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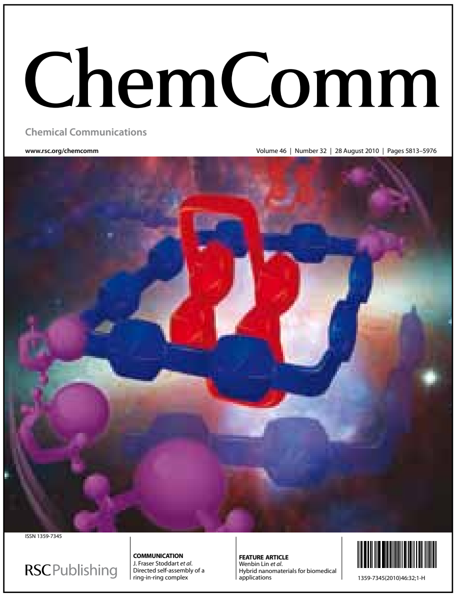

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ARTICLE TYPE

Selective reduction of carboxylic acids to aldehydes through manganese catalysed hydrosilylation

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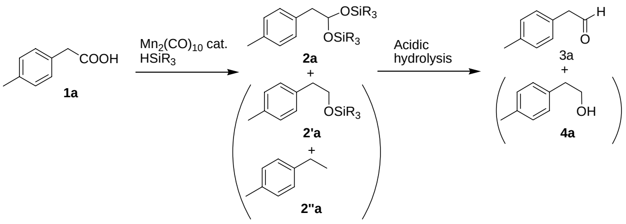
The direct reduction of carboxylic acids to disilylacetals was achieved though manganese catalyzed hydrosilylation reaction in the presence of triethylsilane under mild conditions, at r.t. and under UV irradiation (350 nm). The aldehydes were obtained in good to excellent yields after an acidic hydrolysis.

Aldehydes are key building blocks in organic synthesis due to their high reactivity and are valuable compounds in flavour and fragrance industry.[1] Among the various methods developed for the preparation of aldehydes, the direct reduction of carboxylic acids to aldehydes is a straightforward reaction, which usually suffers from selectivity issues due to the over-reduction to alcohols.[2, 3] Often, a two-step procedures have to be employed for the synthesis of aldehydes, either through full reduction to alcohols prior to re-oxidation to aldehydes[4] or through the transformation of the carboxylic acids to more reactive acid derivatives, such as esters, acyl halides and anhydrides, prior to reduction.[5] During the last years, hydrosilylation has emerged as an elegant and efficient methodology for the reduction of carboxylic acid derivatives under mild conditions with high chemoselectivity.[6] Usually carboxylic acids react with one equivalent of silane to give the corresponding silyl esters.[7] Nevertheless lately, the selective hydrosilylation of carboxylic acids to form aldehydes has been reported: Nagashima[8] performed the reduction with (μ_3, η^2, η^3, η^5-acenaphthylene)$Ru_3(CO)_7$ as the catalyst and with a bis-silane, 1,2-bis(dimethylsilyl)benzene. Brookhart[9] achieved the transformation with the strong Lewis acid, $B(C_6F_5)_3$ as the catalyst, and with triethylsilane. Finally, we have employed an iron catalyst, namely (PBO)$Fe(CO)_3$, (PBO = *trans*-4-phenyl-but-3-en-2-one) combined with 1,1-3,3-tetramethyldisiloxane.[10] In the three cases, the formation of in situ stable disilylacetals intermediates, converted into aldehydes upon hydrolysis, allows the transformation to proceed with high chemoselectivity.

