

## VIP Very Important Paper

## Photocatalytic Dehydroformylation of Benzyl Alcohols to Arenes

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In the last decades, many C–C bond-forming reactions have been developed, whereas less attention has been paid to the design of strategies involving C–C bond cleavage. We report a photocatalytic dehydroformylation sequence for the conversion of benzyl alcohols to arenes in a one-pot two-step process. Herein, the initial dehydrogenation of the benzyl alcohols to the corresponding benzaldehydes is combined with an addi-

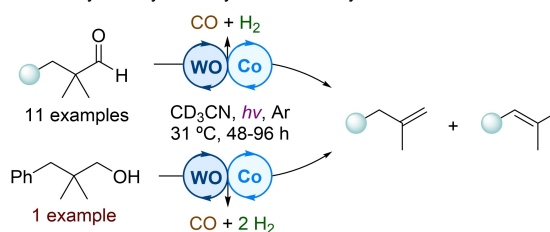
tional decarbonylation step yielding arenes. As a result, a broad range of benzyl alcohols can be easily transformed in short times under mild photocatalytic conditions. The conducted mechanistic studies indicate that our cooperative hydrogen atom transfer (HAT)-cobalt system proceeds through the formation of  $\alpha$ -alkoxy- and acyl radicals as key intermediates, involving concomitant syngas (CO + H<sub>2</sub>) generation.

## Introduction

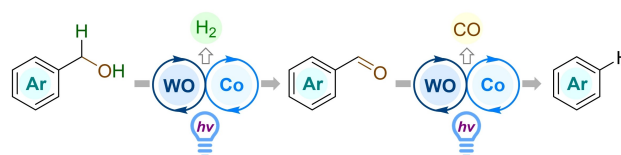
Hydroformylation, the functionalization of an alkene with carbon monoxide and hydrogen to generate the corresponding aldehyde, is one of the largest chemical transformations employed in industry, with an overall output of 10.4 megatons of products generated in the year 2008.<sup>[1]</sup> As a result, this process gives access to a myriad of intermediates with indispensable industrial applications such as methacrolein (acrylic glass manufacture),<sup>[2]</sup> or 2-methyl butanal (isoprene precursor).<sup>[3]</sup> Moreover, the rich reactivity profile of the aldehyde functionality gives rise to a plethora of follow-up transformations such as oxidation to acids, amides and lactones, or reductions to amines and alcohols.<sup>[4]</sup> In contrast, the reverse transformation, cleaving off syngas (CO + H<sub>2</sub>) to form an alkene has historically been less relevant, as aldehydes are generally less available substrates.

The fossil fuel-based chemical industry of the last century was focused on building molecular complexity from simple, unfunctionalized aliphatics and olefins. Going forward, future chemical production will employ complex, biologically derived starting materials like sugars or lignin, transforming them into simpler building blocks. As an example, photocatalytic deoxygenations involving gas evolution can be fruitful strategies that allow to modify complex natural products such as sugars,<sup>[5]</sup> or degrade polymers in a straightforward fashion.<sup>[6]</sup>

Initially, the dehydroformylation reaction was explored with aldehydes, using stoichiometric or catalytic amounts of metal complexes.<sup>[7]</sup> More recently, primary alcohols were reported to undergo dehydroformylation and oxidative dehydroxymethylation in the presence of ruthenium and rhodium complexes respectively.<sup>[8]</sup> In this context, pioneering work by the Sorensen group provided the first photocatalytic version of these transformations by employing a dual HAT-cobalt system under mild conditions.<sup>[9]</sup> Herein, alkenes could be prepared from  $\alpha$ -quaternary aldehydes via dehydroformylation, and in a single instance from an alcohol via dehydroxymethylation (Scheme 1a). Alternatively, the Zuo group successfully employed cerium complexes for the photocatalytic transformation of alcohols by formaldehyde extrusion.<sup>[10]</sup> Inspired by these methodologies and

a) Photocatalytic dehydroformylation of aldehydes: Sorensen 2017.<sup>[9]</sup>b) Photocatalytic decarbonylation of benzaldehydes: König 2023.<sup>[11]</sup>

c) This work: Photocatalytic dehydroformylation of benzyl alcohols.



