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Synthesis of diols using the hypervalent iodine(III) reagent, phenyliodine(III) bis(trifluoroacetate)

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Abstract—1,2- and 1,3-Bis(trifluoroacetoxy) alcohols are easily obtained from the one-pot reaction of alkenes with phenyliodine(III) bis(trifluoroacetate) (PIFA) in the absence of any additive or catalyst. The products were converted into the corresponding diols by ammonolysis. The use of bicyclic alkenes has shown that rearranged 1,3-diacetoxy alcohols are mostly formed as the major products.
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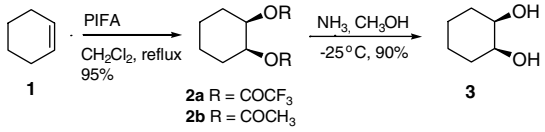
Alkene oxidation is a subject of general interest, which profoundly influences the development of synthetic organic chemistry.[1] For example, *cis*-dihydroxylation[2] of alkenes by OsO_4 provides an efficient synthetic route to *cis*-diols, which are important precursors for a variety of synthetic applications[3] where this functionality is found in various pharmaceuticals. Due to the high cost and toxicity of OsO_4, there is a need to search for alternative metal catalysts for alkene *cis*-dihydroxylations.[4] 1,3-Diols have attracted considerable attention in recent years due to the ubiquitous presence of this moiety in macrolide antibiotics.[5,6] Therefore, the development of methodologies for the preparation of 1,2- and 1,3-diols are of considerable interest. We report herein a new procedure for the synthesis of these diols based on the reaction of olefins with the hypervalent iodine compound, phenyliodine(III) bis(trifluoroacetate) (PIFA).[7]

Hypervalent iodine(III) reagents have recently received much attention due to their low toxicity, easy handling, and reactivities, which are similar to those of heavy metal reagents. We focused our studies on the hydroxylation of various alkenes using PIFA.

To a solution of cyclohexene dissolved in methylene chloride, PIFA was added portionwise to give the product **2**. Ammonolysis of *cis*-1,2-trifluorobisacetoxy-cyclohexane **2a** with ammonia afforded *cis*-1,2-cyclohexanediol **3**[8] in 95% yield (Scheme 1, Table 1, entry 1), which was transformed into diacetate **2b**. The *cis*-geometry in **3** was confirmed by comparison of the ^{1}H NMR spectrum with those of authentic *cis*- and *trans*-1,2-cyclohexanediol. Koser et al.[9] and Zefirov et al.[10] have reported the formation of *cis*-1,2-bis(tosyloxy)cyclohexane and *cis*-1,2-(perchloryloxy)cyclohexane upon treatment of cyclohexene with appropriate hypervalent iodine compounds.

The oxidation of 1,4-cyclohexadiene **4** (entry 2) took place in 20 h to give bis(trifluoroacetate) **5** as the major product (59%), which was hydrolyzed to the corresponding *cis*-diol.[11] The tetraacetate **6**[12] was formed as a minor product in 11% yield. The presence of a cyclopropane ring in **5** was established by measuring the coupling constants $^1J_{CH} = 161.7$ and 162.2 Hz for the cyclopropyl carbons with attached protons. The lack



Scheme 1.

Keywords: Phenyliodine(III) bis(trifluoroacetate); PIFA; Oxidation; Rearrangement; 1,2-Diols; 1,3-Diols.
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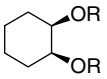
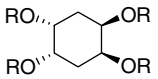
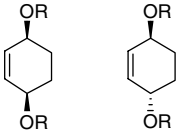
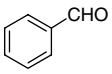
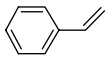
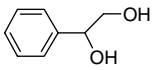
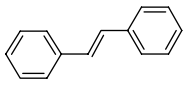
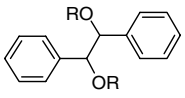
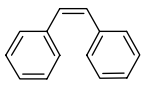
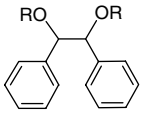
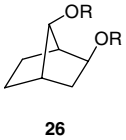
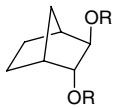
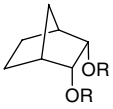
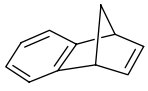
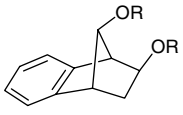
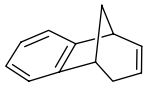
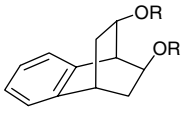
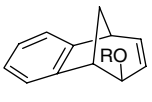
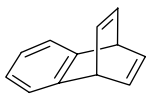
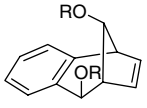
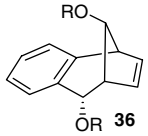
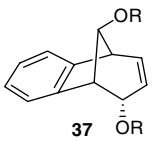
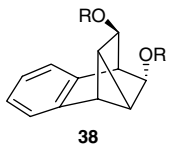
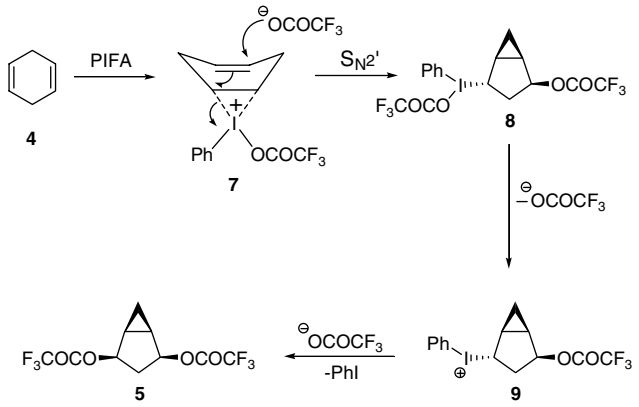
Table 1. Bis(trifluoromethylacetoxy)hydrocarbons from the reaction of alkenes with PIFA

