RSC Advances

Check for updates

Iodine as an efficient initiator for the transfer-hydrogenation from 1,4-cyclohexadiene to aryl-substituted alkenes and the deoxygenation of benzylic alcohols

Sascha Kail and Gerhard Hilt (ID) *

The transfer-hydrogenation emerged as an interesting alternative to traditional hydrogenations with H_2 under transition metal catalysis. Herein, we describe I_2 as an initiator for the catalysis in CH_2Cl_2 for the transfer-hydrogenation from 1,4-cyclohexadiene to aryl-substituted alkenes as well as for the deoxygenation of benzylic alcohols at room temperature.

Historically, there is a one-reaction-publication by Eberhardt in 1967 reporting the transfer-hydrogenation from CHD to styrene utilising a I_2/CHD system to generate ethylbenzene.[1] However a broader investigation on the scope and limitations of this very simple and easy applicable system is missing in the literature. The transfer-hydrogenation from dihydroaromatic compounds to carbon–carbon double bonds was investigated in great detail by Oestreich in utilising boron-based Lewis acids, such as $B(C_6F_5)_3$, as catalysts (Scheme 1).[2–6] Thereafter several reports appeared with different Lewis acids, such as $InBr_3$,[7] [IPrGaCl2] [SbF_6][8] or alkaline-earth metal catalysts[9] which led to milder reaction conditions and an increased substrate scope.

Eventually, in 2024 we reported the $FeBr_3$ catalysed transfer-hydrogenation with 1,4-cyclohexadiene (CHD) which could be performed at ambient temperature.[10] Meanwhile the regio-selective H-D addition to alkenes[11] as well as an asymmetric version for the transfer-hydrogenation to alkenes were also reported.[12]

In a recent report, Xu and Liu disclosed the transfer-hydrogenation utilizing cyclic ketones, such as cyclo-heptanone or cyclododecanone, as the hydrogen donor for the hydrogenation of 1,1-diarylethene derivatives (Scheme 2).[13] Unfortunately, high reaction temperatures and sometimes prolonged reaction times are needed to accomplish this highly interesting transformation.

However, the fact that the α-position of ketones can be easily transformed into α-perdeuterated ketones and these derivatives were applied in the regioselective H-D transfer to the 1,1-di-arylethenes is of considerable interest.

Based on these latest reports, and the initial report by Eberhardt,[1] we became interested in expanding the application

of I_2 as the catalyst (or initiator) for the transfer-hydrogenation from CHD as H_2-surrogate to a broader range of alkenes. For this purpose, we selected 1,1-diphenylethene **1a** as a substrate for the conversion with CHD (1.1 eq.) under I_2 catalysis for the optimisation of the reaction conditions (Table 1).

The optimisation of the transfer-hydrogenation from CHD to aryl-substituted alkenes, such as **1a**, at ambient temperatures was initiated by test reactions in dichloromethane utilising increasing amounts of I_2 (Table 1, entries 1–4). The best results were obtained when 20 mol% of I_2 were employed which led to 95% yield determined by GC analysis after 15 minutes reaction time (isolated yield of **2a**: 95%; see Scheme 3). Similar results were obtained for hexane as solvent (entry 5) which gave 95%
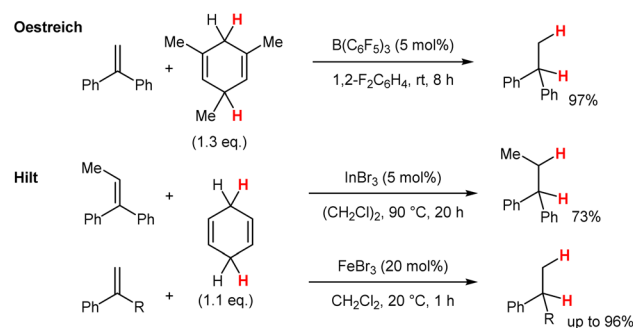
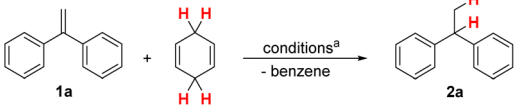Scheme 1 Transfer-hydrogenations with Lewis acid catalysts.
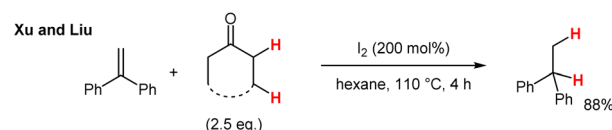
Scheme 2 Transfer-hydrogenation from ketones to alkenes with I_2 as the "catalyst".