**Scheme 1.** Photocatalytic dehydroformylation and decarbonylation methodologies. WO = decatungstate. TX = thioxanthone.

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by our previous work on the photocatalytic decarbonylation of benzaldehydes (Scheme 1b),<sup>[11]</sup> we hypothesized that a two-step dehydroformylation sequence might unlock benzyl alcohols as substrates for their defunctionalization to arenes (Scheme 1c). For this purpose, an acceptorless light-driven HAT-cobalt system held positive prospects. In our opinion, a photochemical hydrogen atom abstraction at the activated benzylic position should be an efficient way to generate a benzylic radical. This open-shell species could then engage in a dehydrogenation event with a cobalt complex, giving the corresponding benzaldehyde, which upon decarbonylation would yield the unfunctionalized arene.

## Results and Discussion

4-*tert*-Butylbenzyl alcohol (**1a**) was chosen as model substrate to test the dehydroformylation reaction. At first, a range of photoexcitable HAT-agents and cobalt complexes were screened in different loadings (Tables S1 and S2). Here, the combination of tetra-*n*-butylammonium decatungstate (TBADT) and cobaloxime pyridine chloride (COPC) as hydrogen evolution catalyst proved optimal. When screening different solvents, non-dried acetonitrile was found to be the best option (Table S3), proving the system to be non-moisture sensitive. Additionally, different concentrations (Table S4) and several LEDs were tested (Table S5). The optimized system was found to involve low loadings of TBADT and COPC, acetonitrile as solvent, and a 385 nm LED (4.7 W) as irradiation source. To our delight, with these conditions, product **1b** was obtained in very good yield after 6 h (85%) (Table 1, entry 1), in a two-step process, corresponding to an average yield of 92% per step. Furthermore, the reaction was successfully conducted on a 0.3 mmol scale, albeit requiring longer reaction times and a higher substrate concentration (entry 2). The replacement of any of the reaction components led in all cases to a significant decrease in yield. Sodium decatungstate (NaDT), despite its similar H-atom abstracting ability to TBADT, led to lower yield presumably due to its poor solubility in acetonitrile (entry 3). Several cheaper photocatalysts such as benzophenone, anthraquinone, or thioxanthone (entries 4–6) were also found

compatible. Similarly, using a different cobalt catalyst (entry 7) rendered acceptable results. With the optimized conditions in hand, we investigated the substrate scope (Scheme 2) with benzyl alcohol (**2a**) and several naturally occurring derivatives.<sup>[12]</sup> Both alkyl and alkoxy-substituted substrates (**3a–16a**), gave the corresponding arenes in good yields (47–84%). To our delight, the conditions could be easily tuned for sterically hindered *ortho*-substituted derivatives (**3a**, **8a** and **14a**). For these substrates, increasing the reaction time to 16 h led to comparable yields to *para*- and *meta*-substituted homologues. The presence of activated C–H bonds with low bond dissociation energies (BDEs) such as secondary and tertiary benzylic positions (**6a** and **7a**) was well tolerated. Similarly, the highly activated benzyloxy position displayed by **16a** was found compatible with our system, albeit giving **16b** in low yield after 16 h of irradiation. Herein, the photocatalyst is believed to engage in undesired HAT events with the mentioned position, consequently decelerating the dehydroformylation process.

Derivatives with ester groups as substituents (**17a–19a**) were successfully converted. Unfortunately, **17a** and **19a** were found to degrade with increasing reaction time. In addition, the methodology was applied for the dehydroformylation of vanillyl alcohol (**20a**). Hereof, guajacol (**20b**) was obtained in low yield, presumably due to the presence of the unprotected phenol moiety. Aryl methanols displaying extended  $\pi$ -systems reacted smoothly, furnishing the corresponding arenes (**21b–23b**) in good yields (60–69%). Here, the more sterically hindered 1-naphthalenemethanol (**22a**), required longer reaction times in comparison to 2-naphthalenemethanol (**23a**). The dehydroformylation of substrate **24a** gave acetanilide (**24b**) in very good yield (72%). Next, the substrate scope was expanded with several halogenated substrates (**25a–29a**), wherein chlorinated derivatives (**28a** and **29a**) gave better results than fluorinated homologues (**25a–27a**). According to literature, the electron donating/withdrawing ability of the substituents can have a direct impact on the BDE and overall stability of benzylic radicals.<sup>[13]</sup> Hereof, radicals with higher lifetimes are more likely to be trapped by cobalt (II), accelerating the first dehydrogenation step of the dehydroformylation sequence. Lastly, the methodology was applied for the two-fold defunctionalization of 1,3-benzenedimethanol (**30a**) to benzene (**30b**), obtaining benzaldehyde as main side product.

