Acknowledgment. Thanks are due to Professor Jun-ichi Aihara of Shizuoka University for his valuable discussions and Mr. Haruo Inoue of Inoue Firebrick Ind. Co. (Sapporo) for presenting some of the clay samples.

(8) If the initial unbalancing of *d* and *l* ligands is $[d\text{-L}]/[l\text{-L}] = 1 + \alpha$ ($\alpha \ll 1$) and the ligand stereoselectivity is given by $[(+)\text{-M}(d\text{-L})]/[(-)\text{-M}(d\text{-L})] = 1 + \beta$ ($0 < \beta$), the resultant unbalancing of the configurational isomers is $[(+)\text{-M}(d\text{-L}) + (+)\text{-M}(l\text{-L})]/[(-)\text{-M}(d\text{-L}) + (-)\text{-M}(l\text{-L})] = 1 + \gamma$ with $\gamma = \alpha\beta(2 + \alpha + \beta)^{-1}$. If the racemic adsorption occurs between the different configurational isomers irrespective of the ligand asymmetry, the ratio of [*d*-L] to [*l*-L] remaining in solution becomes $(1 + \alpha)(1 + \beta)$. In other words, the *d*-L isomer is enriched by a factor of $1 + \beta$.

Diphenylselenium Bis(trifluoroacetate): A New Reagent for Biomimetic Oxidations of Amines and Amino Acids

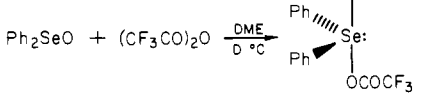
J. P. Marino* and Robert D. Larsen, Jr.

Department of Chemistry, University of Michigan
Ann Arbor, Michigan 48109

Received March 18, 1981

As part of an effort to develop mild and selective two electron oxidants for phenolic compounds,[1] we have been investigating the chemistry of diarylselenuranes[2] bearing heteroatoms. The classical role of selenium dioxide in organic synthesis has been expanded to include a number of organoselenium reagents of various oxidation states for selenium.[3] Balenovic was the first to report that diphenyl selenoxide is an effective oxidant for hydrazides, amines,[4] and catechols.[5] Recently, we have applied the selective oxidation of catechols by diphenyl selenoxide to phenolic coupling processes in the isoquinolines.[6] In this communication, we report a new selenium(IV) reagent, diphenylselenium bis(trifluoroacetate) (**1**), for the controlled oxidations of heterocyclic amines and α-amino acids.

Paetzold[7] first reported the preparation of selenurane **1** in 1973 from the reaction of diphenylselenium dibromide with silver trifluoroacetate. We have found a more convenient preparation of **1** from diphenyl selenoxide.[8,9] Addition of 1 equiv of trifluoroacetic anhydride to a solution of diphenyl selenoxide in dimethoxyethane (DME) provides reagent **1** in quantitative yield.[10]



1

(1) (a) For a summary of sulfur cations in phenolic oxidation processes see: Marino, J. P. *Top. Sulfur Chem.* **1976**, *1*, 1. (b) Marino, J. P.; Samanen, J. M. *Tetrahedron Lett.* **1973**, 4553.

(2) The term selenurane has been used for tetravalent Se(IV) compounds by analogy to sulfurane (Martin, J. C., Arhart, R. J. *J. Am. Chem. Soc.* **1971**, *93*, 2339). There is, however, a possible ambiguity with derivatives of the uranyl ion (UO_2^{2+}) and the suffix for selenurane. There is currently under consideration by the IUPAC Commission on Nomenclature of Organic Chemistry a proposal to use the name λ^4-selane to denote tetravalent Se(IV) compounds (Smith, P. A. S., private communication).

(3) For a review of selenoxides as oxidizing agents, see: Reich, H. J. "Oxidations in Organic Reactions, Part C"; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; Chapter 1.