Manganese is an earth-abundant element and therefore would be a sustainable, economical alternative source for developing new catalytic process. To the best of our knowledge, the use of manganese as a catalyst in homogeneous reduction such as hydrogenation and hydrogen transfer reaction is extremely rare.[11,12] Besides, in the field of hydrosilylation reactions, compared to other transition metals of the first row of the periodic table, manganese promoted reductions are also quite rare, even for alkenes and carbonyl derivatives[11, 13-18] It is noteworthy that for carboxylic acid derivatives, two isolated examples of reduction of amides to amines were reported, catalysed by $Mn_2(CO)_{10}$[17a] and $CpMn(CO)_3$.[17b] More interestingly, in 1995, Cutler described the hydrosilylation of esters to form ethers with a manganese carbonyl acetyl complex, $(CO)_5MnC(O)CH_3$, as an efficient catalyst with phenylsilane.[18] In the continuation of our reports on the iron catalyzed reduction of carboxylic acid derivatives,[19] herein we report the first application of manganese complex as the catalyst for the challenging transformation of carboxylic acids into aldehydes.



Sheme 1: Hydrosilylation of carboxylic acids with manganese

Table 1. Optimization of the reaction parameters [a]

Entry	Silane (equiv.)	Solvent	Time (h)	Conv. [%][b]
1[c]	Et_3SiH (4)	toluene	24	0
2[d]	Et_3SiH (4)	toluene	24	10
3	Et_3SiH (4)	toluene	24	97
4[e]	Et_3SiH (4)	toluene	24	81
5	Et_3SiH (3.3)	toluene	3	93
6	Et_3SiH (3.3)	Et_2O	3	92
7	Et_3SiH (4)	pentane	8	26
8	Et_3SiH (4)	THF	8	0
9	Et_3SiH (4)	CH_3CN	8	0
10	Et_3SiH (4)	CH_2Cl_2	8	64

[a] Reaction conditions: 4-methylphenylacetic acid **1a** (0.5 mmol), Et_3SiH (3.3 - 4 equiv.), $Mn_2(CO)_{10}$ (5 mol%) in 1 mL of solvent at room temperature under UV irradiation (350 nm) for 3 – 24 h. [b] The conversion was determined by ^1H NMR spectroscopy for the formation of the disilylacetal **2a**. [c] The reaction was carried out at 100 °C, without UV irradiation. [d] The reaction was carried out at 100 °C, with visible light irradiation (24 W fluocompact light bulb). [e] $Mn_2(CO)_{10}$ (2.5 mol%) was used.

We started our investigation with the reduction of 4-methylphenylacetic acid (**1a**) as the model substrate with triethylsilane as the reducing agent and with $Mn_2(CO)_{10}$[20] as the catalyst (Scheme 1, Table 1). Under thermal activation, at 100 °C in toluene, after 24 h, no reaction occurred, whereas under visible light irradiation, at 100 °C after 24 h of reaction,

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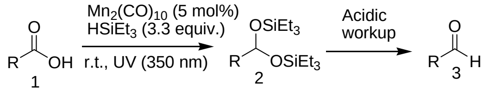
10% of the disilylacetal **2a** was formed (Table 1, entries 1-2). To our delight, the reduction undergoes smoothly under UV irradiation (350 nm) at room temperature: after 24 h, in toluene, with 5 mol% of catalyst and 4 equiv. of Et_3SiH, a full conversion into **2a** was obtained (entry 3). It is noteworthy that no over-reduction to alkyl silyl ether **2'a** nor to fully reduced *p*-ethyltoluene **2''a** was detected by ^1H NMR of the crude mixture. A lower catalyst loading (2.5 mol%) decreases the conversion to 81% (Entry 4), but only 3.3 equiv. of silane and 3 h are sufficient to reach high yield in **2a** (93%, entry 5). Among the various solvent tested, toluene and Et_2O gave satisfactory results. (Table 1, entries 5-10)