Institute of Chemistry, Carl von Ossietzky University Oldenburg, Carl-von-Ossietzky-Str. 9-11, 26129 Oldenburg, Germany. E-mail: Gerhard.Hilt@uni-oldenburg.de

Paper

Table 1 Optimisation of the transfer-hydrogenation from CHD to alkenes with I_2 as the catalyst/initiator under a N_2 atmosphere

| Entry	I_2 loading (mol%)	Solvent	Yield[b] (after 15 min)	Yield[b] (after 1 h)
1	5	CH_2Cl_2	42%	59%
2	12	CH_2Cl_2	55%	68%
3	15	CH_2Cl_2	67%	78%
4	**20**	**CH_2Cl_2**	**95%**	**95%**
5	20	Hexane	95%	95%
6	20	$CHCl_3$	56%	73%
7	20	THF	0%	0%
8	20	MeCN	0%	0%
9	20	DMF	0%	0%
10	20	DMSO	0%	0%

[a] Reaction conditions: **1a** (0.5 mmol), CHD (0.55 mmol), solvent (0.5 mL), N_2 atm., rt. [b] Determined by GC analysis of the crude mixture with mesitylene as internal standard, added from a stock solution after the reaction.

yield after 15 minutes as well. Other solvents, such as chloroform (entry 6) were inferior and more polar solvents (entries 7–10) prohibited the desired transformation completely.

With the optimised reaction conditions for the transformation of **1a** in hand, we then investigated other substrates of type **1** for the transfer-hydrogenation from CHD to these aryl-substituted alkenes (Scheme 3). For this set of experiments, we applied 20 mol% of I_2 in dichloromethane as solvent at ambient temperature. Further substituents (R^1/R^2) were incorporated to determine the electronic effects rather than steric effects on the transfer-hydrogenation. The results for these transformations are given together with our previous results utilising $FeBr_3$ as Lewis acid catalyst when available for comparison.[10]

The basic system **1a** gave the desired product **2a** in a very similar yield as the previously described $FeBr_3$ catalyst system. But since I_2 is less sensitive to water compared to anhydrous $FeBr_3$, this is a significant advantage over the $FeBr_3$ system. Then simple alkyl-substituted diaryl alkenes (**1b** and **1c**) were tested and, in these transformations, the products **2b** and **2c** could be isolated in good yields after 15 minutes reaction time. When methoxy groups were incorporated in the substrates, such as in **2d** and **2e**, the reaction led to high conversions, as well as with a thioether substituent in **2f** affording product **2f** in 83% yield, although the reaction time had to be slightly expanded to 30 minutes.

