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PALLADIUM-CATALYZED REDUCTION OF ENOL TRIFLATES TO ALKENES

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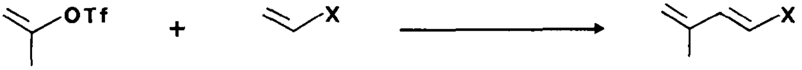
Summary: Enol triflates react with trialkylammonium formate-palladium reagent to give alkenes.

A recent contribution from our laboratories has shown that enol triflates, now available through a good general method from carbonyl compounds,[1] can be involved as vinyl donors in a palladium-catalyzed coupling with olefinic systems.[2]



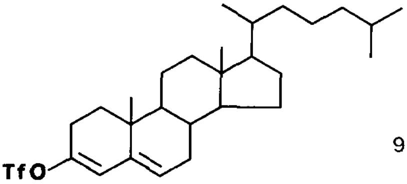
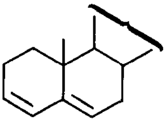
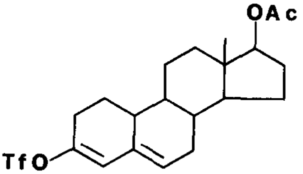
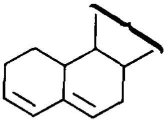
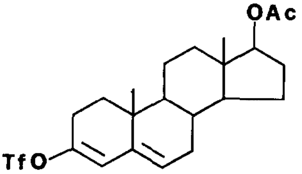
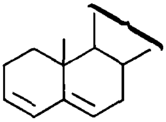
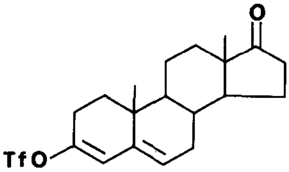
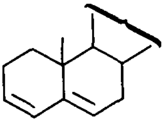
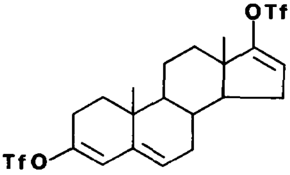
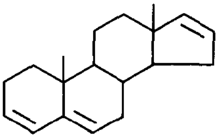
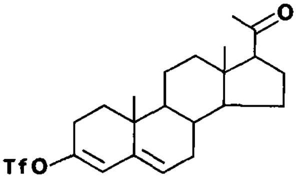
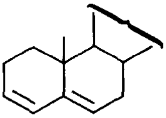
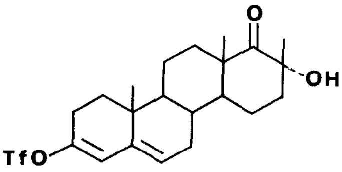
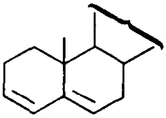
X = COR, CO_2R, CH_2OH, Alkyl, Aryl; Tf = SO_2CF_3

As part of a program on this subject, we investigated the reactivity of enol triflates toward trialkylammonium formate-palladium reagent.

Ammonium[3] and trialkylammonium[4] formate-palladium reagents have been reported to allow the reduction of a variety of functional groups, the synthesis of conjugate addition-type products from α,β-unsaturated carbonyl compounds and aryl iodides,[5] and of trisubstituted alkenes from alkynes and aryl or heteroaryl iodides.[6]

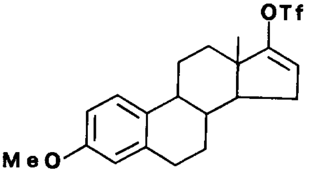
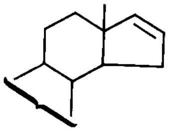
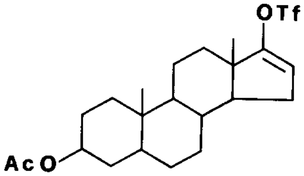
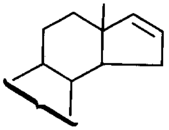
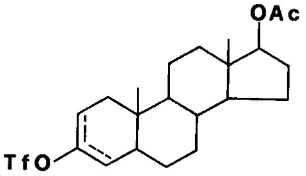
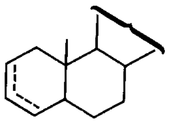
We report here that this reagent can be successfully used to perform an efficient and exceedingly simple reduction of enol triflates to alkenes.

