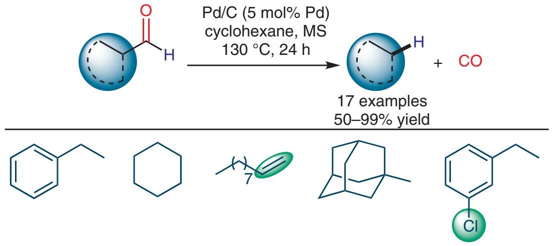
Reevaluation of the Palladium/Carbon-Catalyzed Decarbonylation of Aliphatic Aldehydes

Vladimir Ajdačić[a]
Andrea Nikolić[a]
Michael Kerner[b]
Peter Wipf[b]
Igor M. Opsenica*[a]

[a] Faculty of Chemistry, University of Belgrade, PO Box 51, Studentski trg 16, 11158 Belgrade, Serbia
igorop@chem.bg.ac.rs
[b] Department of Chemistry, University of Pittsburgh, 219 Parkman Avenue, Pittsburgh, PA 15260, USA



Received: 15.05.2018
Accepted after revision: 22.05.2018
Published online: 28.06.2018
DOI: 10.1055/s-0037-1610433; Art ID: st-2018-r0310-l

Abstract An improved method for the decarbonylation of aliphatic aldehydes by using a commercially available Pd/C catalyst is described. The reaction conditions are suitable for linear, cyclic, or sterically demanding substrates, as they afford the corresponding alkanes in yields of up to 99%. In addition, this Pd/C-catalyzed method exhibits good functional-group tolerance. A comparison of previously reported methods with the present one showed that the reaction conditions play a crucial role in the outcome of the reaction. The method can also be applied in a two-step reaction sequence for the synthesis of industrially important compounds.

Key words decarbonylation, aldehydes, palladium catalysis, adamantine, alkylated aromatic compounds, natural products

The removal of functional groups from densely functionalized molecules represents a valuable transformation in synthetic organic chemistry and process research.[1] Whereas carbonyl groups are often essential to the efficient and convergent assembly of target structures, many final products lack carbonyl groups, and consequently there is a need for the development of decarbonylation processes. In particular, the decarbonylation of aldehydes has been shown to be an important step in syntheses of industrial chemicals from biomass[2] or of complex intermediates;[3] it can also provide an in situ source of carbon monoxide.[4] The decarbonylation of aliphatic aldehydes is a step in the biosynthesis of linear carbohydrates, which are important for the survival and reproduction of microorganisms,[5] plants,[6] and animals.[7]

The decarbonylation of aromatic compounds leads to alkylated benzenes, which are a common substructure in natural products (Figure 1).[8] In addition, alkylated aromatic compounds are valuable intermediates that are widely used in the synthesis of industrially important compounds, such as pesticides, dyes, and surfactants that are key ingredients of detergents (Figure 1).[9,10] Palladium and rhodium[11] are the most frequently used metals in the transition-metal-catalyzed decarbonylation of aldehydes.[12] Several methods for the removal of aldehyde functional group employ a solid-supported palladium catalyst.[2,13] The palladium/carbon-catalyzed decarbonylation of aromatic aldehydes has been known since the1960s,[12a] but the Pd/C catalyzed decarbonylation of aliphatic aldehydes had not been investigated in detail[14] not even when it was reported for the first time by Hawthorne and Wilt who used palladium/carbon at elevated temperatures.[12a] Also, Tsuji and co-workers reported the palladium-catalyzed decarbonylation of aliphatic aldehydes in the gas phase by using palladium/carbon.[12b,12c] Despite their importance, these procedures had several drawbacks: high temperatures were required (>180 °C), and complex reaction mixtures were obtained that included products of dehydrogenation, isomerization, and decarbonylation. Recently, Monguchi and Sajiki and their co-workers accomplished a Pd/C-catalyzed decarbonylation of dihydrocinnamaldehydes in isopropanol at 120 °C under an oxygen atmosphere.[15] The addition of Na_2CO_3 promoted the retro-hydroformylation reaction, and the corresponding styrene derivatives were obtained in good yields.

