An Efficient Procedure for Palladium-Catalyzed Reduction of Aryl/Enol Triflates

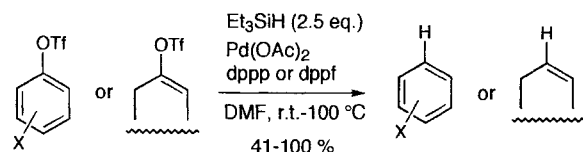Hiyoshizo Kotsuki,*[a] Probal Kanti Datta,[a] Hiroyuki Hayakawa,[a] Hitoshi Suenaga[b]

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An efficient procedure to deoxygenate phenols and enols via trifluoromethanesulfonates is presented. Their reduction with triethylsilane in the presence of a catalytic amount of palladium acetate and bidentate phosphine ligands such as 1,3-bis(diphenylphosphino)propane or 1,1'-bis(diphenylphosphino)ferrocene proceeds efficiently to afford a variety of aromatic, heteroaromatic, and olefinic compounds.
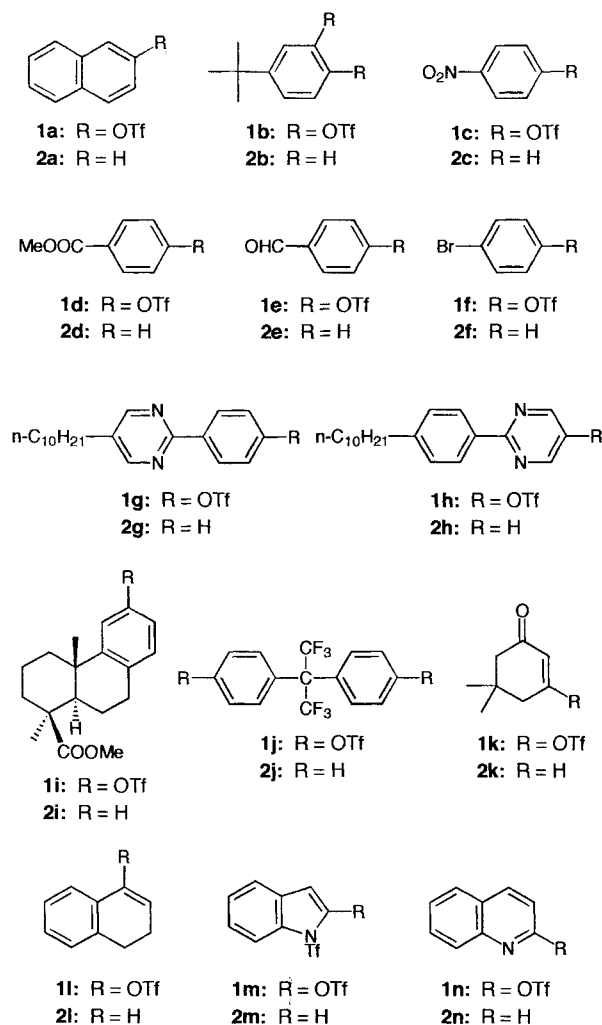
Due to the great reactivity of trifluoromethanesulfonates (triflates) as a leaving group, aryl and enol triflates can serve as versatile intermediates in organic synthesis for preparing variously substituted aromatic, heteroaromatic, and olefinic compounds at the triflate carbon center.[1] In our continuing interest in this field,[2] we are particularly interested in the development of an efficient method to deoxygenate phenols or enols. The importance of this kind of transformation is well-recognized and several procedures have appeared in the literature.[3] One of the simplest relies on palladium-catalyzed reduction of the corresponding triflates by using hydrogen[4] or formic acid[5] as a conventional reducing agent. In 1988 Scott and Stille[6] briefly mentioned the utility of Pd(PPh₃)₄ and triethylsilane as an alternative mild reagent for the conversion of enol triflates into alkenes. Despite its attractive reducing properties, the general applicability of this reaction remains unclear. In this paper we describe an improved procedure to deoxygenate a variety of phenols, enols, and amides via the corresponding triflates using triethylsilane[7] as a reducing agent (Scheme 1). A catalytic system consisting of palladium(II) acetate and bidentate phosphine ligands such as 1,3-bis(diphenylphosphino)-propane (dppp) or 1,1'-bis(diphenylphosphino)ferrocene (dppf) was particularly efficient.

careful inspection of the crude product by GC-MS analysis revealed the presence of hexaethyldisiloxane as the only detectable byproduct.[8]