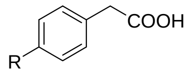
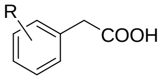
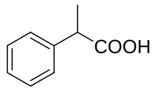
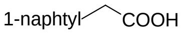
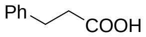
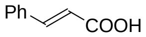
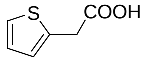
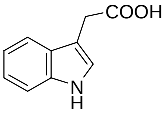
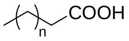
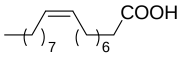
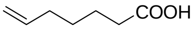
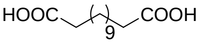
The choice of the silane is of crucial importance for the selectivity of this reduction: with monosilanes, such as Et_3SiH, Ph_2MeSiH and $PhMe_2SiH$, after an acidic work, 97% of the aldehyde **3a** was formed; with Ph_3SiH, the reaction did not take place, while with secondary silanes like Ph_2SiH_2, Et_2SiH_2, 1,1,3,3-tetramethyldisiloxane (TMDS), the alcohol **4a** was formed as the major product (from 80 to 97%, see Supporting Information).

Having optimized the reaction conditions ($Mn_2(CO)_{10}$ (5 mol%), Et_3SiH (3.3 equiv.), toluene or Et_2O,[21] UV irradiation at 350 nm, rt, 3 h), we then investigated the scope of this selective reduction of carboxylic acids to aldehydes. (Table 2) Under these conditions, phenylacetic acid, and its substituted derivatives with a methyl or a methoxy group at the para-position undergo hydrosilylation to produce the corresponding disilylacetals derivatives **1a-c** with high yields in 3 h (entries 1-3). The presence of an amino group does not inhibit the reaction, and the corresponding protected aminoaldehyde is produced with 85% isolated yield. (Entry 4) The reduction of the 4-hydroxyphenylacetic acid leads to the formation of the corresponding disilylacetal with the concomitant silylation of the hydroxyl group: thus the conversion was slightly increased with the use of 5 equiv. of Et_3SiH instead of 4 equiv. (Entry 5) This reduction is also tolerant toward halides, as no dehalogenation was observed during the reduction. However, a longer reaction time (24 h) was needed to reach good conversions, which might be due to the electronic effect of the halides. (Entries 6-8) On the opposite, nitro group inhibits the reaction (entry 9). A control experiment was carried out: the reduction **1a** in the presence of one equivalent of nitrobenzene confirmed the deleterious effect of nitro group on the catalytic system, as no conversion was detected. These results could be explained by the formation of an adduct between the nitro group and manganese carbonyl species that deactivates the catalytic system.[22]

The steric hindrance has a noticeable effect on this catalytic reduction as shown by the influence of the position of the substitution on the phenyl ring in **1j** (ortho position) compared to **1a** and **1k** (respectively para and meta position), and by the absence of reaction of **1l** (entries 1, 10-12). Similar behaviour has been found previously for the hydrolysis of silanes catalyzed by $Mn_2(CO)_{10}$.[14a,15f] Interestingly 1-naphtylacetic acid **1m** was converted in good yield to the corresponding disilylacetal. (77%, entry 13) The reduction of 3-phenylpropionic and cinamic acids lead to the same product, as the conjugated C=C bond of **1o** is fully reduced under these conditions. (entries 14 and 15)

Table 2. Scope of the hydrosilylation of carboxylic acids to give aldehydes under the catalysis of $Mn_2(CO)_{10}$



Entry	Substrate		[a]	Conv.[%][b]	Yield [%][c]
1		**1a,** R = Me	**A**	93	90
2		**1b,** R = H	**A**	85	83
3		**1c,** R = OMe	**A**	>97	93
4[d]		**1d,** R = NH_2	**B**	-	85
5[d]		**1e,** R = OH	**B**	85	74
				90[e]	82[e]
6[d]		**1f,** R = F	**A**	89	87
7[d]		**1g,** R = Cl	**A**	88	82
8[d]		**1h,** R = Br	**A**	91	86
9[d]		**1i,** R = NO_2	**A**	0	-
10[d]		**1j,** R = *o*-Me	**A**	61	60
11[d]		**1k,** R = *m*-Me	**B**	89	87
12[d]		**1l**	**B**	< 3	-
13[d]		**1m**	**A**	93	77
14[d]		**1n**	**A**	>97	96 (71)[f]
15[d]		**1o**	**A**	78	70
16[d]		**1p**	**A**	82	70
17[d]		**1q**	**B**	>97	88
18[d]		**1r,** n = 13	**B**	>97	98 (92)
19		**1s,** n = 10	**A**	>97	92 (81)
20		**1t**	**B**	>97	98 (88)
21[g]		**1u**	**B**	92[h]	-
22[i]		**1v**	**B**	97	97
23[g]	CH_3COOH	**1w**	**B**	>97	95 (81)[j]
24[g]	HCOOH	**1x**	**B**	>97	97 (52)[j]
25[d]	CF_3COOH	**1y**	**A**	0	

