130 (47), 88 (69), 87 (59), 84 (100); HR-MS (ESI): *m/z* = 266.1008, calcd. for C<sub>11</sub>H<sub>17</sub>NO<sub>5</sub> + Na<sup>+</sup>: 266.0999; elemental analysis: calcd. (%) for C<sub>11</sub>H<sub>17</sub>NO<sub>5</sub>: C, 54.31; H, 7.04; N, 5.76. found: C, 54.51; H, 7.16; N, 5.84.

Pure major *E*-isomer and a fraction containing concentrated Z-isomer in mixture with *E*-isomer were isolated by additional column chromatography. <sup>1</sup>H NMR (300.13 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (*E*-isomer)=4.22 (q, *J*=7.1 Hz, 2H, OCH<sub>2</sub>), 2.18 (s, 6H, CH<sub>3</sub>), 2.16 (s, 3H, CH<sub>3</sub>), 1.50 (s, 3H, CH<sub>3</sub>), 1.23 (t, *J*=7.1 Hz, 3H, CH<sub>3</sub>);  $\delta$  (*Z*-isomer)=4.32 (q, *J*=7.1 Hz, 2H, OCH<sub>2</sub>), 2.13 (s, 6H, CH<sub>3</sub>), 2.06 (s, 3H, CH<sub>3</sub>), 1.42 (s, 3H, CH<sub>3</sub>), 1.30 (t, *J*=7.1 Hz, 3H, CH<sub>3</sub>). The structures and configurations of **14**-*E* and **14**-*Z* were confirmed by HMBC and NOESY 2D NMR (see the Supporting Information).

N-[(3-Methyl-2,4-dioxopentan-3-yl)oxy]propionimidoyl cyanide (Mixture of E and Z isomers 4:1) (15): Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  (*E*-isomer)=2.64 (q, J=7.7 Hz, 2H, CH<sub>2</sub>), 2.18 (s, 6H, CH<sub>3</sub>), 1.64 (s, 3H, CH<sub>3</sub>), 1.28 (t, J=7.7 Hz, 3H, CH<sub>3</sub>);  $\delta$  (Z-isomer)=2.52 (q, J=7.5 Hz, 2H, CH<sub>2</sub>), 2.23 (s, 6H, CH<sub>3</sub>), 1.60 (s, 3H, CH<sub>3</sub>), 1.22 (t, J = 7.5 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$ (E-isomer)=201.9 (C=O), 143.3 (C=N), 113.4 (CN), 96.6 (CON), 26.02, 21.9, 19.2, 9.7 (CH<sub>3</sub>, CH<sub>2</sub>);  $\delta$  (Z-isomer) = 202.3 (C=O), 137.1 (C=N), 109.8 (CN), 96.2 (CON), 26.2, 25.95, 19.0, 10.7 (CH<sub>3</sub>, CH<sub>2</sub>); IR (thin layer):  $v_{max} = 2985$ , 2943, 2886 (CH<sub>2</sub>, CH<sub>3</sub>), 1740, 1718, 1358, 1120, 993 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 169 (48), 87 (100), 71 (66); HR-MS(ESI): m/z = 233.0889, calcd. for  $C_{10}H_{14}N_2O_3 + Na^+$ : 233.0897; elemental analysis: calcd. (%) for  $C_{10}H_{14}N_2O_3$ : C 57.13, H 6.71, N 13.33; found: C 57.17, H 6.55, N 13.39.

3-{[(2,4-Dimethylpentan-3-ylidene)amino]oxy}-3-methylpentane-2,4-dione (16): Colorless oil; <sup>1</sup>H NMR  $(300.13 \text{ MHz}, \text{ CDCl}_3): \delta = 3.11 \text{ (heptet, } J = 7.1 \text{ Hz}, 1 \text{ H}, \text{ CH}),$ 2.52 (heptet, J = 6.8 Hz, 1H, CH), 2.17 (s, 6H, O=CCH<sub>3</sub>), 1.49 (s, 3 H, CH<sub>3</sub>), 1.19 (d, J = 7.1 Hz, 6 H, CH<sub>3</sub>), 1.04 (d, J =6.8 Hz, 6H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 205.1$ (C=O), 170.9 (C=N), 94.1 (CON), 31.5, 28.7 (CH), 26.3, 21.3, 19.1, 19.0 (CH<sub>3</sub>); IR (thin layer):  $v_{max} = 2969$ , 2936, 2875 (CH, CH<sub>3</sub>), 1740, 1715 (C=O), 1355, 1117, 1101, 900 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 88 (16), 72 (18), 71 (100); HR-MS (ESI): m/z = 264.1559, calcd. for  $C_{13}H_{23}NO_3 + Na^+$ : 264.1570; elemental analysis: calcd. (%) for C<sub>13</sub>H<sub>23</sub>NO<sub>3</sub>: C 64.70; H 9.61, N 5.80; found: C 64.41, H 9.51, N 5.71.

