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Heavier Alkaline Earth Amides as Catalysts for the Tischenko Reaction

Mark R. Crimmin,[†] Anthony G. M. Barrett,*[,†] Michael S. Hill,*[,†] and Panayiotis A. Procopiou[‡]

Department of Chemistry, Imperial College London, Exhibition Road, South Kensington, London SW7 2AZ, U.K., and GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, U.K.

mike.hill@imperial.ac.uk

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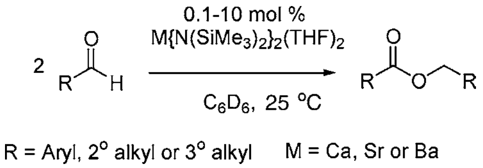
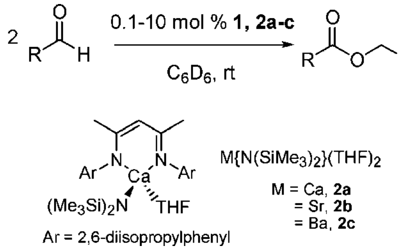
ABSTRACT



Homoleptic heavier alkaline earth amides, $M\{N(SiMe_3)_2\}_2(THF)_2$ (M = Ca, Sr, and Ba) are reported as precatalysts for the dimerization of aldehydes to the analogous carboxylic esters (Tischenko reaction).

Recent years have witnessed a dramatic growth in the coordination chemistry of the heavier alkaline earth metals.[1] Although it has long been speculated that the highly ionic and nondirectional bonding in heavier alkaline earth compounds, coupled with the preclusion of redox behavior, may afford a catalytic reaction chemistry paralleling that of lanthanide(III) organometallics, well-defined examples of such reactivity have only recently begun to emerge. Explorations by Harder of the reactivity of homoleptic heavier alkaline earth benzyl complexes have shown that they may act as catalysts for both the polymerization of styrene and the hydrosilylation of moderately activated alkenes.[2] Furthermore, we have found that the β-diketiminato-stabilized calcium amide **1** (Scheme 1) is an effective catalyst for the intramolecular hydroamination and intermolecular hydrophosphination of alkenes and alkynes.[3]

Scheme 1. Heavier Alkaline Earth Catalyzed Tischenko Reaction



The dimerization of aldehydes to the analogous carboxylic esters, or the Tischenko reaction, has been known for over a century. The reaction represents an atom-efficient synthesis of esters and is industrially relevant as the homodimers of simple aldehydes have found numerous applications in the food and perfume industries. A number of transition metal and main group compounds are reported to catalyze the reaction. Although aluminum alkoxides are typically employed as homogeneous catalysts,[4] $K_2[Fe(CO)_4]$,[5] Cp_2MH_2 (M = Zr, Hf),[6] and $B(OH)_3$[7] also display moderate activities

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[†] Imperial College London.

[‡] GlaxoSmithKline Medicines Research Centre.

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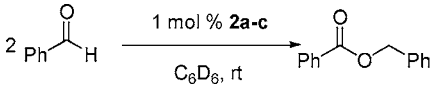
for the dimerization of benzaldehyde to benzyl benzoate. More recently, homoleptic lanthanide amides, $M[N(SiMe_3)_2]_3$ (M = Sc, Y, La), have been reported as highly active catalysts for the Tischenko reaction, mediating the dimerization of aromatic and aliphatic aldehydes to the carboxylic esters with turnover frequencies (TOF) ranging from 2 to 1500 h^{-1}.[8] In this instance, the reaction mechanism has been investigated and proposed to occur via the formation of an intermediate lanthanide(III) alkoxide.[8]

We now present a preliminary report that the heteroleptic calcium amide **1** and the readily synthesized homoleptic alkaline earth amides **2a**−**c** are competent precatalysts for the dimerization of aldehydes to carboxylic esters (Scheme 1).

