A Direct Reduction of Aliphatic Aldehyde, Acyl Chloride, Ester, and Carboxylic Functions into a Methyl Group

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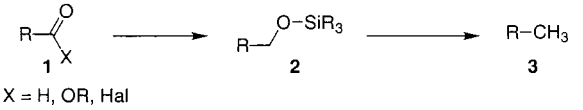
The aliphatic carboxylic group was efficiently reduced to the methyl group by $HSiEt_3$ in the presence of catalytic amounts of $B(C_6F_5)_3$. To the best of our knowledge, this is the first example of a direct exhaustive reduction of *aliphatic* carboxylic function. Aliphatic aldehydes, acyl chlorides, anhydrides, and esters also underwent complete reduction under similar reaction conditions. Aromatic carboxylic acids, as well as other carbonyl functional equivalents, underwent smooth partial reduction to the corresponding TES-protected benzylic alcohols. It was shown that, unlike the reduction of aliphatic substrates, the exhaustive reduction of aromatic substrates was not straightforward: a concurrent Friedel−Crafts-like alkylation process competed with the reduction yielding trace to notable amounts of dimeric products, thus decreasing the overall selectivity of the reduction process.

It is difficult to overstate the importance of Lewis acids in various types of organic transformations involving carbonyl groups and their equivalents.[1] Reduction of carbonyl compounds with hydrosilanes in the presence of Lewis acids is also well-known. Most known reduction methods of this type require a stoichiometric amount of Lewis acid.[2] However, a partial reduction of carbonyl compounds with hydrosilanes in the presence of a catalytic amount of a nontraditional Lewis acid, such as $B(C_6F_5)_3$, was recently reported by Piers and co-workers.[3] At the same time, we have demonstrated that catalytic amounts of $B(C_6F_5)_3$ in together with a stoichiometric amount of hydrosilane was enough for the effective cleavage of alkyl ethers and exhaustive reduction of alcohols into the corresponding hydrocarbons.[4] Having in hand our methodology for the transformation of alcohols and ethers into hydrocarbons,[4] and keeping in mind Piers' reduction protocol,[3] we attempted to combine these methodologies toward the development of a convenient one-pot procedure for a direct conversion of carbonyl compounds into the hydrocarbons.

Herein we report the first examples of an efficient direct transformation of the aliphatic carboxylic function into the methyl group[5] by $HSiEt_3$ in the presence of a catalytic amount of $B(C_6F_5)_3$. An exhaustive reduction of aliphatic carbonyl functional equivalents into the hydrocarbons and partial reduction of their aromatic counterparts, as well as aromatic carboxylic acids, into the silyl benzyl ethers is also described.

Results and Discussion

$B(C_6F_5)_3$-Catalyzed Reduction of Aldehydes, Acyl Chlorides, and Esters with Hydrosilanes. It was found that *n*-dodecanal (**1a**) in the precence of 5 mol % of $B(C_6F_5)_3$ and 3 equiv of $HSiEt_3$ was easily reduced into the *n*-dodecane in excellent yield (**3a**, eq 1, Table 1, entry 1). Similarly, aliphtic acyl chloride **1b** and ester **1c** under



(1)

similar conditions (see Experimental Section for details) were also smoothly reduced to give the corresponding hydrocarbons **3b,c** in virtually quantitative isolated yields (entries 2,3). Cyclic aryl ester **1d** underwent lactone ring cleavage and subsequent exhaustive reduction of the carbonyl group to give the aryl TES-ether **3d** quantitatively (entry 4).

Exhaustive reduction of aromatic carbonyl compounds, in contrast, did not prove so simple. Thus, reduction of aromatic carbonyl compounds **1e−g** with excess trieth-

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(1) For general reviews, see: (a) Yamaguchi, M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, Chapter 1.11. (b) *Lewis Acid Chemistry*; Yamamoto, H., Ed.; Oxford University Press: New York, 1999.

(2) For reduction of ketones with a hydrosilane−Lewis acid system, see: (a) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Tetrahedron Lett.* **1987**, *28*, 6331. (b) Kitazume, T.; Kobayashi, T.; Yamamoto, T.; Yamazaki, T. *J. Org. Chem.* **1987**, *52*, 3218. (c) Dailey, O. D., Jr. *J. Org. Chem.* **1987**, *52*, 1984. (d) Doyle, M. P.; West, C. T.; Donnely, S. J.; McOsker, C. C. *J. Organomet. Chem.* **1976**, *117*, 129. For reductive cleavage of acetales and ketales with hydrosilanes, see: (e) Jun, J.-G. *J. Heterocycl. Chem.* **1997**, *34*, 633. (f) Olah, G. A.; Yamato, T.; Iyer, P. S.; Prakash, G. K. S. *J. Org. Chem.* **1986**, *51*, 2826. (g) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1979**, 4679. (h) Kotsuki, H.; Ushio, Y.; Yoshimura, N.; Ochi, M. *J. Org. Chem.* **1987**, *52*, 2594.