Then, we tested additional halide substituents on the phenyl rings to determine their influence on the reaction performance. The 4,4'-difluoro derivative **2g** was obtained in similar yields compared to the $FeBr_3$ system which resulted in similar results after 1 h reaction time. The conversion of the 4-chloro derivative **1h** for the formation of **2h**, the 3-bromo derivative to generate product **2i** as well as the 4,4'-dibromo derivative **2j** were successful and the desired products could be isolated in overall
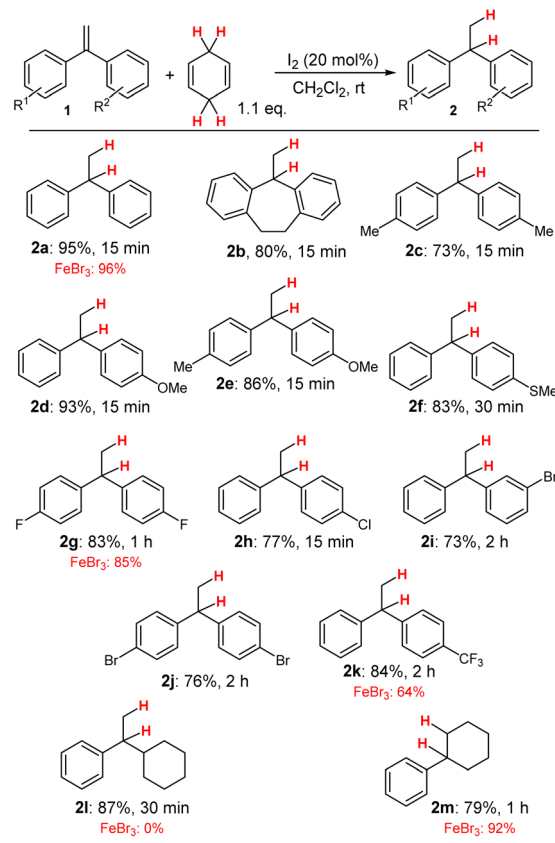
Scheme 3 Scope of the transfer-hydrogenation from CHD to aryl-substituted utilising I_2 as catalyst under N_2 atmosphere. Reaction conditions: **1** (0.5 mmol), CHD (0.55 mmol), CH_2Cl_2 (0.5 mL), N_2 atm., rt.

good yields. Surprisingly, when a substrate with a strong electron-withdrawing substituent in the *para*-position of the arene moiety was investigated, herein the CF_3-substituted substrate **1k**, which destabilize the proposed carbenium ion intermediate (see below), the desired product **2k** could be isolated in a good yield for of 84%, which is superior to the $FeBr_3$/CHD catalysed system.

For this type of transformation, where the stability of a transition carbenium ions is essential, the less stabilizing arene substituents are encountered, the less efficient the hydrogen-transfer reaction will be performed.

Therefore, we became increasingly interested, whether I_2/CHD or the $FeBr_3$/CHD system would make any difference. Compared to the $FeBr_3$/CHD system, the I_2/CHD system performed very efficient for the synthesis of product **2l** but a little less effective for the synthesis of **2m**, which was isolated in 79% yield compared to 92% when the reaction was catalysed by $FeBr_3$.

Nevertheless, the I_2/CHD system exemplified itself as an easily applicable system which is highly cost-efficient and of low harm and is an excellent method for the transfer-hydrogenation from CHD to aryl-substituted alkenes. Therefore, we also became interested in similar transformations which were realised with I_2 as a reagent or catalyst to realise reductions.[14,15]

Under these preconditions, we came across I_2-promoted transformations for the deoxygenation of alcohols and ketones.
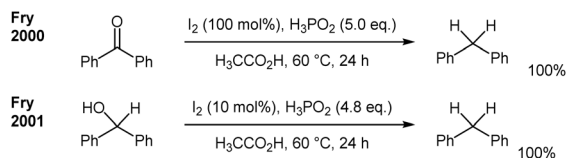
Scheme 4 Deoxygenation of benzylic ketones and benzylic alcohols with I₂/H₃PO₂ in acetic acid under reflux conditions.

Table 2 Optimisation of the deoxygenation with I₂ and CHD

| Entry	I₂ loading (mol%)	Solvent	Yield[b]				
			1 h	2 h	3 h	4 h	20 h
1	10	CH₂Cl₂	5%	6%	7%	9%	15%
2	20	CH₂Cl₂	16%	26%	37%	48%	68%
3	30	CH₂Cl₂	21%	38%	50%	75%	86%
4	**40**	**CH₂Cl₂**	**57%**	**85%**	**98%**	**98%**	**98%**
5	40	Hexane	54%	83%	98%	98%	98%
6	20	CHCl₃	6%	12%	18%	25%	39%
7	20	THF	0%	0%	0%	0%	0%

^{a} Reaction conditions: **3a** (0.5 mmol), CHD (0.55 mmol), solvent (0.5 mL), N₂ atm., rt. ^{b} Determined by GC analysis of the crude mixture with mesitylene as internal standard, added from a stock solution after the reaction.