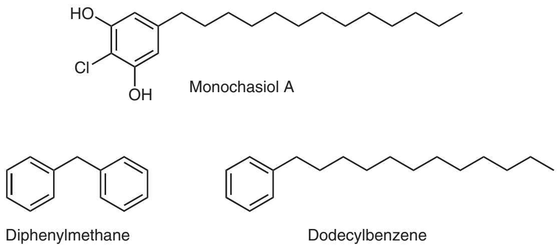


Figure 1 Representative alkylated aromatic compounds

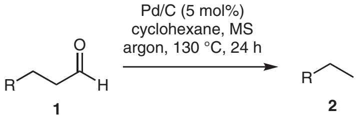
© Georg Thieme Verlag Stuttgart · New York

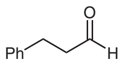
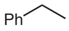
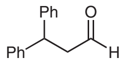
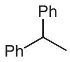
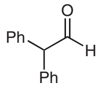
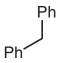
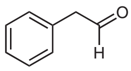
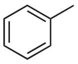
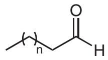
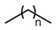
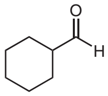
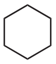
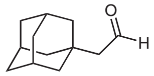
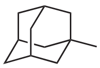
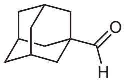
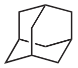
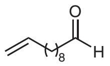
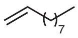
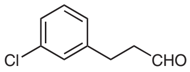
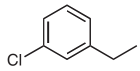
Heruntergeladen von: University of Sussex. Urheberrechtlich geschützt.

We recently developed a method for decarbonylation of aromatic aldehydes by using a maghemite-supported palladium catalyst.[16] As a continuation of this research, we examined the use of a Pd/C catalyst for the decarbonylation of aliphatic aldehydes and the formation of the corresponding alkanes.

As presented in Table 1, we found that palladium/carbon afforded good to excellent yields of the corresponding decarbonylated products in cyclohexane at 130 °C. The decarbonylation of hydrocinnamaldehyde (**1a**) and phenylacetaldehyde (**1d**) resulted in good yields of the desired products, ethylbenzene (**2a**) and toluene (**2d**), respectively (Table 1).

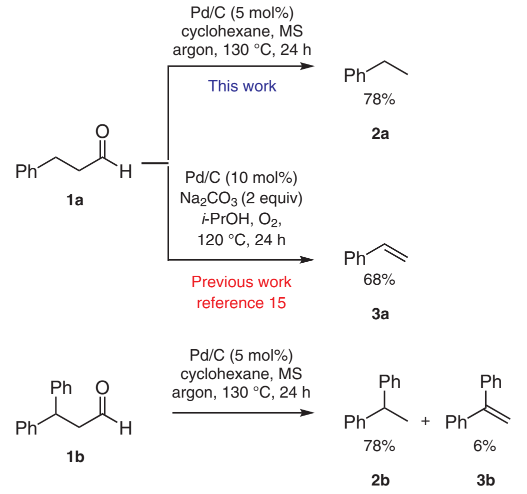
Table 1 Scope of Pd/C-Catalyzed Decarbonylation of Aliphatic Aldehydes



Aldehyde	Product
 **1a**	 **2a** (67%)[a] (78%)[b]
 **1b**	 **2b** (78%)[c]
 **1c**	 **2c** (69%)[c]
 **1d**	 **2d** (82%)[a]
 **1e**, *n* = 5 **1f**, *n* = 6 **1g**, *n* = 7 **1h**, *n* = 8	 **2e**, *n* = 5 (64%)[a] **2f**, *n* = 6 (50%)[a] **2g**, *n* = 7 (54%)[a] **2h**, *n* = 8 (99%)[a]
 **1i**	 **2i** (74%)[d]
 **1j**	 **2j** (78%)[c,e,f]
 **1k**	 2k (54%)[c,e,f]
 **1l**	 **2l** (72%)[a]
 **1m**	 **2m** (51%)[b]

[a] Yields by GC/MS with naphthalene as an internal standard.
[b] Yield by NMR spectroscopy. (The reaction was performed in C_6D_6, and methyl benzoate was used as an internal standard.)
[c] Isolated yield.
[d] Yield by NMR spectroscopy. (The reaction was performed in C_6D_6, and naphthalene was used as an internal standard.)
[e] 10 mol% Pd/C.
[f] The reaction time was 48 h.

Furthermore, 3,3-diphenylpropanal (**1b**) gave 1,1-diphenylethane (**2b**) as the major product, along with 1,1-diphenylethylene (**3b**) as the minor product (Table 1 and Scheme 1).