(4) Poje, M.; Balenovic, K. *Bull. Sci., Sect. A (Zagreb)* **1975**, *20*, 1. *Chem. Abstr.* **1975**, *83*, 43558u.

(5) (a) Perina, I.; Bregant, N.; Balenovic, K. *Bull. Sci., Sect. A (Zagreb)* **1973**, *18*, 3. *Chem. Abstr.* **1973**, *79*, 50966. (b) Balenovic, K.; Bregant, N.; Perina, I. *Synthesis* **1973**, 172.

(6) Marino, J. P.; Schwartz, A. *Tetrahedron Lett.* **1979**, 4553.

(7) Horn, V. V.; Patezold, R. *Z. Anorg. Allg. Chem.* **1973**, *398*, 186.

(8) Leicester, H. M., "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 238. Also commercially available from Eastman Chemicals.

(9) Cinquini, M.; Colonna, S.; Giovanni, R. *Chem. Ind. (London)* **1969**, 1737.

By analogy to sulfuranes[11] and from spectral properties, the diphenylselenium bis(trifluoroacetate) is best represented as a neutral selenurane (**1**), possessing trigonal-bipyramid geometry as opposed to an ionic selenonium trifluoroacetate. Although compound **1** and related dioxyselenuranes have been known since 1973,[12] their use in oxidation chemistry has not been previously reported.[13]

In this report, we wish to focus on the oxidation of secondary and tertiary amines of substituted tetrahydropyridine systems. Initially, a representative series of 1-substituted 1,2,3,4-tetrahydroisoquinolines[14] (**2b–d**) were oxidized with reagent **1** at room temperature and in high yields to their 3,4-dihydroisoquinoline derivatives.[15] In the oxidations of **2b,c**, a small amount (10%) of the isoquinoline derivatives **4b** and papaverine (**4c**) was isolated.[16,17] Attempts at further oxidation of the 3,4-dihydro compounds **2a,b,d** with large excesses of **1** failed to yield the isoquinolines. However, when **2c** was reacted with 6 equiv of reagent **1** for 12 h at room temperature and then 12 h at reflux (DME), a 75% yield of papaveraldine,[18] **4** [$R_2 = (MeO)_2C_6H_3CO$], was obtained. Tetrahydroisoquinoline-3-carboxylic acid (**2e**)[19] and its methyl ester **2f** oxidized directly to isoquinoline systems with 3 equiv of selenurane **1** at room temperature. The reaction of the free amino acid **2e** proved to be complicated in that both aromatization to the isoquinoline acid (isolated as methyl ester **4e**, 40%) and oxidative decarboxylation to isoquinoline itself (26%) occurred. This latter process represents one of the mildest, nonaqueous oxidative decarboxylations of an α-amino acid. The amino ester **2f** was quantitatively oxidized to isoquinoline **4f**.

As a further test of the compatibility of reagent **1** with other nitrogen heterocycles, we examined the oxidation of the medicinally important 1,2,3,4-tetrahydrocarbolines **5** and **6**.[20] With 1.2 equiv of selenurane **1** (room temperature), **5** was oxidized to its 3,4-dihydro derivative[21] in 85% yield. Increasing the oxidant to 3 equiv produced the β-carbolines **7** and **8**[21] in yields of 61% and 70%, respectively. Undoubtedly, the indole ring influences

(10) General experimental procedure: Dried diphenyl selenoxide (vacuum desiccation, 10^{-1} torr, 90 °C, 24 h) is dissolved in dry DME (1 g per 40 mL) and an equimolar amount of trifluoroacetic anhydride (freshly distilled from phosphorus pentoxide) is added via a syringe. This solution is stirred at 25 °C for 15 min and then added dropwise to a DME solution of the amine over a one-half-hour period. The oxidation reactions are normally complete after 3–12 h. Selenurane **1** is a white hygroscopic solid that can be isolated and stored at 0 °C under an inert atmosphere. Data for **1**: mp 175–176 °C (lit.[7] mp 172–174 °C); ^{1}H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 7.65 (br s); ^{19}F NMR (100 MHz, $CDCl_3$) (CF_3CO_2D, external) δ 2.0 (s); IR ($CHCl_3$) 1730, 1716, 1215, 1150 cm^{-1}. Anal. Calcd for $C_{16}H_{10}F_6O_4Se$: C, 41.85; H, 2.20; F, 24.82. Found: C, 41.61; H, 2.20; F, 24.70.

