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Organoselenium Reagents in the Tandem β-Fragmentation-Cyclization of Carbohydrate Anomeric Alkoxy Radicals

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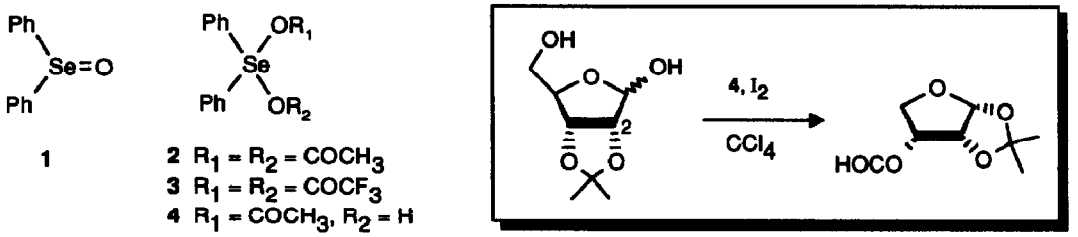
Abstract: *Carbohydrates possessing a suitably positioned hydroxyl group in the presence of organoselenium reagents and iodine under an argon atmosphere undergo intramolecular β-fragmentation-cyclization reaction to give aldofuranose and aldopyranose forms of carbohydrates, specifically.*

The stereochemical properties of carbohydrates combined with their ready availability make them attractive starting material for the enantiospecific synthesis of many highly functionalized compounds.[1] Recently, we have reported new methods for the synthesis of four- and five-carbon chiral building blocks by β-fragmentation[2] and by tandem β-fragmentation-cyclization[3] reaction on appropriate sugar derivatives promoted by hypervalent iodine compounds.

As a part of our ongoing program to develop new oxidizing agents we are exploring the seldom investigated chemical properties of organoselenium (IV) derivatives,[4] such as diphenylselenoxide (1),[5] diphenylselenium diacetate (2),[6] diphenylselenium bis(trifluoro)acetate (3)[4b,c] and diphenylselenium hydroxyacetate (4)[7] (Scheme). This last compound, a stable, non-hygroscopic, crystalline and readily available solid, proved to be an excellent reagent for the generation of alkoxy radicals which on suitable substrates can undergo intramolecular hydrogen abstraction[7a] to afford cyclic ethers and β-fragmentation[7b] to give cyclic imides. These features encouraged us to study the capacity of selenium(IV) derivatives to promote carbohydrate anomeric alkoxy radicals.



Scheme

Preliminary results and conditions are specified in the Table. Firstly, the carbohydrate derivatives (5)[8] and (7) were treated with diphenylselenoxide (1) in the presence of iodine under an inert atmosphere (Table, entries 1 and 2) producing the unwanted oxidation reaction, in accordance with the known oxidizing properties of selenoxides,[5] to give the D-ribonolactone derivatives (6)[8] and (8), that have been used in recent years as versatile chiral intermediates.[9] Noteworthy is the selective oxidation of the anomeric alcohol for the

substrate (**7**) leading to the unchanged secondary alcohol at C-3. Unfortunately, when the reagent used with these substrates (**5**) and (**7**) was diphenylselenium hydroxyacetate (**4**), mixtures of products were obtained.

Nevertheless, when a second set of carbohydrate derivatives with a suitably positioned hydroxyl group was submitted to the reaction conditions, in the presence of diphenylselenium hydroxyacetate (**4**) and iodine, products resulting from a tandem β-fragmentation-cyclization reaction were, successfully, obtained. Thus, the readily available 2,3-*O*-isopropylidene-D-ribofuranose (**9**)[8] gave a sole isomer of the erythrose derivative (**10**)[3a] although in low yield (25%) (Table, entry 3). The stereochemistry of **10** has been established by the coupling constant relationships, the observed $J_{1,2}$ = 3.7 Hz and $J_{2,3}$ = 3.7 Hz being consistent with a *cis* stereochemistry for protons at C_1, C_2 and C_3. A differently protected D-ribose, 2,3-*O*-cyclohexylidene-D-ribofuranose (**11**), produced only a slight improvement of the yields, attaining 34% of the corresponding erythrose derivative (**12**)[10] (Table, entry 4). These tetrahydrofuranoses have been widely used as chiral templates.[11] A similar yield was obtained for the threose derivative (**14**)[12] (37%) when 2,3-*O*-isopropylidene-D-lyxose (**13**) was submitted to the reaction conditions. For this compound the *trans*-stereochemistry between the protons at C_2 and C_3 was confirmed by a coupling constant $J_{2,3}$ = 0 Hz. This threose derivative (**14**) has been used recently as a chiral template for the total synthesis of (-)-echinosporin.[12]