Scheme 1 Comparative study of the decarbonylation of hydrocinnamaldehyde and 3,3-diphenylpropanal

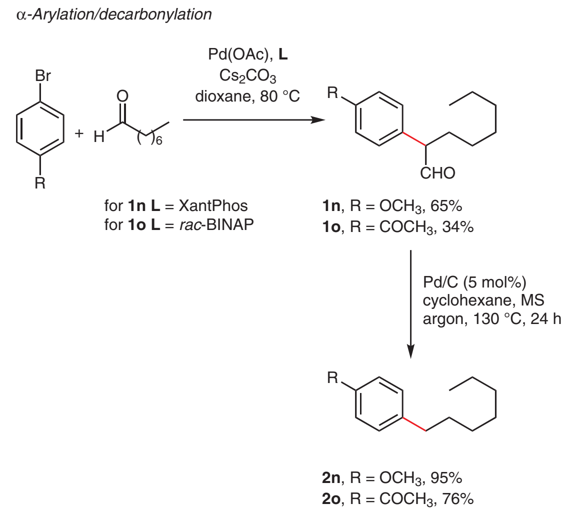
A comparison of these experimental results with those obtained by Monguchi, Sajiki, and co-workers[15] suggested that the outcome of the decarbonylation reaction is strongly dependent on the reaction conditions (Scheme 1). The presence of Na_2CO_3 and an oxygen atmosphere promote the retro-hydroformylation reaction and the formation of the corresponding styrene.

Heruntergeladen von: University of Sussex. Urheberrechtlich geschützt.

The decarbonylation was also applicable to long-chain aliphatic aldehydes (Table 1). Nonanal (**1f**) was completely consumed to give octane (**2f**) in 50% yield. Notably, oct-1-ene was not detected by GC-MS. The lower yield is presumably due to co-evaporation of the desired product during the reaction. In addition, undecanal (**1h**) was converted completely into decane (**2h**). For octanal (**1e**) and decanal (**1g**), the corresponding alkanes **2e** and **2g** were obtained as the major products, along with mixtures of alkenes in 14% and 13% yield, respectively. The decarbonylation of the sterically demanding adamantanes 1-adamantylacetaldehyde (**1j**) and adamantane-1-carbaldehyde (**1k**) gave the desired products 1-methyladamantane (**2j**) and adamantane (**2k**) in 78% and 54% isolated yield, respectively. For the adamantane aldehydes, we observed that the reaction was not completed with 5 mol% of Pd/C; instead the use of a 10 mol% loading of Pd/C and an extension of the reaction time to 48 hours were required to attain full conversion of the starting materials. Moreover, alkenyl aldehyde **1l** gave the desired decarbonylated product **2l** in good yield. Notably, the decarbonylation could also be extended to aryl chlorides. The decarbonylation of 3-(3-chlorophenyl)propanal (**1m**) afforded 1-chloro-3-ethylbenzene (**2m**) in 51% yield, along with a 15% yield of 1-chloro-3-ethenylbenzene.

To gain a better insight into the outcome of the decarbonylation reaction, we performed the decarbonylation of hydrocinnamaldehyde (**1a**) and cyclohexanecarbaldehyde (**1i**) in C_6D_6, at 130 °C for 24 hours, and analyzed the spectra of the reaction mixtures (Table 1 and Supporting Information). As expected, the starting material was consumed and the corresponding decarbonylated products, ethylbenzene (**2a**) and cyclohexane (**2i**) were obtained in good yields as the only products. Notably, the formation of styrene and cyclohexene was not detected.

The use of the aldehyde functional group as a protective group[17] or as a transient directing group[18] makes the decarbonylation reaction very appealing for the synthesis of diverse organic compounds, including several natural products.[19] The utility of the decarbonylation reaction was further demonstrated in the syntheses of alkylated aromatic compounds (Scheme 2). The α-aryl carbonyl compounds **1n** and **1o** were synthesized by a previously reported method,[20,21] involving the Pd-catalyzed α-arylation of octanal with the corresponding bromoarenes. The α-aryl carbonyl compounds **1n** and **1o** were successfully decarbonylated to give the corresponding products **2n** and **2o** in good to excellent yields (Scheme 2).