In this context, in the past there were several remarkable reports from the Fry group regarding the deoxygenation of 1,1-diarylketones[16] and the deoxygenation of 1,1-diarylmethanol derivatives with I₂ and over-stoichiometric amounts of H₃PO₂ (Scheme 4).[17–19] Also remarkable are reports for the reductive deoxygenation utilising silanes, such as polymethylsiloxane (PMHS) as reducing agents under iodide catalysis (HI)[20] and the divergent transformations of benzylic alcohols under I₂ catalysis.[21]

For the deoxygenation of benzylic alcohols, we choose diphenylmethanol **3a** as the test substrate and tested different amounts of I₂ in a small number of solvents under ambient temperatures. The results of this optimisation are summarised in Table 2.

Compared to the previous disclosed transfer-hydrogenation from CHD to aryl-substituted alkenes, the deoxygenation needed higher I₂ loadings and extended reaction times. However, when 40 mol% of I₂ were applied, the desired product **4a** was detected by GC analysis in almost quantitative yield (98%) after 3 h reaction time (entry 4).

Again, dichloromethane and hexane (entries 4/5) exhibited similar performance, while chloroform (entry 6) proved to be inferior again and tetrahydrofuran (THF; entry 7) is not suited for this transformation.
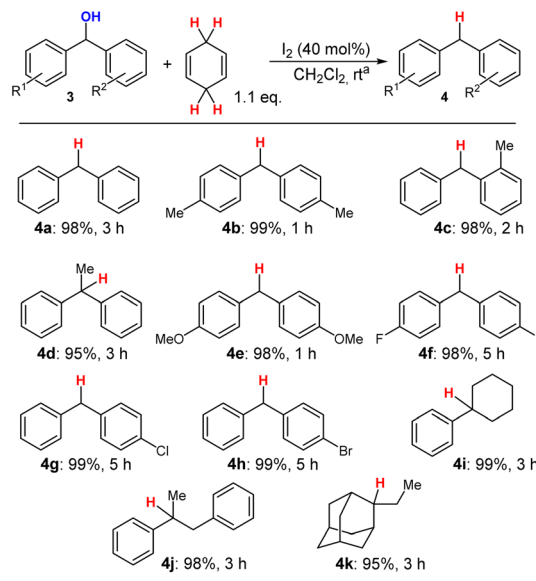
Scheme 5 Scope of the I₂-promoted deoxygenation of alcohols with CHD. ^{a}Reaction conditions: **3** (0.5 mmol), CHD (0.55 mmol), CH₂Cl₂ (0.5 mL), N₂ atm., rt.
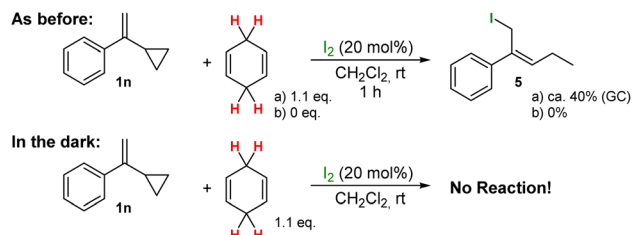
Scheme 6 Reactions with cyclopropyl-substituted substrate **1n** under the optimised conditions, in the absence of CHD and in the dark.

The other polar solvents investigated in Table 1 were not tested for this transformation, as dichloromethane and hexane proved to be very well suited for this deoxygenation reaction.

With these reaction conditions in hand, we then tested several carbinol derivatives of type **3** to generate the deoxygenated products of type **4** under mild reaction conditions. The results of these transformations are summarised in Scheme 5.

In general, the applied carbinol-type substrates **4a–4h** were deoxygenated in very high yields (>95%) and only the reaction time had to be adjusted for each substrate, ranging from 1 to 5 hours. We then tested also aryl-alkyl substituted benzylic alcohols and the products **4i** and **4j** could be obtained in very high yields (>98%) as well. Also, the adamantly derivative **3k** was converted into **4k** in an excellent yield of 95% which shows that this transformation has the potential be applicable also for non-benzylic alcohols in the future.