[a] Reaction conditions: carboxylic acid (1 mmol), Et_3SiH (3.3 mmol, 3.3 equiv.), $Mn_2(CO)_{10}$ (5 mol%), room temperature, UV irradiation (350 nm), 3 h, toluene (2 mL) (**A**) or Et_2O (2 mL) (**B**). [b] The conversion to the silyl intermediate **2** was determined by ^1H NMR spectroscopy. [c] Isolated yield for **2** after purification by column chromatography. The numbers in parentheses are the yields of isolated aldehydes **3**. [d] Et_3SiH (4 equiv.) was used and the reaction was irradiated under UV for 24 h. [e] 5 equiv. of Et_3SiH was used instead of 4 equiv. [f] The conjugated C=C bond was fully reduced. [g] Et_3SiH (4 equiv.) was used. [h] 60% of the insaturated disilylacetal and 32% of the trisilylated product resulting from the hydrosilylation of both the acid and the alkene groups were formed. [i] The reaction was carried out with

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$Mn_2(CO)_{10}$ (10 mol%), Et_3SiH (10 equiv.), for 24 h under UV irradiation. [j] The product was isolated as the 2,4-dinitrophenylhydrozone adduct after hydrolysis.

It is noteworthy that heteroaromatic carboxylic acids such **1p** and **1q** bearing respectively a thiophenyl and an indolyl moieties are reduced in good yields (70% and 88%, respectively, entries 16 and 17). On the other hand, aliphatic carboxylic acids, such as palmitic (**1r**) and tetradecanoic (**1s**) acids gave after hydrolysis the corresponding aldehydes in very good yields (92 and 81%, entries 18 and 19). The presence of internal, non conjugated C=C double bond is tolerated, as shown by the sole reduction of the carboxylic group in the oleic acid **1t** (entry 20), whereas in the case of a terminal C=C double bond like in the hept-6-enoic acid **1u**, a mixture resulting from the partial hydrosilylation of the alkene moieties was obtained (60% of the insaturated disilylacetal and 32% of the trisilylated product resulting from the hydrosilylation of both the acid and the alkene groups (entry 21). Interestingly, the diacid **1v** leads to the formation of the protected dialdehyde in excellent yield (97%, entry 22). Finally, acetic acid and formic acid were also nicely converted to the corresponding aldehydes, which were isolated as their hydrazone derivatives in good yields (81 % and 52%, entries 23 and 24). In contrast, trifluoroacetic acid was not reduced under similar condition (entry 25).

The reactivity of benzoic carboxylic acid derivatives was also investigated under similar conditions: the reduction of benzoic acid, *p*-methyl and *p*-methoxybenzoic acids leads to the exclusive formation of the corresponding aldehydes in modest yields, respectively 39%, 29% and 35% yields after hydrolysis (See Electronic Supporting Information).

In summary, we have developed the first reduction of carboxylic acids to aldehydes catalysed by commercially available and inexpensive manganese carbonyl complex $Mn_2(CO)_{10}$ in the presence of triethylsilane as an affordable and stable reducing agent. The reaction proceeds at room temperature under UV irradiation. Of notable interest is the isolation of the stable protected aldehydes as their disilylacetals, which can be hydrolysed to the corresponding aldehydes.