Entry	Alkene	Product[a]	Yield	Conditions	Ref.[b]
1	 **1**	 **2a**	95%	CH^2Cl^2, reflux 36 h	8
2	 **4**	 **5**  **6**	70% (5:1)	CH_2Cl_2, reflux 20 h	11 12
3	 **10**	 **11** **12**	98% (55:45)	CH_2Cl_2, reflux 12 h	13
4	 **13**	 **18**	Quantitative	CH_2Cl_2, reflux 18 h	
5	 **19**	 **20**	90%	CH_2Cl_2, reflux 36 h	
6	 **21**	 **22**	95% (97:3) **22:23**	CH_2Cl_2, reflux 11 d	14
7	 **24**	 **23**	92% (95:5) **23.22**	CH_2Cl_2, reflux 11 d	14
8	 **25**	 **26**  **27**  **28**	90% (6:3:1)	CH_2Cl_2, reflux 36 h	15
9	 **29**	 **30**	95%	CH_2Cl_2, reflux 12 h	16 18
10	 **31**	 **32**  **33**	94% (3:7)	CH_2Cl_2, reflux 24 h	18
11	 **34**	 **35**  **36**  **37**  **38**	90% (68:22:7:3) **35:36:37:38**	CH_2Cl_2, reflux 36 h	

[a] R = $COCF_3$. The formed trifluoroacetates were transformed into the diols.
[b] The references are for the corresponding diols and acetates.



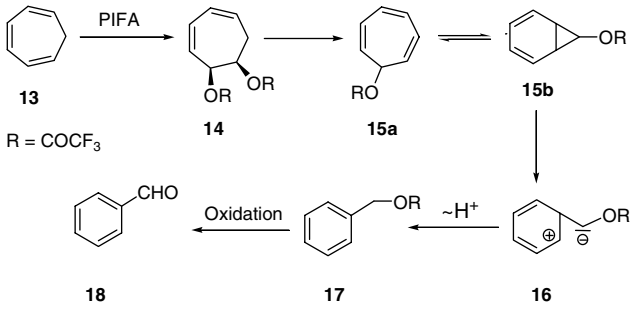
Scheme 2.

of coupling between the protons $J_{1,2}(J_{4,5})$ indicated the *cis–syn*-configuration of the hydroxyl groups.

For the formation of **5** we suggest the following reaction mechanism (Scheme 2). The stereochemical outcome is consistent with the formation of a cyclic organoiodo intermediate **7**. Electrophilic attack of the phenyl(trifluoroacetoxy)iodonium ion will generate the intermediate **7**, which can undergo homoallylic substitution reaction S_N2'-type substitution to give **8**. Nucleophilic displacement of iodobenzene by the trifluoroacetate anion in **9** with inversion of the configuration at carbon would give the bis(trifluoroacetate) derivative **5.**

1,3-Cyclohexadiene **10**, in contrast to 1,4-cyclohexadiene **4**, underwent 1,4-dihydroxylation resulting in the formation of the 1,4-bis-trifluoroacetoxycyclohex-2-enes (**11** and **12**) (entry 3). To characterize these compounds, the trifluoroacetyl groups were removed, and the resulting diols were then converted into the corresponding known diacetates.[13] Treatment of cycloheptatriene **13** with PIFA at room temperature gave benzaldehyde **18** in quantitative yield. We assume that PIFA first oxidizes one of the double bonds to form bis(trifluoroacetate) **14**, which undergoes elimination to give **15a**. The cycloheptatriene derivative **15a** exists in equilibrium with its valence isomer, norcaradiene **15b**. Ring opening of norcaradiene **15b** followed by oxidation may result in the formation of benzaldehyde as depicted in Scheme 3.