1a: R = OTf
2a: R = H

1b: R = OTf
2b: R = H

1c: R = OTf
2c: R = H

1d: R = OTf
2d: R = H

1e: R = OTf
2e: R = H

1f: R = OTf
2f: R = H

1g: R = OTf
2g: R = H

1h: R = OTf
2h: R = H

1i: R = OTf
2i: R = H

1j: R = OTf
2j: R = H

1k: R = OTf
2k: R = H

1l: R = OTf
2l: R = H

1m: R = OTf
2m: R = H

1n: R = OTf
2n: R = H

Et₃SiH (2.5 eq.)
Pd(OAc)₂
dppp or dppf
DMF, r.t.-100 °C
41-100 %

Scheme 1

When the reaction of 2-naphthyl triflate (**1a**) with 2.5 equiv of triethylsilane was conducted in *N,N*-dimethylformamide at 60 °C in the presence of palladium(II) acetate (2 mol%) and 1,3-bis(diphenylphosphino)propane (2 mol%), quantitative formation of naphthalene (**2a**) (GC analysis) was observed within 5 h. In this case, to complete the reaction, the use of 2.5 equiv of triethylsilane was essential and the use of lesser amounts of the reagent significantly retarded the reaction progress, e. g., the reaction using 1.4 equiv of triethylsilane at 60 °C for 3 d gave only 51 % of **2a** along with 49 % of **1a**. In addition,

General aspects of this transformation can be easily identified from the results compiled in the Table. Thus, in many cases, the reaction proceeded cleanly in almost quantitative yields. Although stabilized triflates such as **1c, h,** and **j** were less reactive towards the catalytic system using 1,3-bis(diphenylphosphino)propane, when the ligand was replaced by 1,1'-bis(diphenylphosphino)ferrocene, the reactions were completed in a very short period to produce quantitatively **2c, h,** and **j**. Ditriflates **1b** and **j** required the use of twice the amounts of the reagents to convert efficiently into **2b** and **j**, respectively. Highly

Table. Compounds 2 Prepared

Product	Temp. (°C)/ Time[a]	Yield[b] (%)	mp (°C) or bp (°C)/mmHg	Lit. mp (°C) or bp (°C)/mmHg
2a	60/5 h	100[c]	79.5–81.0	80–82[9]
2b	60/22 h[d]	>99[c]	79/40	169[9]
2c	100/7 d	67[c,e]	82/12	210–211[9]
2c	60/20 min[f]	100[c]		
2d	60/14 h	100[c]	84/19	198–199[9]
2e	60/1 h	99[c]	58/12	178–179[9]
2f	43/1 h	90[c]	56/30	156[9]
2g[g]	60/4 h	99	31.0–32.0	
2h[g]	80/9 d	41[h]	33.0–33.5	
2h[g]	60/10 min[f]	100		
2i[g]	60/22 h[i]	92[j]	142.5–144.0	
2j	60/3 d[d]	95[k]	30.5–32.0	75–77/0.1[10]
2j	60/10 min[f]	100		
2k	r.t./40 min[l]	68	71–72/14	77–78/18[11]
2l	60/4 h	88	86/14	89/16[9]
2m	r.t./10 h	83[m]	108–109/15	233[12]
2n	60/4	97	106–107/14	113–114/17[9]

[a] Unless otherwise noted, 2.5 equiv of triethylsilane were used.
[b] Isolated yield based on 1.
[c] Determined by GC.
[d] Twice the amounts of the reagents were used.
[e] 33% of 1c recovered (GC).
[f] Dppf was used in place of dppp.
[g] Satisfactory microanalyses were obtained: C, H, N ± 0.27.
[h] 59% of 1h recovered.
[i] 3 equiv of triethylsilane were used.
[j] 5% of 1i recovered.
[k] 4% of monoreduced compound was also isolated.
[l] 2 equiv of triethylamine were added.
[m] 3% of 1m recovered.

chemoselective reduction was observed in the reaction of 1d, e, f, i, k, and l; ester, aldehyde, bromo, and olefinic groups are completely unaffected under these conditions. Enol triflate 1k was rather labile under these conditions and the addition of triethylamine to the system showed a better result. Thus, treatment of 1k in the presence of 3 equiv of triethylamine at room temperature gave cyclohexenone 2k in 68% yield. Heterocyclic derivatives such as 1m and n were also reduced smoothly to provide 1-trifluoromethanesulfonylindole (2m) and quinoline (2n) in 83 and 97% yield, respectively.

In conclusion, the presented method can be conducted under fairly mild conditions, and byproducts formed during the reaction were easily removed by simple chromatographic separation. In view of the great facility in reduction and also high chemoselectivity, the method should be valuable for deriving aromatic, heteroaromatic, and olefinic compounds, which are not readily accessible by usual reductive transformations.

All reactions were carried out under positive pressure of Ar. DMF was distilled from CaH_2. Commercially available Et_3SiH (Shinetsu Chemical), Pd(OAc)$_2$ (Wako Chemical), dppp (Tokyo Kasei), dppf (Aldrich) and triflic anhydride (Central Glass) were used as received. Preparative TLC was carried out on 2-mm-thick Merck Kieselgel 60PF-254. Wakogel C-300 was employed for column chromatography.

^{1}H NMR spectra were recorded on a Hitachi R-90H spectrometer (90 MHz) in CDCl$_3$ with TMS as an internal standard. High re-

solution FTIR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. High resolution mass spectra were obtained with a JEOL HX-100 spectrometer. Optical rotations were measured on a JASCO DIP-370 polarimeter.

Preparation of Triflates:
Triflates 1a,[13] c,[14] d,[15] e,[14] j,[10] k,[16] l,[17] m,[12] and n[14] were prepared according to literature procedures. The following triflates were prepared analogously from the corresponding precursors in almost quantitative yields by treatment with trifluoromethanesulfonic anhydride in 2,6-lutidine or N,N-diisopropylethylamine. Satisfactory microanalyses (C, H, N ± 0.05) were obtained for compounds 1g, h, and i.