The β-fragmentation reaction does not depend on the C_2 configuration and, in the above cases, the intermediate generated[3b] is trapped by a primary hydroxyl group. However, this can also be trapped by a secondary hydroxyl group as occurred with 6-*O*-*tert*-butyldimethylsilyl-2,3-*O*-isopropylidene-L-gulose (**15**)[13] which led to an L-xylose derivative (**16**)[14] in moderate yield (55%) (Table, entry 6). Furthermore, D-mannose derivative (**17**) with a secondary alcohol produced the corresponding D-arabinose derivative (**18**)[3a] in good yield (73%).

The formation of carbohydrates in pyranose form is also possible through this procedure starting from carbohydrates in furanose or pyranose forms. For instance, the D-arabinose derivative (**20**)[15] in pyranose form was obtained from 2,3,4-tri-*O*-benzyl-D-glucopyranose (**19**) (Table, entry 8) and the L-lyxose pyranose derivative (**22**)[16] could be formed in good yield from 2,3,5-tri-*O*-benzyl-D-galactofuranose (**21**) (entry 9).

In summary, this work is the first example of a selenium(IV)-reagent promoting β-fragmentation of the anomeric centre of carbohydrates and intramolecular cyclization affording chiral templates which can be difficult to prepare by other means.

Experimental Procedure. A solution of 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-isopropylidene-D-mannose (**17**) (105 mg, 0.23 mmol) in dry carbon tetrachloride (10 mL) containing diphenylselenium hydroxyacetate (170 mg, 0.55 mmol) and iodine (58 mg, 0.23 mmol) was stirred under argon atmosphere for 4h at 80 °C. The reaction mixture was then poured into aqueous sodium thiosulfate solution and extracted with methylene chloride. Rotative chromatography of the crude (*n*-hexane/ethyl acetate 85:15 v/v) gave 3-*O*-formyl-6-*O*-(*tert*-butyldiphenylsilyl)-1,2-*O*-isopropylidene-D-arabinofuranose (**18**) (76 mg, 73%).

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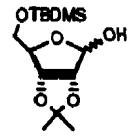
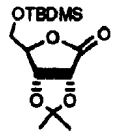
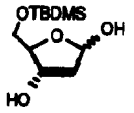
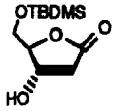
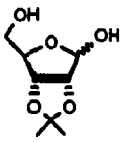
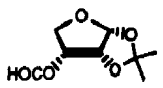
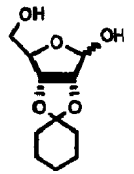
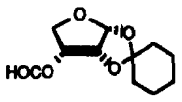
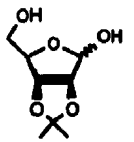
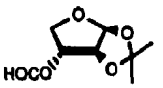
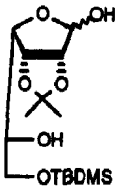
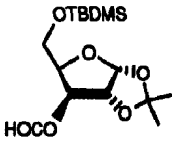
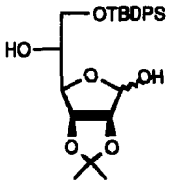
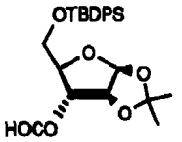
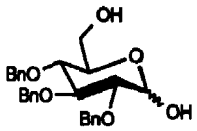
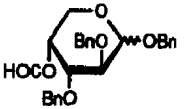
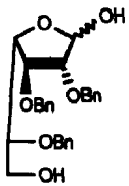
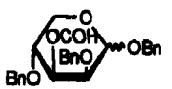
REFERENCES AND NOTES