**3-Methyl-3-[(undecan-6-ylideneamino)oxy]pentane-2,4-dione (17):** Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.45–2.30 (m, 2H, N = CCH<sub>2</sub>), 2.24–2.08 (m, 2H, N = CCH<sub>2</sub>), 2.18 (s, 6H, CH<sub>3</sub>), 1.64–1.40 (m, 4H, CH<sub>2</sub>), 1.50 (s, 3H, CH<sub>3</sub>), 1.40–1.17 (m, 8H, CH<sub>2</sub>), 1.00–0.80 (m, 6H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$  = 205.1 (C=O), 164.1 (C= N), 93.9 (CON), 34.1, 32.2, 31.5, 28.6, 26.2, 25.9, 25.6, 22.48, 22.45, 19.2, 14.07, 14.06 (CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer): v<sub>max</sub> = 2958, 2932, 2872, 2862 (CH<sub>2</sub>, CH<sub>3</sub>), 1740, 1716 (C=O), 1460, 1441, 1420, 1354, 1141, 1113, 1100, 893 cm<sup>-1</sup>; MS (70 eV): m/z (%)=297 (4) [M+], 169 (52), 99 (100), 71 (57); HR-MS (ESI): m/z=320.2196, calcd. for C<sub>17</sub>H<sub>31</sub>NO<sub>3</sub>+Na<sup>+</sup>: 320.2198; elemental analysis: calcd. (%) for C<sub>17</sub>H<sub>31</sub>NO<sub>3</sub>: C 68.65, H 10.51, N 4.71; found: C 68.60, H 10.65, N 4.74.

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Catalysis

Synthesis &

**3-Methyl-3-[(pentan-3-ylideneamino)oxy]pentane-2,4-dione (18):** Slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$ =2.41 (q, *J*=7.6 Hz, 2H, CH<sub>2</sub>), 2.29–2.14 (m, 2H, CH<sub>2</sub>), 2.18 (s, 6H, CH<sub>3</sub>), 1.51 (s, 3H, CH<sub>3</sub>), 1.13 (t, *J*=7.6 Hz, 3H, CH<sub>3</sub>), 1.03 (t, *J*=7.4 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$ =205.1 (C=O), 165.8 (C=N), 93.9 (CON), 27.3, 26.2, 22.0, 19.1, 10.8, 10.4 (CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer):  $v_{max}$ =2976, 2940, 2881 (CH<sub>2</sub>, CH<sub>3</sub>), 1739, 1715 (C=O), 1355, 1141, 1119, 1100, 922, 890 cm<sup>-1</sup>; MS (70 eV): *m/z* (%)=213 (30) [M<sup>+</sup>], 102 (58), 99 (88), 87 (89), 84 (100); HR-MS (ESI): *m/z*=236.1258, calcd. for C<sub>11</sub>H<sub>19</sub>NO<sub>3</sub>+Na<sup>+</sup>: 236.1257.

**3-Butyl-3-{[(2,4-dioxopentan-3-ylidene)amino]oxy}pentane-2,4-dione (19):** Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$ =2.42 (s, 3H, CH<sub>3</sub>), 2.31 (s, 3H, CH<sub>3</sub>), 2.25–2.11 (m, 2H, CH<sub>2</sub>), 2.17 (s, 6H, CH<sub>3</sub>), 1.38–1.22 (m, 2H, CH<sub>2</sub>), 1.22–1.07 (m, 2H, CH<sub>2</sub>), 0.86 (t, *J*=7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$ =201.8, 197.5, 193.7 (C= O), 157.7 (C=N), 100.0 (CON), 32.9, 30.3, 27.0, 25.8, 25.2, 22.8, 13.8 (CH<sub>2</sub>, CH<sub>3</sub>); IR (CHCl<sub>3</sub>): v<sub>max</sub>=2963, 2934, 2875, 2866 (CH<sub>2</sub>, CH<sub>3</sub>), 1725, 1717, 1695 (C=O), 1358, 977 cm<sup>-1</sup>; MS (70 eV): *m*/*z* (%)=173 (68), 172 (72), 130 (100), 129 (71), 85 (77); HR-MS (ESI): *m*/*z*=306.1319, calcd. for C<sub>14</sub>H<sub>21</sub>NO<sub>5</sub>+Na<sup>+</sup>: 306.1312; elemental analysis: calcd. (%) for C<sub>14</sub>H<sub>21</sub>NO<sub>5</sub>: C 59.35, H 7.47, N 4.94; found: C 59.54, H 7.61, N 4.77.