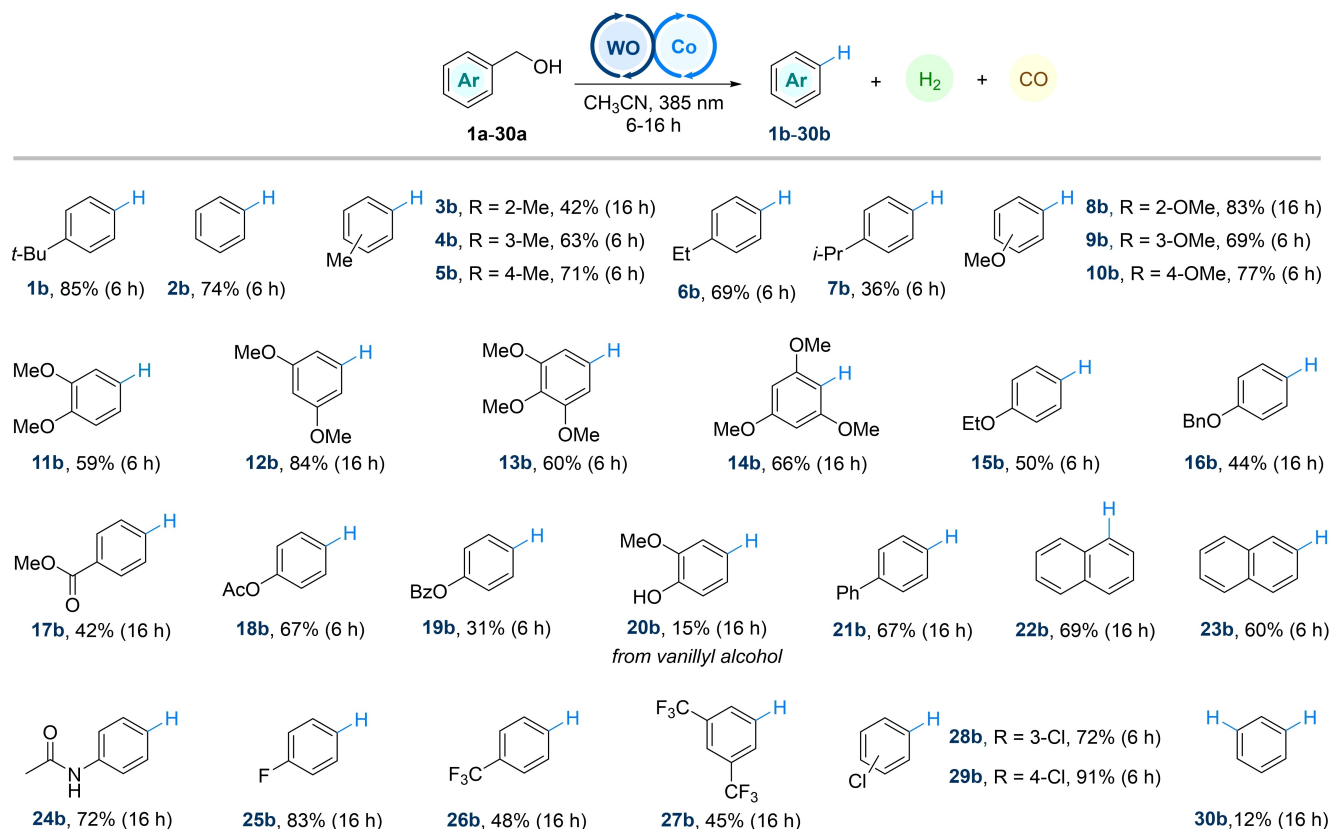
Next, a series of control reactions were carried out with model substrate **1a** (Table 2). All reaction components turned out to be essential for the dehydroformylation reaction, confirming its photocatalytic nature. In absence of TBADT, COPC, or light no product was formed (entries 2–4). Instead, in all these cases the starting material remained unreacted. Similarly, the replacement of light by heat prevented the reaction from occurring (entry 5). In addition, conducting the reaction under air led to a notable decrease in the yield presumably due to quenching of the photocatalyst by oxygen (entry 6). Under these conditions, the formation of 4-*tert*-butyl benzoic acid was observed.

