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Rhodium perfluorobutyramide ($Rh_2(pfm)_4$): a synthetically useful catalyst for olefin aziridinations

Gregg F. Keaney and John L. Wood*

Sterling Chemistry Laboratory, Department of Chemistry, Yale University, New Haven, CT 06520-8107, USA

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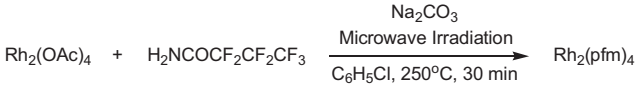
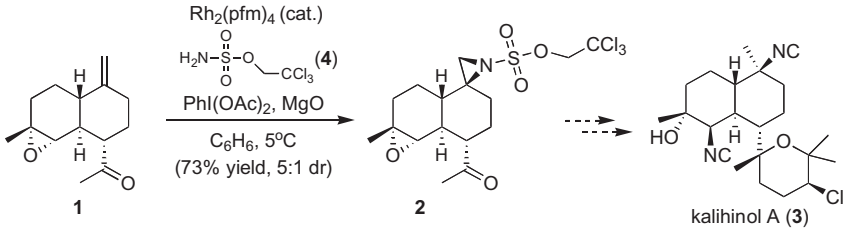
Abstract—Rhodium perfluorobutyramide ($Rh_2(pfm)_4$) has been shown to catalyze the conversion of olefins to trichloroethoxysulfonyl, nosyl, and tosyl aziridines. Advantages of this aziridination procedure include the microwave-assisted preparation of the catalyst and the practical use of the alkene substrate as the limiting reagent.

Recent developments in the transition metal mediated aziridination of olefins (Cu,[1,2] Rh,[3] Mn,[4] Ru,[5] etc.) have resulted in an increased use of aziridines as intermediates in total syntheses.[6] In the course of ongoing synthetic studies directed toward (+)-kalihinol A (**3**), we envisioned the aziridine moiety in intermediate **2** as a key precursor to the tertiary isonitrile found in **3**. Our choice of the specific aziridine variant was inspired by Du Bois' recent successes transferring trichloroethylsulfamate ester (**4**) using rhodium trifluoroacetamide ($Rh_2(tfacam)_4$) as the catalyst.[7] Although we were indeed able to implement Du Bois' protocol, $Rh_2(tfacam)_4$ proved both tedious to prepare and difficult to isolate in high purity.[8] As an alternative to $Rh_2(tfacam)_4$, we explored the use of rhodium perfluorobutyramide ($Rh_2(pfm)_4$), an electronically similar catalyst that had heretofore not been explored for aziridination reactions.[9] We were thus pleased to find that exposure of olefin **1** to the Du Bois aziridination conditions using $Rh_2(pfm)_4$ as the catalyst led to the diastereoselective formation of the desired trichloroethoxysulfonyl aziridine **2** in good yield (Scheme 1).[10]

$Rh_2(pfm)_4$ was initially prepared by a somewhat laborious procedure that involved refluxing rhodium acetate and perfluorobutyramide in chlorobenzene for 60 h under a Soxhlet extraction apparatus.[8a] In search of a more direct method, we eventually found that $Rh_2(pfm)_4$ could be readily prepared in substantially less time by conducting this reaction under microwave irradiation in a sealed vial (Scheme 2).[11]



Scheme 2. Preparation of rhodium perfluorobutyramide.



Scheme 1. Trichloroethoxysulfonyl aziridination toward (+)-kalihinol A.