(3) (a) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440. (b) Parks, D. J.; Blackwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090.

(4) (a) Gevorgyan, V.; Liu, J.-X.; Rubin, M.; Benson, S.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 8919. (b) Gevorgyan, V.; Rubin, M.; Benson, S.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2000**, *65*, 6187.

(5) For the reduction of an aromatic carboxylic function into the methyl group, see: (a) Benkeser, R. A.; Foley K. M.; Gaul, F. M.; Li, G. S. *J. Am. Chem. Soc.* **1970**, *92*, 3232. (b) Li, G. S.; Ehler, D. F.; Benkeser, R. A. *Org. Synth.* **1988**, *50*, 747.

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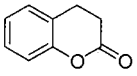
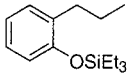
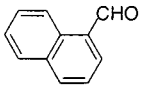
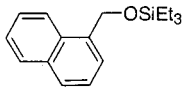
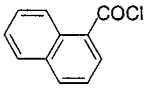
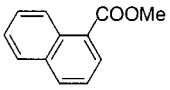
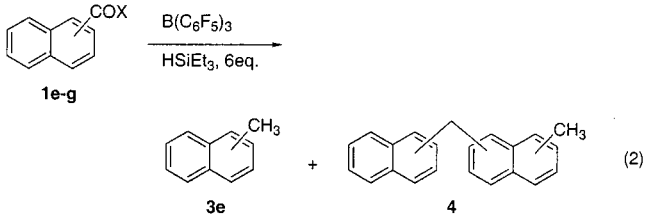
Table 1. Reduction of Aliphatic and Aromatic Carbonyl Function Equivalents[a]

Entry	Substrate, 1	$HSiEt_3$, eq.	Product 2, Yield, %[b] (Method)	Product 3, Yield, %[b] (Method)
1	n-$C_{11}H_{23}CHO$ **1a**	3.0		n-$C_{12}H_{26}$, **3a**, 96 (**A**)
2	n-$C_{15}H_{31}COCl$ **1b**	4.0		n-$C_{16}H_{34}$, **3b**, 97 (**A**)
3	n-$C_{17}H_{35}COOMe$ **1c**	6.0		n-$C_{18}H_{38}$, **3c**, 96 (**A**)
4	 **1d**	6.0		 **3d**, >99 (**C**)
5	 **1e**	1.1	 **2a**, 96 (**C**)	
6	 **1f**	2.2	**2a**, 95 (**C**)	
7	 **1g**	3.3	**2a**, 92 (**C**)	

[a] All reactions were performed on a 5 mmol scale. [b] Isolated yields.

ylsilane in the presence of 5 mol % of $B(C_6F_5)_3$ afforded methylnaphthalene **3e**, as a major reaction product (eq 2). However, in all cases **3e** was accompanied with trace

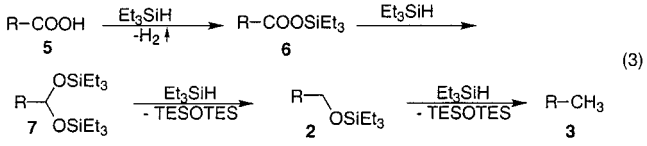


(2)

to notable amounts of inseparable mixtures of dimeric Friedel−Crafts alkylation products **4**[6] (eq 2). Careful studies of the reaction course revealed that the first step(s) of the reduction of the aromatic substrates **1e**−**g** proceeded cleanly to form the TES-ptotected naphthyl alcohols **2** (eq 1). In contrast, the last reduction step, transformation of **2** to **3**, was not so clean: both silyl ethers **2** and methylnaphthalenes **3** underwent partial Friedel−Crafts-type alkylation processes to produce isomeric dimers **4** (eq 2). Although it is apparent that the selective exhaustive reduction of **1e**−**g** into **3e** is problematic, its partial conversion into the silyl ethers **2** can be accomplished without complication. Thus aldehyde **1e**, acyl chloride **1f**, and ester **1g** were efficiently reduced into the TES-ether of naphthylmethanol **2a**[7] with 1, 2, and 3 equiv of $HSiEt_3$, respectively (Table 1, entries 5−7).[8]

$B(C_6F_5)_3$-Catalyzed Reduction of Carboxylic Acids with Hydrosilanes. Direct transformation of a carboxylic function into a methyl group is not a trivial task. Usually, such a transformation can be achieved by reduction of the acid to the alcohol with metal hydrides and conversion of the alcohol to the tosylate, followed by a second reduction with metal hydride reagent.[9] Although a single report on a direct reduction of an *aromatic* carboxyl moiety into a methyl group has been published,[5] to the best of our knowledge, such a transformation of an *aliphatic* carboxyl group is unknown.