Finally, we also tested a cyclopropyl-substituted starting materials to prove that the reaction mechanism is of ionic character and not following radical mechanisms (see Schemes 6/7). For this purpose, substrates **1n** and **3l** were used
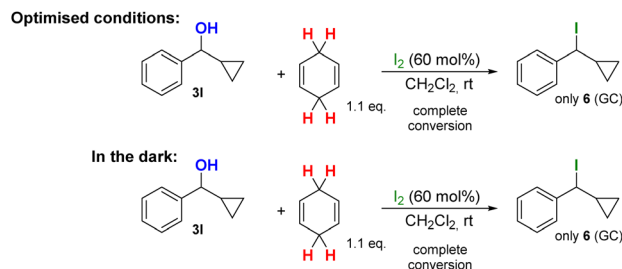
Scheme 7 Reactions with cyclopropyl-substituted substrate 3l under the optimised conditions and in the dark with 60 mol% I_2.

and in contrast to the previous reactions investigated thus far, the following observations were made:

For substrate **1n**:

• The hydrogenation of the cyclopropyl-substituted alkene **1n** gave the product **5** with iodine incorporated in the product. This incorporation was only observed for this transformation!

• In the absence of CHD no reaction was observed.

• When the reactions of **1n** was performed in the dark, no reaction was observed.

For substrate **3l**:

• The brown-coloured reaction solution only decolorised with substrate **3l**. In all other reactions, the coloured solution persisted.

• Only in product **6**, the incorporation of iodine in the product was observed as determined by GCMS and NMR analysis of the crude product.

• When the reactions for the cyclopropyl-substituted alcohol **3l** was performed in the dark, in the presence of CHD complete conversion to **6** was observed.

• In several reactions, a bis-carbinol ether intermediate, such as $Ph_2CH–O–CHPh_2$, was detected by GCMS analysis, indicating that the reaction is most likely following an ionic mechanism for those substrates. When the reaction of **3l** was performed in the dark in the absence of CHD, only the formation of the corresponding two diastereomeric dimers could be observed.

In general, the mechanistic investigations of reactions with cyclopropyl-substituted substrates are a well-accepted method to differentiate between ionic and radical reaction mechanisms. However, we believe that in this special case, the reaction mechanism is for whatever reason, altered when a cyclopropyl substituent alkene or an alcohol are involved, thus leading to completely different products (=**5** and **6**) and different chemical behaviour when the reactions are performed in the absence of light or in the absence of CHD. For substrate **1n**, light and CHD as H• donor seem to be essential for the radical-type ring opening of **1n** to **5**. In contrast, educt **3l** reacts with and without light efficiently to give **6** as single product. Whereas in the absence of CHD, only the formation of the corresponding ether is observed, indicating that this reaction is following an ionic mechanism.

Accordingly, we believe that the transformations outlined in this report are of ionic character. The I_2 is oxidizing CHD to form benzene and HI in small amounts at first.[22] The HI initiates the proton catalysis and is reacting with the starting materials of type **1** (and **3** – not shown) leading to stabilized carbenium ions of type **A** (Scheme 8).
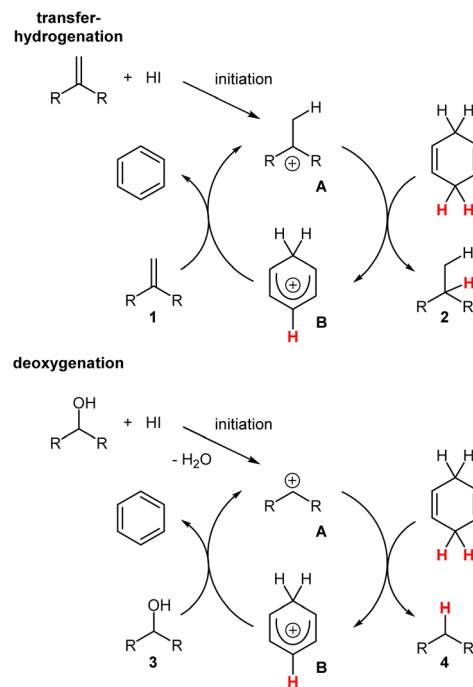
Scheme 8 Proposed mechanism of the transfer-hydrogenation and the deoxygenation with the I_2/CHD system.