Keywords: Kalihinane diterpenoids; Aziridination; Microwave; Nosyl; Tosyl; Trichloroethoxysulfonyl; Rhodium perfluorobutyramide.
* Corresponding author. Tel.: +1 203 432 5991; fax: +1 203 432 6144; e-mail addresses: john.wood@yale.edu; tetlett@yale.edu

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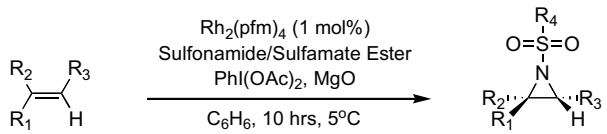
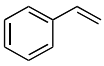
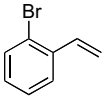
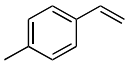
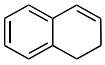
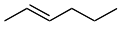
Table 1. Aziridinations using rhodium perfluorobutyramide catalyst[a]



Entry	Substrate	Yield (%)		
		Trichloroethoxysulfonyl[b]	Nosyl[c]	Tosyl[d]
1		87(73)[e]	79	73
2		71	71	64
3		58	58	47
4		60	42	54
5		80	46	48
6		72	44	44
7		55	32	37(75)[f]
8		76	31	54

[a] Reactions were run using 1.0 equiv olefin, 1.1 equiv sulfonamide/sulfamate ester, 1.3 equiv $PhI(OAc)_2$, 2.3 equiv MgO, and 0.01 equiv $Rh_2(pfm)_4$ at 0.5 M [olefin] in C_6H_6 unless otherwise specified.
[b] $R_4 = OCH_2CCl_3$.
[c] R_4 = Ar-*p*-NO_2.
[d] R_4 = Ar-*p*-CH_3.
[e] Yield when crude $Rh_2(pfm)_4$ was used.
[f] Yield when 5.0 equiv olefin were used.

Having developed an improved method for preparing $Rh_2(pfm)_4$, we next examined its generality as an aziridination catalyst. In the event, we found $Rh_2(pfm)_4$ to be effective at promoting the conversion of several olefins to their corresponding trichloroethoxysulfonyl aziridines in 55–87% yield (Table 1).[12] As illustrated, the substrates included conjugated olefins (entries 1–4) as well as endocyclic (entry 5) and acyclic (entries 6–8) isolated olefins. In addition, this catalyst was also shown to be effective for conducting nosyl (*para*-nitrobenzenesulfonyl) and tosyl (*para*-toluenesulfonyl) aziridinations in 31–79% and 37–73% yields, respectively.[13–15]

In summary, we have developed an improved, microwave-assisted method for the preparation of rhodium perfluorobutyramide ($Rh_2(pfm)_4$) and have demonstrated the effectiveness of this catalyst in trichloroethoxysulfonyl, nosyl, and tosyl aziridination processes. This aziridination protocol is operationally simple and practical due to the in situ generation of the iminoiodinane ylide, the low catalyst requirement (1 mol%), and, most notably, the use of the olefinic substrate as the limiting reagent.