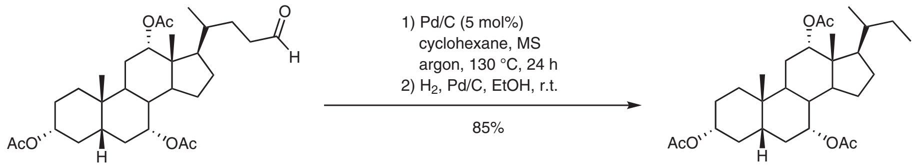
Scheme 2 The scope of the method

We further demonstrated, in one example, that the decarbonylation reaction can be employed on the densely functionalized inexpensive natural product **4** (Scheme 3).

Unfortunately, besides the desired alkane **5**, significant amounts of alkene products were also obtained (alkane/alkene ratio ≤55:45). This drawback was overcome by adding H_2 gas, and after hydrogenation, the corresponding saturated decarbonylated derivative was obtained in a good yield. Despite the low selectivity, with this substrate we demonstrated that the corresponding saturated product could be obtained in good yield by a two-step procedure.

When (±)-citronellal (**6**) was subjected to the decarbonylation reaction, the decarbonylated product **7** and *p*-cymene (**9**) were obtained in 36% and 23% yield, respectively, along with 2,6-dimethylheptane (**8**) and a mixture of dienes and other compounds (Scheme 4). The formation of *p*-cymene might occur through an intramolecular alkene hydroacylation reaction (Scheme 4).

To gain a better insight into the mechanism of the decarbonylation reaction, we performed a deuterium-labeling experiment. (Scheme 5). The decarbonylation of [α-D_1]-1-adamantylacetaldehyde (***d*-1j**) gave [1D_1]-1-methylada-

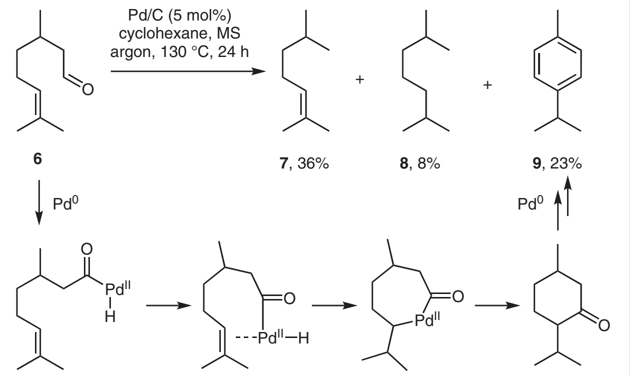


4

5

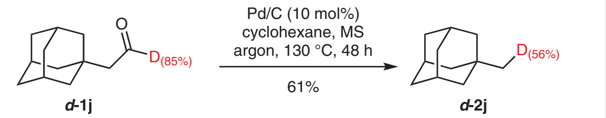
Scheme 3 Decarbonylation of natural product **4**

Heruntergeladen von: University of Sussex. Urheberrechtlich geschützt.



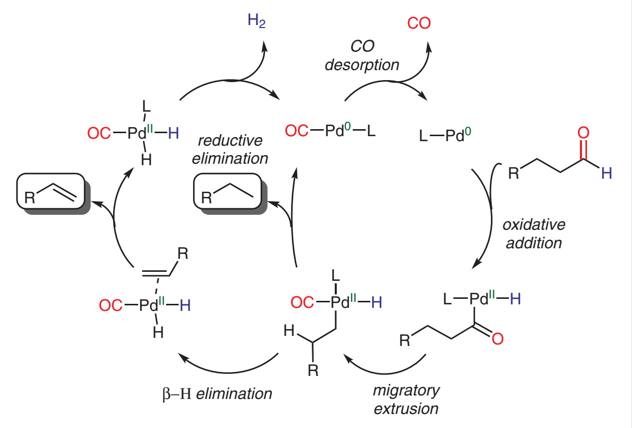
Scheme 4 Decarbonylation of (±)-citronellal (**6**). The GC-MS yield, with naphthalene as an internal standard, is reported.

mantane (***d*-2j**; Scheme 5). The partial loss of the deuterium label suggested that the decarbonylation of ***d*-1j** is slower than that of 1-adamantylacetaldehyde (**1j**).[12h]



Scheme 5 Deuterium labeling experiment

On the basis of the above observed results and previous reports,[12h] we propose the plausible mechanism for the decarbonylation of aliphatic aldehydes shown in Scheme 6.