Table. Palladium-Catalyzed Reduction of Enol Triflates to Alkenes[a]

Entry	Enol Triflate[b,c]	Yield %[d]	Reduction Product[c]	Yield %[d]
1		98		77
2		74		90 72[e]
3		68		80 92[e]
4		81		81
5		11[f]		95
6		53[g]		79
7		27[h]		93

continued

Table (continued).

Entry	Enol Triflate[b,c]	Yield %[d]	Reduction Product[c]	Yield %[d]
8		88		86
9		50		85
10		49[i]		77[j] 90[e,j]

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[a] Reactions were carried out on a 0.5–0.7 mmol scale at 60 °C in DMF under argon atmosphere for 1–3 h with a molar ratio enol triflate : HCO_2H : nBu_3N : $Pd(OAc)_2(PPh_3)_2$ = 1 : 2 : 3 : 0.02, unless otherwise noted. Disappearance of starting material was monitored by TLC.

[b] Preparation of enol triflates was carried out at room temperature according to the procedure of Stang (ref. 1) with a molar ratio steroidal ketone : triflic anhydride : 2,6-di-*t*-butyl-4-methylpyridine = 1 : 2 : 2.2. Purification of reaction mixtures was effected by flash chromatography on silica gel with hexane-ethyl acetate mixtures as eluant.

[c] All new products gave satisfactory microanalyses and spectroscopic data in agreement with the proposed structures.

[d] Yields are given on isolated products and refer to single non optimized runs.

[e] Et_3N was used as the base.

[f] Obtained as the by-product in the preparation of monotriflate of entry 4.

[g] Isolated together with a 34% yield of an about 1:1 isomeric mixture of 3,5,17(20)- and 3,5,20-trien-3,20-yl ditriflates.

[h] Obtained from 17α-hydroxyprogesterone.

[i] Isolated and reacted as an about 80:20 mixture of 2- and 3-en-3-yl triflates.

[j] Isolated as an about 80:20 mixture of 2- and 3-enes.

A typical example is as follows. To a mixture of 17β-acetoxyandrosta-3,5-dien-3-yl triflate (0.31 g, 0.67 mmol), tri-n-butylamine (0.18 g, 2.02 mmol), bis(triphenylphosphine) palladium acetate (0.01 g, 0.013 mmol) and DMF (1.4 ml), was added 99% formic acid (0.05 ml, 1.33 mmol) all at once. The mixture was stirred at 60 °C for 1 h under argon. Ethyl acetate and water were added and the organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified through flash chromatography on silica gel (hexane/ethyl acetate = 95/5 as eluant) to give

17β-acetoxyandrosta-3,5-diene (0.17 g, 80%): mp 125-127 °C (hexane); $[\alpha]_D$ ($CHCl_3$, 1%) -164° (lit.^{7} mp 126 °C; $[\alpha]_D$ -155°); ^1H NMR ($CDCl_3$) δ 5.95 (bd, 1H, J = 9.7 Hz, C_4-H), 5.74-5.50 (m, 1H, C_3-H), 5.47-5.33 (m, 1H, C_6-H); MS (m/e) 314 ($M^{\dot{+}}$).

The table details the results of this investigation. Ketones (entries 4,6,7), esters (entries 2,3,9,10), alcohols (entry 7), and presumably a variety of other functional groups are unaffected by the reduction conditions. Some limitations may arise from the triflating step. In favourable cases, however, good chemoselectivity can be attained without chemical manipulation of the substrate (entries 4,6). A valuable feature of our method is the regioselective and quantitative introduction of a deuterium atom when the reaction is carried out by using DCO_2D.

As an example, treatment of 17β-acetoxyandrosta-3,5-dien-3-yl triflate with DCO_2D under usual conditions gave the corresponding 3-deuterioderivative in 87% yield: mp 125-126 °C (hexane); $[\alpha]_D$ ($CHCl_3$, 1%) -173°; ^1H NMR ($CDCl_3$) δ 5.95 (bs, 1H, C_4-H), 5.50-5.35 (bs, 1H, C_6-H); MS (m/e) 315 ($M^{\dot{+}}$).

To sum up, as enol triflates may be easily prepared and the trialkylammonium formate-palladium reducing system is very simple to use, the present reaction appears as a convenient one for achieving deoxygenation of carbonyl compounds to olefins in two steps and may represent a valuable alternative to the related methods.^{8}

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