Inspired by the successful reduction of the carbonyl functional equivalents with the $HSiEt_3/B(C_6F_5)_3$-cat. system, we attempted to apply this methodology to the direct exhaustive reduction of the aliphatic carboxylic function. It was anticipated that a carboxylic acid **5** in the presence of the $B(C_6F_5)_3$ catalyst would react with 4 equiv of $HSiEt_3$ in a stepwise fashion to produce a hydrocarbon **3** via the intermediates **6**, **7**, and **2** (eq 3).



(3)

Indeed, the first step, the dehydrocondensation of an acid **5** with hydrosilane in the presence of Lewis acids to produce a silyl ester **6**, is known.[10] The last step, the transformation **2** to **3**, should not be a problem as well.[4] We also believed that the transformation **6** → **7** → **2** would have certain chances for success in the remaining steps of the sequence since the carbon analogues of **6**,

(6) Formation of **4** was confirmed by GC/MS and NMR analyses of the crude reaction mixtures.

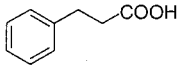
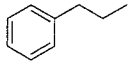
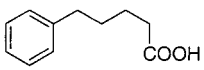
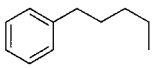
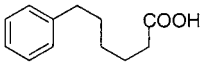
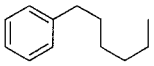
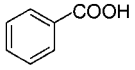
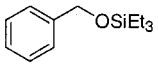
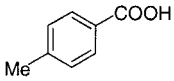
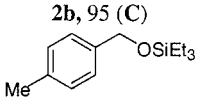
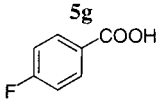
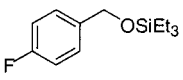
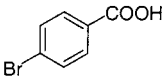
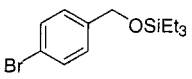
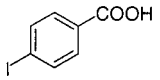
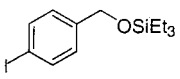
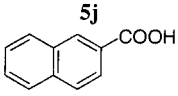
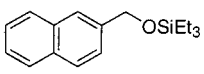
(7) Obviously, the TES-ethers can be easily deprotected into the alcohols upon hydrolysis, see: Greene, T. W.; Wuts, P. G. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999.

(8) A partial reduction of aldehydes into the Ph_3Si-protected ethers has been recently reported; see ref 3.

(9) For a review, see: Seyden-Penne, J. Chapter 2. Cleavage of the Carbon-Heteroatom Single Bond. In *Reductions by the Alumino- and Borohydrides in Organic Synthesis*; Wiley-VCH: New York, 1997

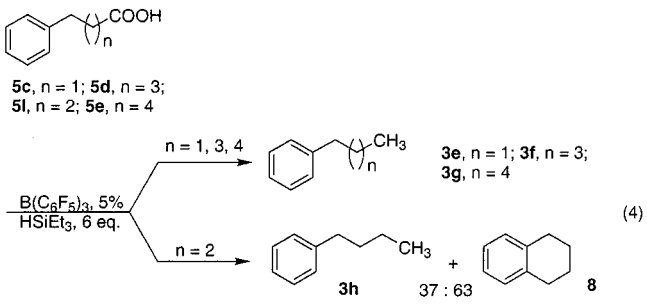
(10) See, for example: (a) Chrusciel, J. *Pol. J. Chem.* **1997**, *71*, 977. (b) Orlov, N. F.; Slesar, L. N. *J. Gen. Chem. USSR (Engl. Trans.)* **1966**, *36*, 1078.