Scheme 6 Proposed mechanism for the decarbonylation of aliphatic aldehydes

Oxidative addition of the C(O)–H bond of the aldehyde to palladium provides an acylpalladium hydride complex. Subsequent migratory extrusion of carbon monoxide and reductive elimination gives the alkane product, while desorption of CO regenerates the catalyst.

In conclusion, we have reassessed the reaction conditions for the decarbonylation of aliphatic aldehydes and the formation of the corresponding alkanes.[22] The reaction conditions that we report are milder than those previously reported, and there are few or no byproducts.[12a–c] The conversion of all substrates resulted in good to excellent yields of the desired products. The reaction conditions could also be applied to sterically demanding substrates. In addition, a variety of functional groups, including alkenyl, ketone, ether, and ester, were well tolerated in this process. The level of functional-group compatibility extends even to reactive aryl halides. The method is also applicable in a two-step procedure for the synthesis of alkylated aromatic compounds that have a variety of uses in industry.

Funding Information

This research was financially supported by the Ministry of Education, Science and Technological Development of Serbia (Grant No. 172008). The authors acknowledge the support of the FP7 RegPot project FCUB ERA GA No. 256716. The EC does not share responsibility for the content of the article.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610433.

References and Notes

(1) Modak, A.; Maiti, D. *Org. Biomol. Chem.* **2016**, *14*, 21.
(2) (a) Huang, Y.-B.; Yang, Z.; Chen, M.-Y.; Dai, J.-J.; Guo, Q.-X.; Fu, Y. *ChemSusChem* **2013**, *6*, 1348. (b) Ishida, T.; Kume, K.; Kinjo, K.; Honma, T.; Nakada, K.; Ohashi, H.; Yokoyama, T.; Hamasaki, A.; Murayama, H.; Izawa, Y.; Utsunomiya, M.; Tokunaga, M. *ChemSusChem* **2016**, *9*, 3441.
(3) (a) Hu, P.; Snyder, S. A. *J. Am. Chem. Soc.* **2017**, *139*, 5007. (b) Biswas, P.; Paul, S.; Guin, J. *Synlett* **2017**, *28*, 1244. (c) Hu, J.; Yu, X.; Xie, W. *Synlett* **2017**, *28*, 2517.
(4) Hattori, T.; Ueda, S.; Takakura, R.; Sawama, Y.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2017**, *23*, 8196.
(5) Schirmer, A.; Rude, M. A.; Li, X. Z.; Popova, E.; del Cardayre, S. B. *Science* **2010**, *329*, 559.
(6) (a) Bernard, A.; Joubès, J. *Prog. Lipid Res.* **2013**, *52*, 110. (b) Wolf, F. R. *Appl. Biochem. Biotechnol.* **1983**, *8*, 249.
(7) (a) Cheesebrough, T. M.; Kolattukudy, P. E. *J. Biol. Chem.* **1988**, *263*, 2738. (b) Yoder, J. A.; Denlinger, D. L.; Dennis, M. W.; Kolattukudy, P. E. *Insect Biochem. Mol. Biol.* **1992**, *22*, 237.
(8) Kikuchi, H.; Ito, I.; Takahashi, K.; Ishigaki, H.; Iizumi, K.; Kubohara, Y.; Oshima, Y. *J. Nat. Prod.* **2017**, *80*, 2716.
(9) Khadilkar, B. M.; Borkar, S. D. *J. Chem. Technol. Biotechnol.* **1998**, *71*, 209.
(10) Wang, J.-J.; Chuang, Y.-Y.; Hsu, H.-Y.; Tsai, T.-C. *Catal. Today* **2017**, *298*, 109.
(11) (a) Tsuji, J.; Ohno, K. *Tetrahedron Lett.* **1965**, *6*, 3969. (b) Ohno, K.; Tsuji, J. *J. Am. Chem. Soc.* **1968**, *90*, 99. (c) Walborsky, H. M.; Allen, L. E. *J. Am. Chem. Soc.* **1971**, *93*, 5465. (d) Doughty, D. H.; Pignolet, L. H. *J. Am. Chem. Soc.* **1978**, *100*, 7083. (e) Fristrup, P.; Kreis, M.; Palmelund, A.; Norrby, P.-O.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 5206.