**Diethyl 2-{[(3-benzyl-2,4-dioxopentan-3-yl)oxy]imino}malonate** (20): Slightly yellow oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.32–7.18 (m, 3H, ArH), 7.12–7.00 (m, 2H, ArH), 4.46–4.30 (m, 4H, OCH<sub>2</sub>), 3.50 (s, 2H, PhCH<sub>2</sub>), 1.96 (s, 6H, CH<sub>3</sub>), 1.38 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>), 1.30 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.3 (C=O), 160.0, 159.1 (COO), 146.9 (C=N), 134.0, 130.5, 128.5, 127.3 (C<sub>Ar</sub>), 100.0 (CON), 63.1, 62.8 (OCH<sub>2</sub>), 38.9, 27.4, 14.2, 14.1 (CH<sub>2</sub>, CH<sub>3</sub>); IR (CHCl<sub>3</sub>):  $v_{max}$ =1745, 1719 (C=O), 1260, 1094 cm<sup>-1</sup>; MS (70 eV): *m/z* (%) = 377 (13) [M<sup>+</sup>], 293 (79), 217 (100), 187 (46), 174 (66); HR-MS (ESI): *m/z* = 400.1362, calcd. for C<sub>19</sub>H<sub>23</sub>NO<sub>7</sub>+Na<sup>+</sup>: 400.1367; elemental analysis: calcd. (%) for C<sub>19</sub>H<sub>23</sub>NO<sub>7</sub>: C 60.47, H 6.14, N 3.71; found: C 60.91, H 6.48, N 4.06.

**3-{[(1-Acetyl-2-oxocyclopentyl)oxy]imino}pentane-2,4-dione (21):** Colorless oil; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta =$ 2.73–2.59 (m, 1H, CH<sub>2</sub>), 2.54–2.31 (m, 2H, CH<sub>2</sub>), 2.37 (s, 3H, CH<sub>3</sub>), 2.33 (s, 3H, CH<sub>3</sub>), 2.31–2.16 (m, 1H, CH<sub>2</sub>), 2.24 (s, 3H, CH<sub>3</sub>), 2.14–1.99 (m, 2H, CH<sub>2</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 209.1$ , 203.2, 197.2, 193.5 (C=O), 157.9 (C=N), 95.9 (CON), 37.0, 31.9, 30.5, 26.6, 25.9, 18.1 (CH<sub>2</sub>, CH<sub>3</sub>); IR (thin layer):  $v_{max} = 2974$ , 2925 (CH<sub>2</sub>, CH<sub>3</sub>), 1758, 1724, 1694 (C=O), 1421, 1359, 1296, 1167, 1029, 989, 964, 940 cm<sup>-1</sup>; MS (70 eV): m/z (%)=141 (100), 113 (19), 100 (16); HR-MS (ESI): m/z = 276.0836, calcd. for C<sub>12</sub>H<sub>15</sub>NO<sub>5</sub>+Na<sup>+</sup>: 276.0842; elemental analysis: calcd. (%) for C<sub>12</sub>H<sub>15</sub>NO<sub>5</sub>: C 56.91, H 5.97, N 5.53; found: C 56.81, H 5.99, N 5.46.