1. a) Hanessian, S. *Total Synthesis of Natural Products. The Chiron Approach*, Pergamon Press, Oxford 1983; b) Hanessian S.; Rauncourt, G. *Pure Appl. Chem.* 1977, *49*, 1201; c) Fraser-Reid, B.; Tom, T.F; Sun, K.M. in *Organic Synthesis, Today and Tomorrow* (Eds.; Trost, B.M.; Hutchinson, C.R.), Pergamon Press, Oxford, 1981; d) Inch, T.D. *Tetrahedron* 1984, *40*, 3161; *Trends in Synthetic Carbohydrate Chemistry* (Eds.: Horton, D.; Hawkins, L.D.; McGarvey, G.J.), ACS, Washington, 1989.

Table. Tandem β-Fragmentation-Cyclization Reaction[a,17]

Entry	Substrate	Time (h)	Product	Yield (%)
1	 5	1.5	 6	67[b]
2	 7	3	 8	77[b]
3	 9	3	 10	25
4	 11	5.5	 12	34
5	 13	5	 14	37
6	 15	5	 16	55
7	 17	4	 18	73
8	 19	2	 20-α 20-β	71[c]
9	 21	1.5	 22-α 22-β	71

[a] All reactions were performed in CCl_4 with the system diphenylselenium hydroxyacetate (4)/iodine (2.4/1.2 mmol per mmol of substrate) at 80 °C. b) In this case the system diphenyl selenoxide/iodine (2.3/1.1 mmol per mmol of substrate) was used. c) 19% of 2,3,4-tri-*O*-benzyl-D-glucopyranolactone was also obtained.