1,2-Bis(trifluoromethanesulfonyloxy)-4-tert-butylbenzene (1b):
Bp = 127°C/14 mmHg.
FTIR (neat): v = 1505, 1433, 1219, 1138, 941, 876, 839, 791, 760 cm^{-1}.
^{1}H NMR: δ = 1.34 (9 H, s), 7.43 (3 H, m).
MS: m/z = 430 (M$^+$, 20), 415 (100), 351 (5), 323 (5), 297 (8), 218 (16), 190 (12), 164 (20), 147 (8), 121 (15), 93 (13), 69 (12), 57 (28), 41 (19).
HRMS: m/z = 429.9951 (M$^+$). Calc. for $C_{12}H_{12}O_6F_6S_2$: 429.9980.

2-(4-Trifluoromethanesulfonyloxyphenyl)-5-decylpyrimidine (1g):
Mp = 45.5–47.5°C (from pentane).
FTIR (KBr): v = 1551, 1503, 1433, 1250, 1213, 1142, 889, 799, 610 cm^{-1}.
^{1}H NMR: δ = 0.88 (3 H, t, J = 6.3 Hz), 1.27 (14 H, br s), 1.4–1.9 (2 H, m), 2.64 (2 H, t, J = 7.5 Hz), 7.37 (2 H, d, J = 8.8 Hz), 8.53 (2 H, d, J = 8.8 Hz), 8.63 (2 H, s).

2-(4-Decylphenyl)-5-trifluoromethanesulfonyloxypyrimidine (1h):
Mp = 81.0–81.5°C (from hexane–EtOH).
FTIR (KBr): v = 1429, 1219, 1142, 885, 608 cm^{-1}.
^{1}H NMR: δ = 0.88 (3 H, t, J = 6.3 Hz), 1.26 (14 H, br s), 1.4–1.8 (2 H, m), 2.68 (2 H, t, J = 7.0 Hz), 7.30 (2 H, d, J = 8.2 Hz), 8.34 (2 H, d, J = 8.2 Hz), 8.72 (2 H, s).

Methyl 1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-6-trifluoromethanesulfonyloxyphenanthrene-1-carboxylate (1i):
Mp = 73.0–74.5°C (from hexane); [α]$_D^{23}$ = + 92.61 (c = 0.95, CHCl$_3$).
FTIR (KBr): v = 1725, 1418, 1235, 1138, 930, 910, 602 cm^{-1}.
^{1}H NMR: δ = 1.03, 1.28 (each 3 H, s), 1.3–2.5 (9 H, m), 2.86 (2 H, m), 3.67 (3 H, s), 6.8–7.2 (3 H, m).

General Procedure for the Reduction of Aryl/Enol Triflates:
To a mixture of the triflate (1 mmol), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol) and dppp (8 mg, 0.02 mmol) in 5 mL of DMF at 60°C was added Et$_3$SiH (0.4 mL, 2.5 mmol). At this time the solution changed color sharply from light brown to deep brown. The stirring was continued until completion of the reaction. After dilution with Et$_2$O, the mixture was successively washed with water, sat. aq NaHCO$_3$, and sat. aq NaCl, dried (Na$_2$SO$_4$), and evaporated. The crude product was purified by preparative TLC or column chromatography to give the desired deoxygenated product. The following are new compounds.

5-Decyl-2-phenylpyrimidine (2g):
FTIR (KBr): v = 1549, 1435, 745, 691, 654 cm^{-1}.
^{1}H NMR: δ = 0.88 (3 H, t, J = 6.2 Hz), 1.27 (14 H, br s), 1.4–1.8 (2 H, m), 2.62 (2 H, t, J = 7.7 Hz), 7.46 (3 H, m), 8.41 (2 H, m), 8.62 (2 H, s).

4-Decyl-1-(2-pyrimidinyl)benzene (2h):
FTIR (KBr): v = 1566, 1549, 1416, 1181, 801 cm^{-1}.
^{1}H NMR: δ = 0.88 (3 H, t, J = 6.2 Hz), 1.26 (14 H, br s), 1.5–2.0 (2 H, m), 2.68 (2 H, t, J = 6.8 Hz), 7.13 (1 H, t, J = 4.8 Hz), 7.29 (2 H, d, J = 7.9 Hz), 8.35 (2 H, d, J = 7.9 Hz), 8.77 (2 H, d, J = 4.8 Hz).

Methyl 1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethylphenanthrene-1-carboxylate (**2i**):

$[\alpha]_D^{22} = +132.95$ ($c = 0.70$, $CHCl_3$).

FTIR (KBr): $v = 1725, 1470, 1238, 1229, 1190, 1150, 762, 731\ cm^{-1}$.

^1H NMR = 1.03, 1.27 (each 3 H, s), 1.3–2.5 (9 H, m), 2.7–3.0 (2 H, m), 3.65 (3 H, s), 6.9–7.3 (4 H, m).

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