The reaction of styrene **19** with PIFA followed by ammonolysis gave 1-phenylethane-1,2-diol **20** in 90% yield (entry 5). On the other hand, *trans*-and *cis*-stilbenes **21** and **24** reacted very slowly with PIFA at reflux in methylene chloride, and formed as the major products, *dl*- and *meso*-1,2-diphenylethane-1,2-bis(trifluoroacetates)[14] **22** and **23** in 95% and 92% yields, respectively (entries 6 and 7).

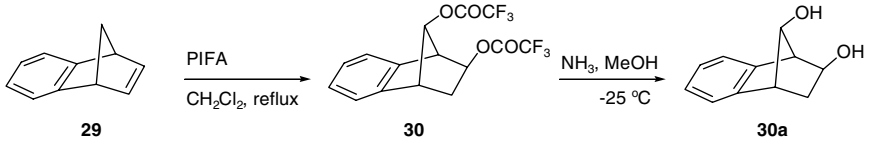


Scheme 3.

We next investigated the reactivity of unsaturated bicyclic systems such as norbornene **25** and its derivatives since these compounds have a large tendency to undergo Wagner–Meerwein-type rearrangement. When norbornene was refluxed in methylene chloride with PIFA, three products (**26**–**28**) were formed, the rearranged product **26** being the major product (54% yield). All three products were transformed into the corresponding diols and characterized as their acetates (entry 8).[15]

Benzonorbornadiene **29** reacted with PIFA and produced the rearranged compound **30** as the sole product (Scheme 4). The structure of the corresponding 1,3-diol **30a** was established by comparison of the spectral data with those reported in the literature.[16] Homobenzobarrelene **31** underwent reaction via a different route and mainly formed the allylic oxidation product **33** in addition to the rearranged product **32** (entry 10). Finally, we investigated the reaction of benzobarrelene **34** with PIFA in methylene chloride. ^1H NMR studies revealed that the reaction mixture consisted of four products, which could be isolated by chromatography on silica gel. The major products **35** and **36** were formed via *endo*-attack of PIFA to the double bond. The structures were determined by comparison of the NMR data with those of the corresponding dibromo compounds.[17]

General procedure: To a magnetically stirred solution of olefin (10 mmol) in methylene chloride (50 mL), PIFA (13 mmol) was added portionwise over a period of 10 min. After completion of the addition, the solution was refluxed for the appropriate amount of time (Table 1). The reaction mixture was washed with water and dried over sodium sulfate. After removal of the solvent, the residue was chromatographed on silica gel eluting with hexane/ethyl acetate (95:5) to give the products. For the hydrolysis of the trifluoroacetate groups, the product was dissolved in anhydrous methanol (10 mL) and dry NH_3 was bubbled through the solution, with stirring for 4 h at −25 °C. Evaporation of the solvent gave the corresponding diol in quantitative yield.



Scheme 4.

In conclusion, the reported procedure is easy to carry out and enables the direct transformation of acyclic as well as cyclic alkenes to 1,2- and/or 1,3-diacetoxy derivatives using PIFA.