2. Armas, P.; Francisco, C.G.; Suárez, E. *Angew. Chem. Int. Ed. Engl.*, **1992**, *31*, 772.
3. a) Armas, P.; Francisco, C.G.; Suárez, E. *J. Am. Chem. Soc.*, **1993**, *115*, 8865; b) Armas, P.; Francisco, C.G.; Suárez, E. *Tetrahedron Lett.*, **1993**, *34*, 7331.
4. a) Togo, H.; Miyagawa, N.; Yokoyama, M. *Chemistry Letters*, **1992**, 1677; b) Marino, J.P.; Larsen, R.D. *J. Am. Chem. Soc.*, **1981**, *103*, 4642; c) Marino, J.P.; Dax, S. *Tetrahedron Lett.*, **1987**, *28*, 4007.
5. Hu, M.X.; Aso, Y.; Otsubo, T; Ogura, F. *Chemistry Letters*, **1985**, 603 and references cited therein.
6. a) Foster, D.G. *Recl. Trav. Chim, Pays-Bas*, **1935**, *54*, 447; b) Horn, V.; Paetzold, R. *Z. Anorg. Allg. Chem.*, **1973**, *186*, 398.
7. a) Dorta, R.L.; Francisco, C.G.; Freire, R.; Suárez, E. *Tetrahedron Lett.*, **1988**, *29*, 5429; b) Dorta R.L.; Francisco, C.G.; Suárez, E. *Tetrahedron Lett., in press.*
8. Kaskar, B.; Heise, G.L.; Michalak, R.S.; Vishnuvajjala, B.R. *Synthesis*, **1990**, 1031.
9. a) Bhat, K.L.; Chen, S.-Y.; Joullié, M.M. *Heterocycles* **1985**, *23*, 691; b) Beer, D.; Menuly, R.; Vasella, A. *Helv. Chim. Acta*, **1982**, *23*, 2570; c) Lim, M.I.; Marquez, V.E. *Tetrahedron Lett.*, **1983**, *24*, 5559; d) Wolfe, M.S.; Anderson, B.L.; Borcherding, D.R.; Borchardt, R.T. *J. Org. Chem.* **1990**, *55*, 4712; e) Chen, S.-Y.; Joullié, M.M. *J. Org. Chem.*, **1984**, *49*, 2168.
10. Compound (**12**): IR ($CHCl_3$) ν_{max} 1737 cm^{-1}; ^1H NMR (200MHz, $CDCl_3$) δ_H 8.08 (1H, d, *J* 0.84 Hz), 5.83 (1H, d, *J* 3.8 Hz), 4.89-5.00 (1H, m), 4.75 (1H, apparent t, *J* 3.9 Hz), 4.11 (1H, dd, *J* 8.4, 6.9 Hz), 3.87 (1H, dd, *J* 8.4, 9.4 Hz), 1.80-1.35 (10 H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 159.98 (s), 114.05 (s), 104.61 (d), 76.46 (d), 71.43 (d), 66.10 (t), 36.16 (t), 36.02 (t), 24.85 (t), 23.86 (t), 23.54 (t); EIMS *m/z* 228.10024 (M^+, 12%), 139 (100%).
11. a) Sulikowski, M.M.; Ellis Davies, G.E.R.; Smith, A.B., III *J. Chem. Soc., Perkin Trans. 1* **1992**, 979; b) Smith, A.B., III; Sulikowski, G.A.; Fujimoto, K. *J. Am. Chem. Soc.*, **1989**, *111*, 8039.
12. Smith, A.B., III; Sulikowski, G.A.; Sulikowski, M.M.; Fujimoto, K. *J. Am. Chem. Soc.*, **1992**, *114*, 2567.
13. Fleet, G.W. J.; Ramsden, N.G.; Witty, D.R. *Tetrahedron*, **1989**, *45*, 319.
14. Compound (**16**): IR ($CHCl_3$) ν_{max} 1738 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ_H 8.07 (1H, s), 5.91 (1H, d, *J* 3.7 Hz), 5.36 (1H, d, *J* 3.0 Hz), 4.52 (1H, d, *J* 3.7 Hz), 4.37-4.33 (1H, m), 3.84 (1H, dd, *J* 5.6, 10 Hz), 3.74 (1H, dd, *J* 7.6, 10.0 Hz), 1.53 (3H, s, CH_3), 1.31 (3H, s, CH_3), 0.86 (9H, s, $SiC(CH_3)_3$), 0.05 (3H, s, CH_3), 0.03 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 159.51 (s), 112.25 (s), 104.83 (d), 83.19 (d), 79.05 (d), 75.55 (d), 59.76 (t), 26.67 (q), 26.24 (q), 25.75 (q), -5.46 (q), -5.57 (q); EIMS *m/z* 317.14190 (M^+-Me, 20%), 229 (100%).