Table 2. Reduction of Aliphatic and Aromatic Carboxylic Acids[a]

Entry	Substrate	$HSiEt_3$, eq.	Product 2, Yield,%[b] (Method)	Product 3, Yield, %[b] (Method)
1	n-$C_{11}H_{23}COOH$ **5a**	6.0		n-$C_{12}H_{26}$, **3a**, 91 (**B**)
2	n-$C_{17}H_{35}COOH$ **5b**	6.0		n-$C_{18}H_{38}$, **3c**, 94 (**B**)
3	 **5c**	6.0		 **3e**, 94 (**D**)
4	 **5d**	6.0		 **3f**, 93 (**D**)
5	 **5e**	6.0		 **3g**, 93 (**D**)
6	 **5f**	3.3	 **2b**, 95 (**C**)	
7	 **5g**	3.3	 **2c**, 91 (**C**)	
8	 **5h**	3.3	 **2d**, 93 (**C**)	
9	 **5i**	3.3	 **2e**, 93 (**C**)	
10	 **5j**	3.3	 **2f**, 94 (**C**)	
11	 **5k**	3.3	 **2g**, 96 (**C**)	

[a] All reactions were performed on a 5 mmol scale. [b] Isolated yields.

the esters **1c** and **1g**, underwent smooth reduction under similar reaction conditions to produce the hydrocarbon **3c** and the silyl ether **2a**, respectively (eq 1, Table 1, entries 3,7).[11] The experiments have proven the above assumptions correct: lauric acid **5a** in the presence of 5 mol % of $B(C_6F_5)_3$ smoothly reacted with excess $HSiEt_3$ at room temperature to produce *n*-dodecane (**3a**) in excellent yield (Table 2, entry 1)! The stepwise nature of the above transformation was also confirmed: all three intermediates, compounds **6**, **7**, and **2**, were detected by GC/MS analyses of the reaction mixtures at early stages. Similarly, other aliphatic acids **5b**−**e** under the same conditions gave the corresponding hydrocarbons **3c,e**−**g** in very high yields (Table 2, entries 2−5). Notably, unlike the homologues with shorter (**5c**) or longer (**5d**,**e**) chains, 4-phenylbutyric acid (**5l**) produced a significant amount of tetraline **8**, (the product of intramolecular Friedel−Crafts-type alkylation process), together with the normal reduction product **3h** (eq 4). Analogous to the reduction



(4)

of the aromatic carbonyl functional equivalents **1e**-**g** (eq 2, Table 1), the exhaustive reduction of aromatic carboxylic acids was not highly selective, as expected. Nevertheless, employment of 3 equiv of $HSiEt_3$ allowed a clean partial reduction of the aromatic substrates **5f**−**k** under mild reaction conditions to give the silyl ethers of

(11) Earlier, Piers and co-workers showed that esters upon the treatment with 1 equiv of Ph_3SiH can be transformed into a mixed silyl acetal, a carbon analogue of **7**; see ref 3.

the benzyl series **2b**−**f** and the silyl ether of the naphthylmethanol **2g** in excellent yields (Table 2, entries 6−11).[7]

Our test experiments indicated that other reducible groups such as ketones, acetales, and nitriles are also susceptible to reduction by our protocol. To date, only phenols, aromatic halides, secondary and tertiary alcohols, and tertiary ethers are irreducible by this method.

In conclusion, we have demonstrated an unprecedented direct transformation of the aliphatic carboxylic function into a methyl group. We have also developed an efficient and mild method for the exhaustive reduction of aliphatic aldehydes, acyl chlorides, and esters into the hydrocarbons. Finally, we elaborated an effective protocol for the partial reduction of aromatic aldehydes, acyl chlorides, esters, and carboxylic acids into the benzylic alcohols.

Experimental Section

General Information. All manipulations were conducted under an argon atmosphere using standard Schlenk techniques. Anhydrous solvents were purchased from Aldrich. All starting materials were commercially available and purchased from Aldrich and Acros. Products **2b**,**c**,[12] **3a-c**,**e-h**,[13] and **8**[13] are known compounds, and their analytical data were in perfect agreement with the literature data. The TES-ethers **2a**,**d**−**g** were deprotected[7] into the corresponding alcohols which showed a perfect match of their ^{1}H and ^{13}C NMR and MS data with those for authentic samples.

$B(C_6F_5)_3$-Catalyzed Reduction of Carboxylic Acids and Carbonyl Function Equivalents with $HSiEt_3$. Procedure A. $HSiEt_3$ was added dropwise under an argon atmosphere to a stirred mixture of $B(C_6F_5)_3$ (5 mol %) and substrate (5 mmol) in anhydrous CH_2Cl_2 (5 mL). After being stirred for 20 h at room temperature, the reaction mixture was quenched (Et_3N, 0.25 mL), filtered (Celite), and concentrated. The residue was mixed with 40% HF (5−7 mL) in ethanol (30 mL) and refluxed for 7 h. Water (60 mL) was added, and the crude product was extracted with pentane (3 × 30 mL). The combined pentane solution was washed with water and dried with magnesium sulfate, and then both solvent and triethylfluorosilane were removed in a vacuum. The residue was purified by flash column chromatography on silica gel.