To elucidate the reaction mechanism, several additional experiments were performed (Scheme 3). First, gas evolution was confirmed by gas chromatography (Figure S9).

**Table 1.** Screening of reaction conditions.

Entry	Deviation from standard conditions	Yield of <b>1b</b> [%] <sup>[a]</sup>
1	None	85
2	0.3 mmol scale, CH <sub>3</sub> CN (0.2 M), 48 h	80
3	NaDT instead of TBADT	43
4	Benzophenone instead of TBADT	45
5	Anthraquinone instead of TBADT	17
6	Thioxanthone instead of TBADT	15
7	Co(dmgH)(dmgH <sub>2</sub> )Cl <sub>2</sub> instead of COPC	47

[a] GC-FID yields determined using mesitylene as internal standard.



**Scheme 2.** Substrate scope for benzyl alcohols. Reaction conditions: **a** (0.05 mmol), TBADT (3 mol%), COPC (2.5 mol%), CH<sub>3</sub>CN (0.5 mL), 385 nm LED (4.7 W), N<sub>2</sub>, 35 °C. GC-FID yields determined using mesitylene as internal standard.

**Table 2.** Control experiments.

Entry	Deviation from standard conditions	Yield of <b>1b</b> (%) <sup>[a]</sup>
1	None	85
2	No TBADT	N.d.
3	No COPC	N.d.
4	No light	N.d.
5	No light; at 60 °C	N.d.
6	Under air	18

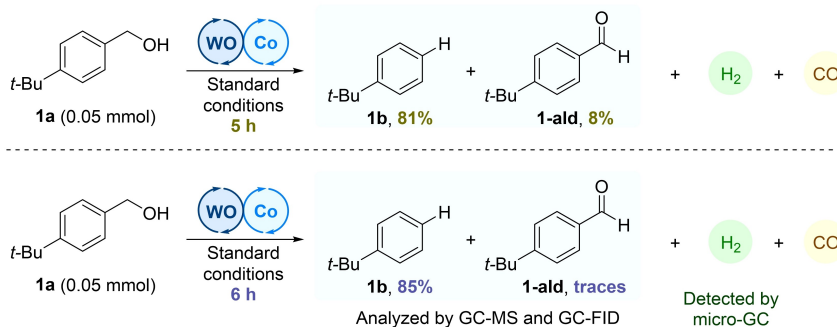
[a] GC-FID yields determined using mesitylene as internal standard.

While the generation of hydrogen could be observed as a clearly defined peak, the detection of carbon monoxide remained elusive. Further analysis by GC-MS and GC-FID of the reaction mixture of **1a** after 5 h of irradiation revealed the presence of 4-*tert*-butyl benzaldehyde (**1-ald**) (Scheme 3a). In contrast, when concluding the reaction after 6 h of irradiation, this product could be only detected in trace amounts, suggesting its role as an intermediate in the dehydroformylation process. This finding is consistent with the postulated initial oxidation step of the alcohol to the corresponding aldehyde via coopera-