15. Compound (**20**-α): IR ($CHCl_3$) ν_{max} 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ_H 8.16 (1H, s), 7.42-7.28 (10 H, Ar), 5.48 (1H, bs, $w_{1/2}$ 10 Hz), 4.90 (1H, d, *J* 3.6 Hz), 4.77 and 4.56 (2H, AB, d, *J* 11.9 Hz, CH_2Ph), 4.73 and 4.57 (2H, AB, *J* 12.3 Hz, CH_2Ph), 4.72 and 4.66 (2H, AB, *J* 11.1 Hz, CH_2Ph), 4.02 (1H, dd, *J* 3.4, 10.0 Hz), 3.91 (1H, dbs, *J* 13.0 Hz, $w_{1/2}$ 5 Hz), 3.83 (1H, dd, *J* 3.6, 10.0 Hz), 3.67 (1H, dd, *J* 2.0, 13.0 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 160.35 (s), 138.38 (s), 137.90 (s), 137.00 (s), 128.4-127.6 (s, Ar), 96.39 (d), 75.90 (d), 75.21 (d), 73.43 (t), 72.63 (t), 69.16 (t), 68.86 (d), 60.64 (t); EIMS *m/z* 357.13311 (M^+-Bn, 1.8%), 341 (M^+-OBn, 100%). Compound (**20**-β): IR ($CHCl_3$) ν_{max} 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ_H 8.19 (1H, s), 7.38-7.26 (15H, m), 5.40 (1H, bs, $w_{1/2}$ 8 Hz), 4.97 and 4.77 (2H, AB, *J* 11.9 Hz, CH_2Ph), 4.92 and 4.67 (2H, AB, *J* 11.9 Hz, CH_2Ph), 4.73 and 4.63 (2H, AB, *J* 11.6 Hz, CH_2Ph), 4.47 (1H, d, *J*, 7.2 Hz), 4.07 (1H, dd, *J* 2.4, 13.2 Hz), 3.75 (1H, dd, *J* 7.2, 9.4 Hz), 3.61 (1H, dd, *J* 3.4, 9.4 Hz), 3.52 (1H, dbs, *J* 13.2, $w_{1/2}$ 4.0 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 160.37 (s), 138.43 (s), 137.58 (s), 137.26 (s), 128.4-127.6 (d, Ar), 102.68 (d), 79.04 (d), 78.21 (d), 75.36 (t), 72.54 (t), 71.05 (t), 67.60 (d), 63.81 (t); EIMS *m/z* 341.13977 (M^+-OBn, 0.04%), 91.05325 (100%).
16. Compound (**22**) (less polar isomer, *n*-hexane-EtOAc, 9:1): IR ($CHCl_3$) ν_{max} 1730 cm^{-1}; ^1H NMR (200MHz, $CDCl_3$) δ_H 8.07 (1H, s), 7.40-7.27 (15H, m, Ar), 5.31 (1H, dd, *J* 3.3, 8.7 Hz), 4.80 (1H, d, *J* 2.9 Hz), 4.64 (4H, s, CH_2Ph), 4.75 and 4.48 (1H, AB, *J* 12 Hz, CH_2Ph), 3.98 (1H, ddd , *J* 4.9, 9.1, 8.9 Hz), 3.87 (1H, t, *J*, 3.0 Hz), 3.82 (1H, dd, *J* 11.2, 4.9 Hz), 3.67 (1H, dd, *J* 11.2, 9.2 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 160.37 (s), 137.98 (Ar), 137.60 (Ar), 137.04 (Ar), 128.46-127.70 (d, Ar), 97.38 (d), 75.64 (d), 73.44 (t), 72.98 (t), 72.89 (d), 72.63 (d), 69.25 (t), 61.44 (t); EIMS *m/z* 357.13632 (M^+-Bn, 1%), 181 (100%). Compound (**22**) (more polar isomer, *n*-hexane-EtOAc, 9:1): IR ($CHCl_3$) ν_{max} 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ_H 8.03 (1H, s), 7.41-7.31 (15H, m, Ar), 5.20 (1H, dd, *J* 3.5, 6.1 Hz), 4.86 and 4.61 (2H, AB, *J* 11.9 Hz, CH_2Ph), 4.72 (1H, *J* 2.4 Hz), 4.67 and 4.60 (AB, *J* 11.9 Hz, CH_2Ph), 4.62 (2H, s, CH_2Ph), 4.03 (1H, dd, *J* 3.3, 12.2 Hz), 3.93 (1H, apparent t, *J* 3.1 Hz), 3.77 (1H, ddd, *J* 3.4, 5.6, 5.7 Hz), 3.41 (1H, dd, *J* 5.3, 12.2 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ_C 160.44 (s), 137.76 (2s), 137.36 (s), 128.5-127.6 (d, Ar), 97.30 (d), 73.25 (d), 72.87 (t), 72.57 (d), 72.31 (t), 69.96 (d), 69.96 (t), 60.51(t); EIMS *m/z* 447.18117 (M^+-H, <1%), 341.13455 (M^+-OBn, 2%), 181 (100%).
17. All new compounds gave satisfactory high resolution mass spectra, consistent with the expected molecular formula.

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