Acknowledgements

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18. Physical data for selected compounds: 4-(acetyloxy)bicyclo[3.1.0]hex-2-yl acetate (**5**, R = Ac): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (t, $J = 2.9$, 2H, H-2 and H-4) 2.07 (s, 6H, –CH_3) 2.0 (m, 1H, H-6$_{endo}$) 1.84 (m, 2H, H-3), 1.72 (dd, $J = 8.8$ and 4.0 Hz, 2H, H-1 and H-5), 0.67 (dt, $J = 8.8$ and 6.2 Hz, 1H, H-6$_{exo}$). ^{13}C NMR (100 MHz, $CDCl_3$, coupled) δ 170.9 (d, $J = 6.9$, C=O), 76.2 (d, $J = 157.2$ Hz, C-2 and C-4), 36.1 (t, $J = 132.0$ Hz, C-3), 22.1 (d, $J = 161.7$ Hz, C-1 and C-5), 21.3 (q, $J = 129.7$ Hz, CH_3), 6.2 (t, $J = 162.2$ Hz, C-6). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.89; H, 7.50. *dl*-1,2-Diphenyl-2-[(2,2,2-trifluoroacetyl)oxy]ethyl-2,2,2-trifluoroacetate (**22**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33–7.18 (m, 10H, aromatic), 6.27, (s, 2H, OCH). ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.2 (q, $^2J_{CH} = 43.3$ Hz, C=O), 134.6, 131,8, 130.8, 129.5, 116,4 (q, $^1J_{CH} = 285.4$ Hz, CF_3), 82.3. Anal. Calcd for $C_{18}H_{12}F_6O_4$: C, 53.21; H, 2.98. Found: C, 53.51; H, 3.09.
2-[(2,2,2-Trifluoroacetyl)oxy]bicyclo[2.2.1]hept-7-yl-2,2,2-trifluoroacetate (**26**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.93 (dd, $J = 7.6$ and 3.6 Hz, 1H, H-2), 4.87 (s, 1H, H-7), 2.70 (d, $J = 4.3$ Hz, 1H, H-1), 2.50 (m, br s, 1H, H-4), 1.17–2.12 (m, 6H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.5 (q, $^2J_{CH} = 42.8$ Hz, 2 × C=O), 116.3 (q, $^1J_{CH} = 285.4$ Hz, 2 × CF_3), 85.5, 82.0, 44.8, 40.3, 38.6, 25.5, 23.3. Anal. Calcd for $C_{11}H_{10}F_6O_4$: C, 41.26; H, 3.15. Found: C, 41.47; H, 3.17.
11-(Trifluoroacetyloxy)tricyclo[6.2.1.0^{2,7}]undeca-2,4,6-trien-9-yl trifluoroacetate (**30**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.37–7.19 (m, 4H, aromatic), 4.97 (dd, $J = 7.0$ and 3.8 Hz, 1H, H_9), 4.93 (s, 1H, H-11), 3.93 (br s, 1H, H-8), 3.64 (d, $J = 1.6$ Hz, 1H, H-1), 2.29–2.24 (m, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ158.8 (q), 158.4 (q), 144.4, 139.0, 130.6, 129.9, 125.5, 124.2, 116.4, (q, $^1J_{CH} = 286.6$), 116.3, (q, $^1J_{CH} = 285.8$), 86.7, 80.5, 52.6, 47.5, 35.5. Anal. Calcd for $C_{15}H_{10}F_6O_4$: C, 48.93; H, 2.74. Found: C, 49.04; H, 2.84.
12-(Trifluoroacetyloxy)tricyclo[6.2.2.0^{2,7}]dodeca-2,4,6-trien-9-yl trifluoroacetate (**32**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36–7.19 (m, 4H, aromatic), 5.05 (dt, $J = 9.7$ and 3.1 Hz, 2H, H-9 and H-12), 3.87 (t, $J = 2.9$ Hz, 1H, H-8), 3.22 (quin., $J = 2.4$ Hz, 1H, H-1), 2.46–2.30 (ddd, A-part of AB-system, $J = 13.3$, 9.7 and 3.0 Hz, 2H, CH_2), 1.96–1.86 (dt, B-part of AB-system, $J = 13.3$, 3.0 Hz, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.2 (q), 144.2, 136.2, 130.7, 129.4, 128.3, 126.2, 116.4 (q, $^1J_{CH} = 285.9$ Hz, CF_3), 77.3, 44.0, 35.7, 35.5. Anal. Calcd for $C_{16}H_{12}F_6O_4$: C, 50.27; H, 3.16. Found: C, 50.04; H, 3.17.
12-(Trifluoroacetyloxy)tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraen-8-yl trifluoroacetate (**35**, R = $COCF_3$): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31–7.1 (m, 4H, aromatic), 6.55 (ddd, $J = 6.0$, 3.5 and 1.0 Hz, 1H, H-10), 6.02, (br s, 1H, H-8), 6.0 (ddd, $J = 6.0$, 4.8 and 2.5 Hz, 1H, H-11), 5.52 (t,

$J = 4.8$ Hz, 1H, H-12), 3.70 (t, $J = 4.0$ Hz, 1H, H-1), 3.42 (br t, $J = 3.2$ Hz, 1H, H-9). ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.2 (q, $^2J_{CH} = 42.8$ Hz, C=O), 158.7 (q, $^2J_{CH} = 42.1$ Hz, C=O), 144.9, 139.9, 132.8, 132.0, 131.0, 130.3, 129.2 (2C), 116.1 (q, $^1J_{CH} = 285.9$ Hz, CF_3), 115.8 (q, $^1J_{CH} = 279.9$ Hz, CF_3), 80.2, 73.7, 48.0, 45.6. Anal. Calcd for $C_{16}H_{10}F_6O_4$: C, 50.54; H, 2.65. Found: C, 51.14; H, 2.75.