An initial reaction between benzaldehyde and 10 mol % of **1** was conducted on an NMR scale in C_6D_6. After 1 h at room temperature, the production of benzyl benzoate was observed as evidenced by the appearance of a characteristic methylene singlet of the product at 5.21 ppm, with a concomitant decrease in intensity of the aldehyde proton of benzaldehyde. The reaction was complete within 2 h, and benzyl benzoate was identified as the major volatile product by NMR and GC-MS analysis. The reaction could be repeated with 1 mol % of **1** with no loss of activity. In both cases, the dimerization of benzaldehyde was accompanied by the production of the protonated ligand ArNHC(Me)CHC(Me)NAr (Ar = 2,6-diisopropylphenyl), observed in the ^1H NMR. This result suggested the catalytically active species was not supported by the spectator ligand. On the basis of this observation, a series of simple homoleptic alkaline earth amides, $M\{N(SiMe_3)_2\}_2(THF)_2$ (M = Ca, Sr, and Ba, **2a**−**c**), were synthesized by metathesis of MI_2 with 2 equiv of $KN(SiMe_3)_2$ in THF, and their catalytic reaction with benzaldehyde was investigated on an NMR scale. The results of these experiments are presented in Table 1. Compounds **2a**−**c** were found to be active catalysts for the dimerization of benzaldehyde to benzyl benzoate. In all cases, the latter was observed as the major product of the reaction. The turnover frequency of the reaction decreases with increasing ionic radius of the alkaline earth metal. This result is in stark contrast to that observed in the lanthanide series, $M\{N(SiMe_3)_2\}_3$ (M = Sc, Y, La), for the same reaction where turnover frequencies increase with increasing ionic radius.[8] Indeed, although the reaction could be catalyzed by $Ba\{N(SiMe_3)_2\}_2(THF)_2$, **2c**, turnover was markedly slow and the reaction took several days to near completion.

Table 1. Dimerization of Benzaldehyde to Benzyl Benzoate Catalyzed by 1 mol % of $M\{N(SiMe_3)_2\}_2(THF)_2$ in C_6D_6 at Room Temperature



catalyst	TOF/h^{-1}	NMR yield/%
2a	52	97
2b	41	78
2c	1.6	86

Recent reports have shown that pretreated alkaline earth oxides, MO (M = Ca, Sr, Ba), may act as heterogeneous catalysts for the Tischenko reaction with activities increasing with the increasing basicity of the M−O bond ($Sr > Ca \gg Ba$).[9] To ascertain that the observed catalytic activity was due to a homogeneous intermediate, and not hydrolysis products, the reaction of benzaldehyde with **2a** was carried out following exposure of the catalyst to an aerobic atmosphere. In these instances, no benzyl benzoate production was observed.

The scope of the reaction was investigated, and a series of aromatic, heteroaromatic, and aliphatic aldehydes were allowed to react with 1−5 mol % of $Ca\{N(SiMe_3)_2\}_2(THF)_2$ **2a**. The reactions were performed on both an NMR and a preparative scale (Table 2). In all cases, the preparative scale yields paralleled those observed by NMR and the products were isolated and fully characterized (see Supporting Information). This study showed that **2a** was an effective catalyst for both the *inter-* and *intramolecular* Tischenko reaction, with the rate of the latter exceeding that of the former. A number of aromatic aldehydes and both enolizable and nonenolizable aliphatic aldehydes are reactive substrates giving the analogous dimeric esters in high yield. The reactivity of enolizable aliphatic aldehydes with **2a** under these conditions is of particular note as the stoichiometric reaction of $Ca\{N(SiMe_3)_2\}_2(THF)_2$ with acetophenone is reported to give a high yield of the corresponding calcium enolate, which has been isolated and characterized in the solid state.[10]

The dimerization of more electron-rich aromatic aldehydes with the calcium amide **2a** proved unsuccessful. Indeed, the attempted dimerization of *N*-methylindole-2-carboxaldehyde, 2-furfuraldehyde, and *p*-*N*,*N*-dimethylbenzaldehyde by **2a** were all ineffective, even at higher reaction temperatures and catalyst loadings. Although it is feasible that heteroatom-substituted substrates may inhibit catalytic turnover by coordination to the electrophilic calcium center, treatment of **2a** with *m*-anisaldehyde gave an almost quantitative yield of 3-methoxybenzyl 3-methoxybenzoate. In contrast, under

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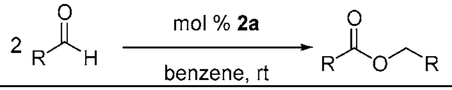
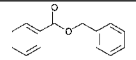
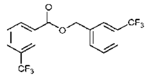
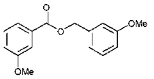
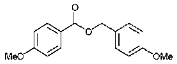
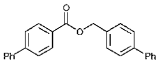
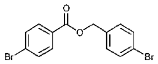
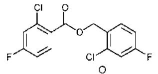
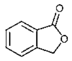
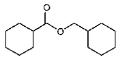
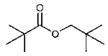
Table 2. Dimerization of Aldehydes to the Analogous Carboxylic Esters Catalyzed by 1−5 mol % of **2a** at Room Temperature in Benzene[a]



entry	product	mol % 2a	NMR Yield / %	isolated Yield / %[b]
1		1	97	74
2		3	99	87
3		3	96	72
4		5	26	10[c]
5		2.5	97	74
6		5	93	70
7		5	48	40[c]
8		1	95	81
9		5	>95	82
10		2	98	96