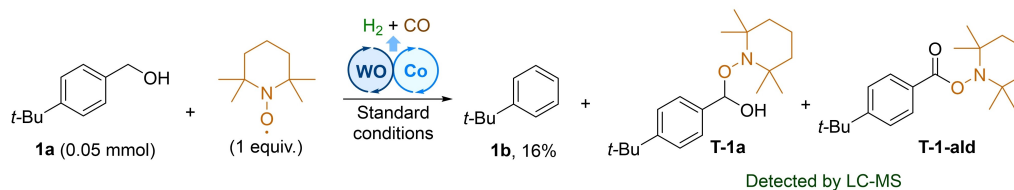
tive HAT-cobalt catalysis (see Scheme 1). Furthermore, a radical trapping experiment was conducted using TEMPO as a scavenger (Scheme 3b). Consequently, two main radical-derived products were observed (**T-1a** and **T-1-ald**), indicating the in-situ generation of benzylic and acyl radicals via HAT. This finding supported a stepwise radical dehydroformylation sequence, wherein the initial dehydrogenation of the alcohol to give the corresponding aldehyde is essential. To further test this hypothesis, we subjected the proposed aldehyde intermediate (**1-ald**) to our reaction conditions (Scheme 3c), which underwent decarbonylation to give **1b** in excellent yield (93%). According to our previous work on the photocatalytic decarbonylation of benzaldehydes,<sup>[11]</sup> such a dual HAT-cobalt system performs well in the defunctionalization of aromatic aldehydes. In contrast, subjecting substrate **31a** to our conditions led to no arene formation (Scheme 3d), as the protection of the alcohol group prevents the initial dehydrogenation event.

Based on the above observations and according to previous studies,<sup>[9,11,14]</sup> we proposed a plausible mechanism for the dehydroformylation of benzyl alcohols (Scheme 4). In the transformation, a stepwise radical mechanism could be involved, proceeding via photoinduced C–H activation. The overall mechanism can be described as the combination of two pairs of consecutive HAT-cobalt catalytic cycles, which ultimately result in the selective cleavage of the aryl-alkyl C–C bond of the benzyl alcohol (**IV**). Consequently, one equivalent each of hydrogen and

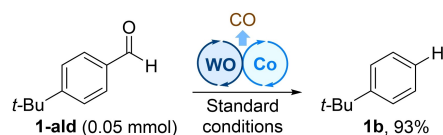
a) Analysis of the reaction mixture of **1a** after 5 h and 6 h reaction.



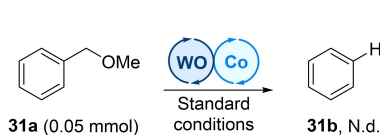
b) Dehydroformylation of **1a** in presence of TEMPO



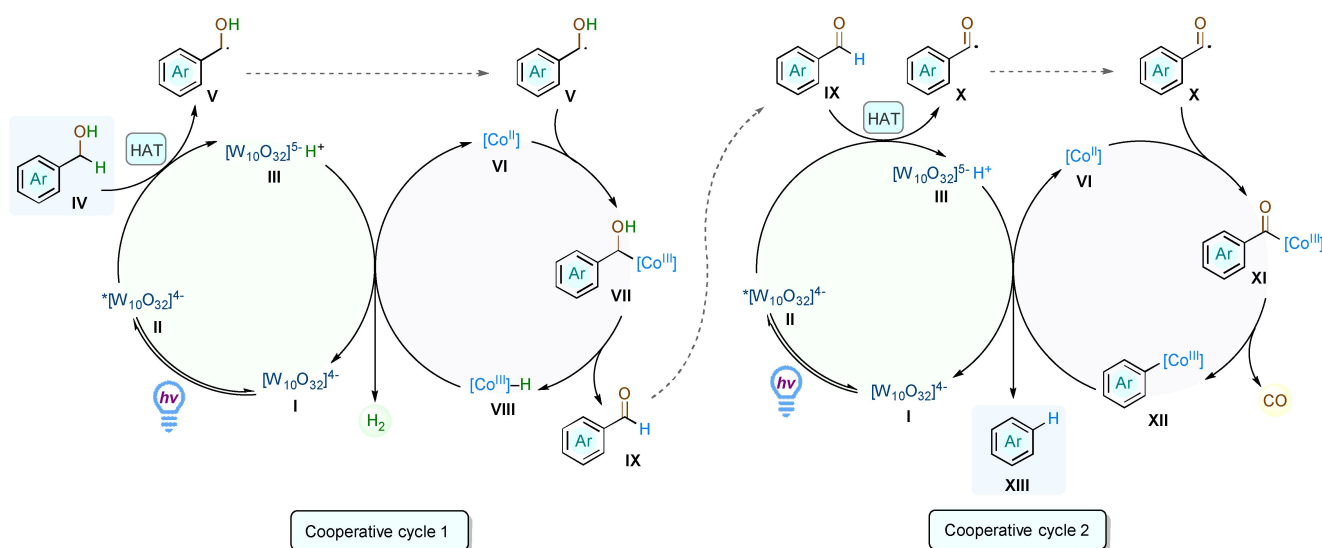
c) Decarbonylation of proposed aldehyde intermediate