Acknowledgements

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9. For examples of previous applications of $Rh_2(pfm)_4$, see: (a) Ref. 8a; (b) Moody, C. J.; Miah, S.; Slawin, A. M. Z.; Mansfield, D. J.; Richards, I. C. *Tetrahedron* **1998**, *54*, 9689–9700; (c) Savinov, S. N.; Austin, D. J. *Chem. Commun.* **1999**, *11*, 1813–1814.
10. All other catalysts (Cu(OTf), $Cu(OTf)_2$, $Rh_2(oct)_4$, $Rh_2(OAc)_4$, $Rh_2(OTFA)_4$, and $Rh_2(pfb)_4$) screened for this reaction led to no appreciable aziridine formation.
11. *$Rh_2(pfm)_4$ Catalyst Preparation*: Rhodium acetate (25 mg, 0.056 mmol, 1.0 equiv), perfluorobutyramide (120 mg, 0.56 mmol, 10.0 equiv), and Na_2CO_3 (60 mg, 0.56 mmol, 10.0 equiv) were dissolved in 3.0 mL of chlorobenzene in a microwave vial. The reaction was conducted under microwave irradiation (Biotage Initiator, 205 W) for 30 min at 250 °C. The purple reaction mixture was cooled to room temperature and extracted with FC-72 (perfluoro-*n*-hexane, Acros) three times. The fluorous extracts were concentrated under reduced pressure. Excess perfluorobutyramide was removed by sublimation. The complex could be used without further purification, or purified by silica gel chromatography (9:1–3:1 hexanes/ethyl acetate) to give $Rh_2(pfm)_4$ (31 mg, 53% yield) as a blue solid. ^{19}F NMR (376 MHz, CD_3CN, $C_6H_5CF_3$ standard at −63.7 ppm) −82.0, −117.8, −127.9 ppm.
12. *Representative Aziridination Procedure*: To a solution of $Cl_3CCH_2SO_3NH_2$[7] (126 mg, 0.55 mmol, 1.1 equiv) in 1.0 mL of C_6H_6 was added olefin substrate (0.50 mmol, 1.0 equiv), MgO (46 mg, 1.15 mmol, 2.3 equiv), and $Rh_2(pfm)_4$ (5.3 mg, 0.005 mmol, 0.01 equiv). The blue mixture was cooled to 5 °C and $PhI(OAc)_2$ (209 mg, 0.65 mmol, 1.3 equiv) was added. The reaction was run at 5 °C for approximately 2 h, and then at room temperature for 8 h. The reaction was filtered through a Celite plug, washed repeatedly with CH_2Cl_2, and the combined filtrates were concentrated under reduced pressure. The material was purified by silica gel chromatography to provide the aziridine product.
13. *N-p*-Nitrobenzenesulfonyl-2-(2-bromophenyl)-aziridine (Entry 2). Cream-colored solid, m.p. 131–132 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.6 Hz, 2H), 8.11 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 7.8 Hz, 1H), 7.15–6.98 (comp m, 3H), 4.03 (dd, J = 4.7, 7.4 Hz, 1H), 3.04 (d, J = 7.2 Hz, 1H), 2.29 (d, J = 4.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 143.7, 134.0, 132.7, 130.1, 129.5, 129.5, 127.9, 127.5, 124.5, 124.5, 123.5, 42.1, 36.5 ppm; IR (thin film/NaCl) 3106 (m), 2871 (w), 1728 (w), 1607 (m), 1531 (s), 1349 (s), 1311 (m), 1167 (s), 1092 (m) cm^{-1}; HRMS (FAB) *m/z* found: 382.9701 [calc'd for $C_{14}H_{12}BrN_2O_4S$ (M+H): 382.9701].
N-p-Nitrobenzenesulfonyl-1,2-(dihydronathalenyl)-aziridine (Entry 4). Cream-colored foam. ^1H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 8.8 Hz, 2H), 8.13 (d, J = 9.2 Hz, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.27–7.23 (m, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.4 Hz, 1H), 3.93 (d, J = 7.0 Hz, 1H), 3.72 (br d, J = 7.0 Hz, 1H), 2.79–2.68 (m, 1H), 2.59 (dd, J = 5.4, 15.8 Hz, 1H), 2.34–2.28 (m, 1H), 1.75 (tdd, J = 1.7, 5.5, 14.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 144.7, 136.6, 129.6, 129.2, 129.0, 128.9, 128.9, 128.6, 126.7, 124.4, 124.4, 43.4, 42.9, 24.7, 20.1 ppm; IR (thin film/NaCl) 3106 (m), 3039 (w), 2940 (m), 2855 (w), 1731 (w), 1607 (m), 1531 (s), 1400 (m), 1349 (s), 1333 (s), 1162 (s), 1090 (m) cm^{-1}; HRMS (FAB) *m/z* found: 331.0752 [calc'd for $C_{16}H_{15}N_2O_4S$ (M+H): 331.0752].