Heruntergeladen von: University of Sussex. Urheberrechtlich geschützt.

(12) (a) Hawthorne, J. O.; Wilt, M. H. *J. Org. Chem.* **1960**, *25*, 2215. (b) Tsuji, J.; Ohno, K.; Kajimoto, T. *Tetrahedron Lett.* **1965**, *6*, 4565. (c) Tsuji, J.; Ohno, K. *J. Am. Chem. Soc.* **1968**, *90*, 94. (d) Wilt, J. W.; Pawlikowski, W. W. Jr. *J. Org. Chem.* **1975**, *40*, 3641. (e) Matsubara, S.; Yokota, Y.; Oshima, K. *Org. Lett.* **2004**, *6*, 2071. (f) Modak, A.; Deb, A.; Patra, T.; Rana, S.; Maity, S.; Maiti, D. *Chem. Commun.* **2012**, *48*, 4253. (g) Modak, A.; Naveen, T.; Maiti, D. *Chem. Commun.* **2013**, *49*, 252. (h) Modak, A.; Rana, S.; Phukan, A. K.; Maiti, D. *Eur. J. Org. Chem.* **2017**, 4168.

(13) Kundu, P. K.; Dhiman, M.; Modak, A.; Chowdhury, A.; Polshettiwar, V.; Maiti, D. *ChemPlusChem* **2016**, *81*, 1142.

(14) Tsuji, J.; Ohno, K. *Synthesis* **1969**, 157.

(15) Hattori, T.; Takakura, R.; Ichikawa, T.; Sawama, Y.; Monguchi, Y.; Sajiki, H. *J. Org. Chem.* **2016**, *81*, 2737.

(16) Ajdačić, V.; Nikolić, A.; Simić, S.; Manojlović, D.; Stojanović, Z.; Nikodinovic-Runic, J.; Opsenica, I. M. *Synthesis* **2018**, *50*, 119.

(17) Smari, I.; Youssef, C.; Yuan, K.; Beladhria, A.; Ben Ammar, H.; Ben Hassine, B.; Doucet, H. *Eur. J. Org. Chem.* **2014**, 1778.

(18) Taarning, E.; Madsen, R. *Chem. Eur. J.* **2008**, *14*, 5638.

(19) Akanksha, ???.; Maiti, D. *Green Chem.* **2012**, *14*, 2314.

(20) Martín, R.; Buchwald, S. L. *Org. Lett.* **2008**, *10*, 4561.

(21) Martín, R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 7236.

(22) **Pd/C-Catalyzed Decarbonylation of Aliphatic Aldehydes: Decarbonylation of 3-phenylpropanal to ethylbenzene (2a); Typical Procedure**
[CAS Reg. No. 100-41-4]
A dry glass reaction tube, purged with argon and equipped with a magnetic stirrer bar, was charged with 3–4 Å MS (100 mg), aldehyde **1a** (50 μL, 0.38 mmol), Pd/C (20 mg, 5 mol% Pd), and cyclohexane (1 mL). The tube was sealed and heated at 130 °C for 24 h. The mixture was then cooled to r.t., filtered through a pad of Celite, and washed with CH_2Cl_2 (15–20 mL), to give PhEt (**2a**) in 67% GC-MS yield (naphthalene as standard); GC-MS: m/z = 106.1 $[M]^+$.
NMR Spectroscopic Analysis: A dry glass reaction tube, purged with argon and equipped with a magnetic stirrer bar, was charged with 3–4 Å MS (100 mg), aldehyde **1a** (40 μL, 0.30 mmol), Pd/C (16 mg, 5 mol% Pd), and C_6D_6 (1 mL). The tube was sealed and heated at 130 °C for 24 h. The mixture was then cooled to r.t. and filtered through a short pad of silica gel to remove the catalyst. The silica gel was then washed with C_6D_6 (2 × 0.5 mL) to give PhEt (**2a**) in 78% NMR yield (BzOMe as standard). ^1H NMR (500 MHz, C_6D_6): δ = 7.10–7.00 (m, 5 H), 2.43 (q, J = 7.5 Hz, 2 H), 1.06 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (125 MHz, C_6D_6): δ = 144.3, 128.6, 128.1, 125.9, 29.2, 15.8..

Heruntergeladen von: University of Sussex. Urheberrechtlich geschützt.