d) Reaction with a substrate displaying a protected alcohol



**Scheme 3.** Mechanistic studies. Standard conditions: substrate (0.05 mmol), TBADT (3 mol%), COPC (2.5 mol%), CH<sub>3</sub>CN (0.5 mL), 385 nm LED (4.7 W), N<sub>2</sub>, 35 °C, 6 h. GC-FID yields determined using mesitylene as internal standard.



**Scheme 4.** Proposed mechanism for the sequential dehydroformylation of benzyl alcohols.

carbon monoxide are generated. In the first cycle, the alcohol (**IV**) is initially oxidized to an aldehyde intermediate (**V**) that can further engage in a second cooperative cycle to undergo decarbonylation and give the corresponding arene product (**XIII**).

First, upon irradiation of the photocatalyst (**I**), its excited state (**II**) abstracts a hydrogen atom from the benzyl alcohol (**IV**) via HAT, consequently generating a benzylic radical (**V**). This

species can be trapped by cobalt (**II**) (**VI**) to form a cobalt (**III**) complex (**VII**). This complex then further reacts, to give a cobalt-hydride complex (**VIII**) and the corresponding benzaldehyde (**IX**). Next, the cobalt hydride complex (**VIII**) reacts with the reduced form of the photocatalyst (**III**) via proton transfer coupled with single electron transfer (SET). Herein, both the cobalt (**II**) complex (**VI**) and the photocatalyst (**I**) are regen-

erated. The resulting benzaldehyde (IX) can then undergo decarbonylation, as its weak C–H bond is prone to be cleaved by the excited photocatalyst (II) to give an acyl radical (X). The combination of this species with cobalt (II) (VI) leads to the formation of an acyl-cobalt complex (XI), which upon extrusion of carbon monoxide yields an aryl-cobalt complex (XII). This last species is postulated to engage with the reduced form of the photocatalyst (III) via another proton transfer coupled with SET, regenerating it to its ground state (I) while giving the aimed unfunctionalized arene product (XIII).

## Conclusions

In summary, we have developed a photocatalytic methodology for the sequential dehydroformylation of benzyl alcohols to arenes. The combination of TBADT as photoexcitable HAT-agent and COPC as co-catalyst results in a cooperative photocatalytic system that generates concomitant syngas (CO + H<sub>2</sub>). The performed mechanistic studies confirmed the in-situ generation of benzylic and acyl radicals, indicating that the transformation proceeds through a stepwise radical pathway. These open-shell intermediates can then be trapped by a cobalt (II) complex, giving access to further transformations, including dehydrogenation and decarbonylation events. With our proposed reaction mechanism, we postulate that the transformation proceeds via selective C–H bond activation and results in C–C bond cleavage.

## Supporting Information

The supporting information includes the general experimental procedure for the photocatalytic dehydroformylation of benzyl alcohols, experimental procedures for the preparation of starting materials, characterization data of starting materials and data related to the conducted mechanistic studies. The authors have cited additional references within the Supporting Information.<sup>[15–17]</sup>

## Acknowledgements

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## Conflict of Interests

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords:** photocatalysis · dehydroformylation · hydrogen atom transfer · cobalt · benzyl alcohols

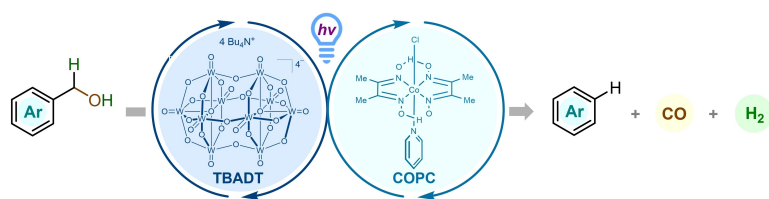
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