N-p-Nitrobenzenesulfonyl-9-azabicyclo[6.1.0]nonane (Entry 5). Cream-colored solid, m.p. 143–144 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.7 Hz, 2H), 8.14 (d, J = 8.9 Hz, 2H), 2.94–2.87 (m, 2H), 2.07–1.98 (m, 2H), 1.67–1.22 (comp m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 145.0, 129.0, 124.4, 45.1, 26.4, 26.3, 25.3 ppm; IR (thin film/NaCl) 3105 (m), 3070 (w), 2924 (s), 2858 (m), 1530 (s), 1351 (s), 1304 (s), 1295 (s), 1159 (s) cm^{-1}; HRMS (FAB) *m/z* found: 311.1065 [calc'd for $C_{14}H_{19}N_2O_4S$ (M+H): 311.1065].
trans-N-Trichloroethoxysulfonyl-2-methyl-3-propylaziridine (Entry 6). Clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 4.78 (s, 2H), 2.79–2.69 (comp m, 2H), 1.77–1.41 (comp m, 4H), 1.53 (d, J = 5.8 Hz, 3H), 0.96 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 93.3, 79.5, 50.8, 46.0, 32.0, 20.2, 14.7, 13.7 ppm; IR (thin film/NaCl) 2962 (m), 2935 (m), 2876 (w), 1450 (w), 1366 (s), 1250 (w), 1181 (s), 1166 (m) cm^{-1}; HRMS (FAB) *m/z* found: 309.9839 [calc'd for $C_8H_{15}Cl_3NO_3S$ (M+H): 309.9838].
cis-N-Trichloroethoxysulfonyl-2-methyl-3-propylaziridine (Entry 7). Clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 4.79 (d, J = 10.5 Hz, 1H), 4.76 (d, J = 10.8 Hz, 1H), 3.03–2.96 (m, 1H), 2.91–2.85 (m, 1H), 1.60–1.45 (comp m, 4H), 1.31 (d, J = 6.1 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 93.2, 79.4, 47.0, 42.5, 28.3, 20.4, 13.8, 12.0 ppm; IR (thin film/NaCl) 2962 (m), 2876 (w), 1466 (w), 1450 (w), 1379 (s), 1367 (s), 1254 (w), 1181 (s) cm^{-1}; HRMS (FAB) *m/z* found: 309.9839 [calc'd for $C_8H_{15}Cl_3NO_3S$ (M+H): 309.9838].
N-Trichloroethoxysulfonyl-2,2,3-trimethylaziridine (Entry 8). Clear oil. ^1H NMR (400 MHz, $CDCl_3$) δ 4.76 (d, J = 10.8 Hz, 1H), 4.71 (d, J = 10.8 Hz, 1H), 2.97 (q, J = 5.9 Hz, 1H), 1.62 (s, 3H), 1.32 (s, 3H), 1.29 (d, J = 5.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 93.3, 79.3, 51.7, 50.1, 20.9, 20.4, 13.0 ppm; IR (thin film/NaCl) 3000 (m), 2972 (s), 2936 (m), 1626 (w), 1462 (s), 1415 (m), 1366 (s), 1253 (m), 1181 (s), 1090 (s) cm^{-1}; HRMS (FAB) *m/z* found: 295.9681 [calc'd for $C_7H_{13}Cl_3NO_3S$ (M+H): 295.9681].
N-p-Nitrobenzenesulfonyl-2,2,3-trimethylaziridine (Entry 8). White solid, m.p. 114–116 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 2H), 8.11 (d, J = 8.8 Hz, 2H), 3.06 (q, J = 6.1 Hz, 1H), 1.76 (s, 3H), 1.33 (s, 3H), 1.17 (d, J = 6.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 147.3, 128.4, 128.4, 124.3, 124.3, 53.6, 49.3, 21.9, 20.9, 13.0 ppm; IR (thin film/NaCl) 3116 (m), 3000 (w), 2968 (w), 2931 (w), 2867 (w), 1607 (m), 1531 (s), 1460 (w), 1380 (m), 1351 (s), 1319 (s), 1300 (s), 1162 (s) cm^{-1}; HRMS (FAB) *m/z* found: 271.0753 [calc'd for $C_{11}H_{15}N_2O_4S$ (M+H): 271.0752].

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15. A significant advantage of using fluorinated rhodium catalysts for olefin aziridination is that moderately high yields can be obtained even when the olefinic substrate is present in limiting quantity.[7] While such conditions are considered to be ideal, most current methods using non-fluorinated catalysts for intermolecular aziridinations require that the olefin be used in 5- to 20-fold excess in order to obtain comparable yields.[1b,e,3b,4a,14a–c]