Notes and references

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† Electronic Supplementary Information (ESI) available. See DOI: 10.1039/b000000x/

[1] (a) R. C. Larock, in Comprehensive Organic Transformations, 2nd ed., Wiley-VCH, New York, 1999; (b) B. Levrand, W. Fieber, J.-M. Lehn and A. Herrmann, *Helv. Chim. Acta*, 2007, **90**, 2281.

[2] J. Seyden-Penne, in Reductions by the Alumino- and *Borohydrides in Organic Synthesis*, 2nd ed., Wiley, New York, 1997.

[3] (a) H. C. Brown, J. S. Cha, B. Nazer and N. M. Yoon, *J. Am. Chem. Soc.*, 1984, **106**, 8001; (b) J. S. Cha, J. E. Kim and K. W. Lee, *J. Org. Chem.*, 1987, **52,** 503; (c) M. Muraki and T. Mukaiyama, *Chem. Lett.*, 1974, 1447; (d) T. D. Hubert, D. P. Eyman and D. F. Wiemer, *J. Org. Chem.*, 1984, **49**, 2279; (e) J. S. Cha, K. D. Lee, O. O. Kwon, J. M. Kim and H. S. Lee, *Bull. Korean Chem. Soc.*, 1995, **16**, 561; (f) J. S. Cha and S. J. Moon, *Bull. Korean Chem. Soc.*, 2002, **23**, 1340; (g) F. M. Marlett and W. S. Park, *J. Org. Chem.*, 1990, **55**, 2968; (h) T. Sato, T. Jinbo and M. Sato, *Synthesis,* 1981, 871; (i) R. J. P. Corriu, G. F. Lanneau and M. Perrot, *Tetrahedron Lett.*, 1987, **28**, 3941.

[4] *Comprehensive Organic Synthesis*, B. M. Trost Ed., Pergamon, Oxford, **1991**, Vol. 8, pp 259-305.

[5] (a) R. Braden and T. Himmler, *J. Organomet. Chem.,* 1989, **367**, C12; (b) T. Fukuyama, S.-C. Lin and L. Li, *J. Am. Chem. Soc*., 1990, **112**, 7050; (c) P. T. Ho and K.-y. Ngu, *J. Org. Chem,*. 1993, **58**, 2313; (d) S. Chandrasekhar, M. Suresh Kumar and B. Muralidhar, *Tetrahedron Lett.,* 1998, **39**, 909; (e) C. O. Kangani, D. E. Kelley and B. W. Day, *Tetrahedron Lett.,* 2006, **47**, 6289; (f) D. V. Gutsulyak and G. I. Nikonov, *Adv. Synth. Catal.,* 2012, **354**, 607. (g) P. Four and F. Guibé, *J. Org. Chem.,* 1981, **46**, 4439; (h) K. Nagayama, I. Shimizu and A. Yamamoto, *Chem. Lett.,* 1995, 367; (i) K. Nagayama, I. Shimizu and A. Yamamoto, *Bull. Chem. Soc. Jpn.,* 2001, **74**, 1803.

[6] D. Addis, S. Das, K. Junge and M. Beller, *Angew. Chem. Int. Ed.,* 2011, **50**, 6004.

[7] M. Chauhan, B. P. S. Chauhan and P. Boudjouk, *Org. Lett.* 2000, **2**, 1027.

[8] K. Miyamoto, Y. Motoyama and H. Nagashima, *Chem. Lett.* 2012, **41**, 229.

[9] D. Bézier, S. Park and M. Brookhart, *Org. Lett.,* 2013, **15**, 496.

[10] L. C. Misal Castro, H. Li, J.-B. Sortais and C. Darcel, *Chem. Commun.,* 2012, **48**, 10514.

[11] R. I. Khusnutdinov, A. R. Bayguzina and U. M. Dzhemilev, *Russ. J. Org. Chem*., 2012, **48**, 309.