[a] Reactions conducted in C_6D_6. TOF: intermolecular aromatic, 2−60 h^{-1}; intramolecular aromatic, >500 h^{-1}; intermolecular aliphatic, >100 h^{-1}. [b]Isolated after stirring with **2a** for 24 h at room temperature in C_6H_6. [c]96 h reaction time.

the same conditions, *p*-anisaldehyde gave 4-methoxybenzyl 4-methoxybenzoate in a low yield (Table 2, entries 3 and 4). This observation suggests that the electronic character of the aldehyde determines its ease of dimerization with **2a** and that more electron-rich aldehydes react more slowly. Similarly, it has been reported that La{N(SiMe$_3$)$_2$}$_3$ demonstrates low catalytic activity for the dimerization of heteroaromatic and electron-rich aromatic aldehydes.[8]

To investigate the limits of the catalysis, a further reaction was conducted between benzaldehyde and 0.1 mol % of **2a** using a 0.5 mol quantity of the aldehyde. The reaction was conducted without solvent, and after 88 h at ambient temperature, benzyl benzoate could be isolated in 63% yield. This lower turnover frequency, longer reaction time, and lower reaction yield as compared to the NMR scale reaction are most likely a reflection of the lower catalyst loading, as the catalyst may be destroyed by reaction with trace impurities or water present in the benzaldehyde. Repeating the reaction using 0.2 mol % of **2a** allowed an optimization of the yield to 74% after only 48 h at room temperature.

The homoleptic or heteroleptic calcium amide catalysts could also be applied to the polymerization of dialdehydes, and the reaction of 1 mol % of **1** or **2a** with terephthaldicarboxaldehyde (1,4-(CHO)$_2$C$_6$H$_4$) in benzene gave the corresponding polyester in high yield. Characterization of the polymer by ^{1}H NMR spectroscopy revealed that there were numerous aldehyde endgroups present, and consistent with the expected step-growth polymerization mechanism, GPC analysis showed a polydisperse high molecular weight material along with low molecular weight oligomers (see Supporting Information).

The dimerization of 2 equiv of benzaldehyde to benzyl benzoate formally involves the oxidation of 1 equiv of aldehyde and the reduction of another. Given the redox inability of the group 2 complexes, it is clear that this process must occur by a net hydride transfer from one aldehyde to the other. In an attempt to understand the reaction further, the dimerization of benzaldehyde to benzyl benzoate catalyzed by 10 mol % of **2a** was studied in more detail. Quenching the reaction after 5 min at room temperature and analyzing by GC-MS and ^{1}H NMR spectroscopy revealed that both benzyl alcohol and *N*,*N*-bis(trimethylsilyl)benzamide were initial byproducts of the reaction. Given this observation, it is likely that the reaction occurs via a calcium alkoxide intermediate which may originate from a Meerwein−Ponndorf−Verley-type reduction of benzaldehyde. Subsequent addition to a second equivalent of aldehyde followed by a hydride transfer would result in the formation of benzyl benzoate with regeneration of the calcium alkoxide. Further evidence for an alkoxide intermediate was provided by a crossover experiment. Thus, the reaction of a 1:1 mixture of benzaldehyde and 4-bromobenzyl 4-bromobenzoate with 5 mol % of **2a** gave, in addition to benzaldehyde, benzyl benzoate, and 4-bromobenzyl 4-bromobenzoate, the crossover product benzyl 4-bromobenzoate as identified by GC-MS. This latter result may be attributed to the ester product undergoing transesterification with an intermediate calcium alkoxide.

In summary, the heteroleptic calcium amide **1** and homoleptic heavier alkaline earth amides **2a**−**c** are effective catalysts for the dimerization of electron-deficient aromatic and aliphatic aldehydes to the analogous carboxylic esters. We are continuing to study the mechanism and scope of this reaction.

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Supporting Information Available: Full experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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