**2-{[(2,4-Dioxopentan-3-ylidene)amino]oxy}-2-methylcyclohexane-1,3-dione (22):** White crystals; mp 115–116 °C; <sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.87–2.62 (m, 4H, CH<sub>2</sub>), 2.37 (s, 3H, CH<sub>3</sub>), 2.25 (s, 3H, CH<sub>3</sub>), 2.02–1.84 (m, 2H,

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CH<sub>2</sub>), 1.57 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>):  $\delta = 203.1$ , 197.3, 193.8 (C=O), 157.0 (C=N), 94.5 (CON), 38.3, 30.4, 25.8, 18.9, 17.9 (CH<sub>2</sub>, CH<sub>3</sub>); IR (KBr):  $v_{max} = 2972$ , 2916, 2871 (CH<sub>2</sub>, CH<sub>3</sub>), 1742, 1715, 1691 (C=O), 1130, 1016, 969, 571 cm<sup>-1</sup>; MS (70 eV): m/z (%) = 114 (62), 99 (68), 72 (65), 56 (100); HR-MS (ESI): m/z = 276.0833, calcd. for C<sub>12</sub>H<sub>15</sub>NO<sub>5</sub> + Na<sup>+</sup>: 276.0842; elemental analysis: calcd. (%) for C<sub>12</sub>H<sub>15</sub>NO<sub>5</sub>: C 56.91, H 5.97, N 5.53; found: C 57.00, H 5.99, N 5.51.

#### **Experiments for Table 3**

Since  $Mn(OAc)_3 \cdot 2H_2O$ ,  $KMnO_4$  and  $(NH_4)_2Ce(NO_3)_6$  are poorly soluble in AcOH, it was impossible to prepare solutions of these oxidants at concentrations appropriate for experiments. Hence, different procedures were used in runs 1-5 (heterogeneous reaction mixture) and runs 6-9 (homogeneous reaction mixture). In all experiments, the complete conversion of oxime 2a into iminoxyl radical A corresponds to the concentration of the latter equal to 0.005 mol/L. The concentration of radical A was determined by the double integration of the ESR spectrum. Solutions of the stable nitroxyl radical 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) were used as concentration standards in MeCN (to estimate the concentration of A in runs 6 and 7 in MeCN) and in EtOAc (to estimate the concentration of A in runs 1–5 and 8 and 9 in AcOH). It is incorrect to use a solution of TEMPO in AcOH as a concentration standard because this nitroxyl radical can disproportionate in an acidic medium.<sup>[148,149]</sup> Hence, ethyl acetate was used instead of AcOH because these solvents have similar relative permittivities (dielectric constants):<sup>[150]</sup> 6.02 for EtOAc and 6.15 for AcOH.[151]

In runs 1–5, a solution of 3-(hydroxyimino)pentane-2,4dione **2a** (32.3 mg, 0.25 mmol) in AcOH (50 mL) was added to the oxidant (the amounts are given below). Then the mixture was continuously shaken, and samples were taken at certain time intervals for ESR measurements. In run 2, a solution of **2a** in acetic acid contained  $Mn(OAc)_2$ ·4H<sub>2</sub>O (49.0 mg, 0.2 mmol). The amounts of the oxidant were as follows:  $Mn(OAc)_3$ ·2H<sub>2</sub>O 95% (70.6 mg, 0.25 mmol, run 1), KMnO<sub>4</sub> (7.90 mg, 0.05 mmol, runs 2 and 3), KMnO<sub>4</sub> (15.8 mg, 0.1 mmol, run 4), (NH<sub>4</sub>)<sub>2</sub>Ce(NO<sub>3</sub>)<sub>6</sub> (137 mg, 0.25 mmol, run 5). "Fine powdered" KMnO<sub>4</sub> was used for ESR experiments (see Figure 1, sample 3).

In runs 6 and 7, a solution of  $Fe(ClO_4)_3$ ,  $nH_2O$  or  $Cu(ClO_4)_2$ ,  $6H_2O$  in MeCN (0.01 mol/L, 1.0 mL) was mixed with a solution of oxime **2a** in MeCN (0.01 mol/L, 1.0 mL) at room temperature. Then ESR spectra of the solution were registered at certain time intervals.

In runs 8 and 9, a solution of  $Pb(OAc)_4$  or  $PhI(OAc)_2$  in AcOH (0.005 mol/L, 1.0 mL) was mixed with a solution of oxime **2a** in AcOH (0.01 mol/L, 1.0 mL) at room temperature. Then ESR spectra of the solution were registered at certain time intervals.

### Acknowledgements

This work was supported by the Russian Foundation for Basic Research (Grant 13-03-12074) and the Programs "Molecular and Cell Biology" and " Development of methodology of organic synthesis and design of compounds with valuable applied properties" of the Presidium of the Russian Academy of Sciences. High resolution mass spectroscopy and electron microscopy were performed in the Department of Structural Studies of Zelinsky Institute of Organic Chemistry, Moscow.

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Adv. Synth. Catal. 2014, 356, 1-16

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