[12] (a) M. C. Berndt, J. de Jersey and B. Zerner, *J. Am. Chem. Soc.,* 1977, **99**, 8335; (b) R. Sweany, S. C. Butler and J. Halpern, *J. Organomet. Chem.,* 1981, **213**, 487; (c) J. F. Garst, T. M. Bockman and R. Batlaw, *J. Am. Chem. Soc.,* 1986, **108**, 1689.

[13] (a) S. L. Pratt and R. A. Faltynek, *J. Organomet. Chem.,* 1983, **258**, C5; (b) H. S. Hilal, M. Abu-Eid, M. Al-Subu and S. Khalaf, *J. Mol. Catal*., 1987, **39**, 1; (c) N.A. Kuz'min, L.V. Il'inskaya, R.G. Gasanov, E.Ts. Chukovskaya and R.Kh. Freidlina, *Izv. Akad.* Nauk SSSR, Ser. Khim., 1986, 212.

[14] (a) H. S. Hilal, S. Khalaf, M. Al Nuri and M. Karmi, *J. Mol. Catal.* 1986, **35**, 137; (b) B. T. Gregg and A. R. Cutler, *Organometallics* 1994, **13**, 1039.

[15] (a) P. K. Hanna, B. T. Gregg and A. R. Cutler, *Organometallics,* 1991, **10**, 31; (b) B. T. Gregg, P. K. Hanna, E. J. Crawford and A. R. Cutler, *J. Am. Chem. Soc.,* 1991, **113**, 384; (c) M. D. Cavanaugh, B. T. Gregg and A. R. Cutler, *Organometallics,* 1996, **15**, 2764; (d) M. D. Cavanaugh, B. T. Gregg, R. J. Chiulli and A. R. Cutler, *J. Organomet. Chem.,* 1997, **547**, 173; (e) S. U. Son, S.-J. Paik, I. S. Lee, Y.-A Lee, Y. K. Chung, W. K. Seok and H. N. Lee, *Organometallics*, 1999, **18**, 4114; (f) S. U. Son, S.-J. Paik and Y. K. Chung, *J. Mol. Catal. A*, 2000, **151**, 87; (g) M. Igarashi, Y. Sugihara and T. Fuchikami, *Tetrahedron Lett.,* 1999, **40**, 711.

[16] B. T. Gregg and A. R. Cutler, *Organometallics,* 1993, **12**, 2006.

[17] (a) M. Igarashi and T. Fuchikami, *Tetrahedron Lett.,* 2001, **42**, 1945; (b) R. Arias-Ugarte, H. K. Sharma, A. L. C. Morris and K. H. Pannell, *J. Am. Chem. Soc.,* 2012, **134**, 848.

[18] Z. Mao, B. T. Gregg and A. R. Cutler, *J. Am. Chem. Soc.,* 1995, **117**, 10139.

[19] (a) D. Bézier, G. T. Venkanna, L. C. Misal Castro, J. Zheng, T. Roisnel, J.-B. Sortais and C. Darcel, *Adv. Synth. Catal.,* 2012, **354**, 1879; (b) D. Bézier, G. T. Venkanna, J.-B. Sortais and C. Darcel, *ChemCatChem.,* 2011, **3**, 1747; (d) H. Li, L. C. Misal Castro, J. Zheng, T. Roisnel, V. Dorcet, J.-B. Sortais and C. Darcel, *Angew. Chem. Int. Ed.* 2013, **52**, 8045.

[20] $Mn_2(CO)_{10}$ 98% was purchased from Strem and ICP-MS analysis were performed. For critical review about the impurities in catalysis see: I. Thomé, A. Nijs and C. Bolm, *Chem. Soc. Rev.,* 2012, **41**, 979.

[21] The choice of the solvent depends on the solubility of the starting carboxylic acid.

[22] A. Alberti and C. M. Camaggi, *J. Organomet. Chem.,* 1980, **194**, 343.