Procedure B. Substrate (5 mmol, neat or dissolved in dry CH_2Cl_2) was added dropwise under an argon atmosphere to a stirred mixture of $B(C_6F_5)_3$ (5 mol %) and $HSiEt_3$ in anhydrous CH_2Cl_2 (5 mL). After being stirred for 20 h at room temperature, the reaction mixture was worked up and the product was isolated and purified in the same manner as described in Procedure A.

Procedure C. $HSiEt_3$ was added dropwise under an argon atmosphere to a stirred mixture of $B(C_6F_5)_3$ (5 mol %) and substrate (5 mmol) in anhydrous CH_2Cl_2 (5 mL). After being stirred for 20 h at room temperature, the reaction mixture was quenched (Et_3N, 0.25 mL), filtered (Celite), and concentrated. The residue was purified by flash column chromatography on silica gel.

Procedure D. Substrate (5 mmol) was added dropwise under an argon atmosphere to a stirred mixture of $B(C_6F_5)_3$ (5 mol %) and $HSiEt_3$ in anhydrous CH_2Cl_2 (5 mL). After being stirred for 20 h at room temperature, the reaction mixture was worked up and the product was isolated and purified in the same manner as in Procedure C.

2a. ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ 8.08 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.67 d (d, J = 7.0 Hz, 1H), 7.59−7.51 (m, 3H), 5.28 (s, 2H), 1.06 (t, J = 7.9 Hz, 9H), 0.76 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 137.06, 133.98, 131.28, 129.05, 128.09, 126.29, 126.00, 125.93, 124.38, 123.77, 63.52, 7.31, 5.00; GC/MS m/z 272 (M^+, 3%), 243 (M − Et, 34%), 141 (100%).

2d. ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ 7.33 (dd, J_{HH} = 8.5 Hz, $^4J_{HF}$ = 5.8 Hz, 2H), 7.05 (ps-t, J_{HH} = 8.5 Hz, $^3J_{HF}$ = 8.5 Hz, 2H), 4.73 (s, 2H), 1.01 (t, J = 7.9 Hz, 9H), 0.68 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 161.39 (d, $^1J_{CF}$ = 244 Hz), 137.40, 128.25 (d, $^3J_{CF}$ = 7.8 Hz), 115.35 (d, $^2J_{CF}$ = 21.2 Hz), 64.50, 7.19, 4.88; ^{19}F NMR ($CDCl_3$, 470.55 MHz) δ −117.66; GC/MS m/z 240 (M^+, <1%), 221 (M − Et, 76%), 109 (100%).

2e. ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ 7.48 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 4.71 (s, 2H), 1.02, 0.68 (q, J = 8.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 140.81, 131.67, 128.25, 121.07, 64.45, 7.16, 4.91; GC/MS m/z 300 (M^+, 1%), 271 (M − Et, 77%), 169 (100%).

2f. ^{1}H NMR ($CDCl_3$, 400.13 MHz) δ 7.65 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.3 Hz, 2H), 4.68 (s, 2H), 0.98 (t, J = 7.9 Hz, 9H), 0.65 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100.61 MHz) δ 141.07, 137.25, 128.11, 92.14, 64.08, 6.78, 4.46; GC/MS m/z 348 (M^+, 4%), 319 (M − Et, 100%).

2g. ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ 7.88 (m, 4H), 7.52 (m, 3H), 4.97 (s, 2H), 1.09 (t, J = 7.9 Hz, 9H), 0.77 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 139.29, 133.86, 133.21, 128.36, 128.32, 128.14, 126.39, 125.96, 125.21, 124.99, 65.37, 7.31, 5.01; GC/MS m/z 272 (M^+, 4%), 243 (M − Et, 38%), 141 (100%).

3d. ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ 7.18 (d, J = 7.4 Hz, 1H), 7.11 (ps-t, J = 7.8 Hz, 1H), 6.93 (ps-t, J = 7.4 Hz), 6.84 (d, J = 7.8 Hz, 1H), 2.64 (ps-t, J = 7.7 Hz, 2H), 1.68 (ps-sextet, J = 7.6 Hz, 2H), 1.08 (t, J = 8.0 Hz, 9H), 1.02 (t, J = 7.3 Hz, 3H), 0.85 (q, J = 8.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 154.11, 133.54, 130.56, 127.01, 121.27, 118.63, 33.18, 23.64, 14.57, 7.15, 5.82; GC/MS m/z 250 (M^+, 56%), 221 (M − Et, 100%); FTIR (CCl_4) 1599, 1581, 1260, 1123 cm^{-1}.

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