The intermediate **A** then abstracts a hydride ion from CHD to form the desired products **2** and simultaneously generates the arenium ion **B** (= Wheland complex), which acts as a strong Brönstedt acid, to protonate the starting materials **1** and thereby closes the catalytic cycle. For the starting materials of type **3**, water is formed as a good leaving group, but the deoxygenation reaction also follows the same principle. However, in these reactions radical mechanisms cannot be excluded.

In summary, we have developed an I_2-initiated transfer-hydrogenation of aryl-substituted alkenes under very mild conditions utilising CHD as a H_2-surrogate. Also, the I_2-initiated deoxygenation of benzylic alcohols was investigated which led to excellent results when the reaction time is adjusted to the substrate. In addition, this transformation could be conducted ambient reaction conditions and opens the way for further investigations with the I_2/CHD system for more sophisticated deoxygenations that we have in mind.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information is available. See DOI: **https://doi.org/10.1039/d5ra07048a**.

Notes and references

1 M. K. Eberhardt, *Tetrahedron*, 1967, **23**, 3029.

2 A. Simoneneau and M. Oestreich, *Angew. Chem., Int. Ed.*, 2013, **52**, 11905.

3 A. Simoneneau, J. Friebel and M. Oestreich, *Eur. J. Org Chem.*, 2014, 2077.

4 J. Mohr and M. Oestreich, *Angew. Chem., Int. Ed.*, 2014, **53**, 13278.

5 I. Chatterjee and M. Oestreich, *Angew. Chem., Int. Ed.*, 2015, **54**, 1965.

6 W. Yuan, P. Orecchia and M. Oestreich, *Chem. Commun.*, 2017, **53**, 10390.

7 L. Li, S. Kail, S. M. Weber and G. Hilt, *Angew. Chem., Int. Ed.*, 2021, **60**, 23661.

8 B. Michelet, C. Bour and V. Gandon, *Chem.–Eur. J.*, 2014, **20**, 14488.

9 H. Bauer, K. Thum, M. Alonso, C. Fischer and S. Harder, *Angew. Chem., Int. Ed.*, 2019, **58**, 4248.

10 S. Kail and G. Hilt, *Synlett*, 2024, **35**, 1011.

11 L. Li and G. Hilt, *Org. Lett.*, 2020, **22**, 1628.

12 B. Wolff, Z.-W. Qu, S. Grimme and M. Oestreich, *Angew. Chem.*, 2023, **135**, e202305295.

13 Y. Duan, W. Zhong, Z. Zeng, J. Feng, J. Xu, F. Yang and J. Liu, *Chem. Commun.*, 2024, **60**, 75.

14 J. A. Luján-Montelongo, J. B. Mateus-Ruiz and R. M. Valdez-García, *Eur. J. Org Chem.*, 2023, **26**, e202201156.

15 L. D. Hicks, J. K. Han and A. J. Fry, *Tetrahedron Lett.*, 2000, **41**, 7817.

16 P. E. Gordon and A. J. Fry, *Tetrahedron Lett.*, 2001, **42**, 831.

17 A. J. Fry, M. Allukian and A. D. Williams, *Tetrahedron*, 2002, **58**, 4411.

18 P. E. Gordon, A. J. Fry and L. D. Hicks, *ARKIVOC*, 2005, 393.

19 M. Allukian, P. E. Gordon, G. S. Han, L. D. Hicks and A. J. Fry, *ARKIVOC*, 2002, 76.

20 X. Ye, J. Zhang, H. Yang, S. Yang, Q. Ren and Y. Peng, *Org. Biomol. Chem.*, 2025, **23**, 2878.

21 M. Jereb and D. Vražič, *Acta Chim. Slov.*, 2017, **64**, 747.

22 I. Chatterjee and M. Oestreich, *Org. Lett.*, 2016, **18**, 2463.