(11) For structural and spectral characterization of oxysulfuranes, see: Martin, J. C.; Livant, P. *J. Am. Chem. Soc.* **1977**, *99*, 5761 and references cited therein.

(12) Paetzold, R.; Reichenbacher, M. *Org. Selenium Compd.: Their Chem. Biol.* **1973**, 305.

(13) Schwartz, Alan Ph.D. Thesis, University of Michigan, 1979.

(14) **2a**: Buck, J. S. *J. Am. Chem. Soc.* **1974**, *56*, 1769. **2b**: Spaeth, E.; Dengel, F. *Chem. Ber.* **1938**, *71*, 113. **2c**: Falck, J. R.; Miller, L. L.; Stermitz, F. R. *Tetrahedron* **1974**, *30*, 391. **2d**: Hershenson, F. M. *J. Org. Chem.* **1975**, *40*, 740.

(15) **3a**: Ban, Y.; Yonemitsu, O.; Terashima, M. *Chem. Pharm. Bull (Tokyo)* **1960**, *8*, 183, 194. **3b**: Bruderer, H.; Brossi, A. *Helv. Chim. Acta* **1965**, *48*, 1945. **3c**: Wehrli, P. A.; Schaer, B. *Synthesis* **1974**, 288. Data for **3d**: mp 178–179 °C; ^{1}H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 3.3 (m, 2 H), 4.0 (m, 2 H), 4.0 (m, 2 H, buried), 4.0 (s, 3 H), 4.1 (s, 3 H), 6.9 (s, 1 H), 7.9 (s, 1 H); MS *m/e* 235 (M^+), 191 ($M^+ - 44$), 176 ($M - 59$). Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.26; H, 5.58; N, 5.96. Found: C, 60.98; H, 5.42; N, 5.58.

(16) Umezawa, B.; Hoshina, O.; Sawaki, S. *Chem. Pharm. Bull. (Tokyo)* **1969**, *17*, 1115.

(17) Rosenmund, K. W.; Nothnagel, M.; Riesenfeldt, H. *Chem. Ber.* **1927**, *60*, 392.

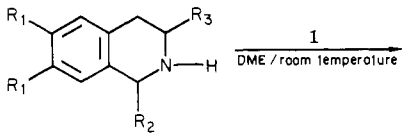
(18) Buck, J. S.; Haworth, R. D.; Perkin, W. H. *J. Chem. Soc.* **1924**, *125*, 2176.

(19) **2e**: Julian, P. L.; Karpel, W. J. *J. Am. Chem. Soc.* **1948**, *70*, 180. **2f**: Soxena, A.; Jain, P. C.; Anand, N. *Indian J. Chem.* **1975**, *13*, 230.

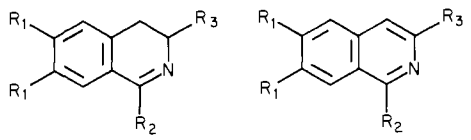
(20) **5**: Ho, B. T.; Walker, K. E. *Org. Synth.* **1971**, *51*, 136. **6**: Snyder, H. R.; Hansch, C. H.; Katz, L.; Parameter, S. M.; Spaeth, E. C. *J. Am. Chem. Soc.* **1948**, *70*, 219.

(21) O'Rell, D.D.; Lee, F. G. H.; Boekelheide, V. *J. Am. Chem. Soc.* **1974**, *94*, 3205. **7**: Speitel, R.; Schlitter, *Helv. Chim. Acta* **1949**, *32*, 860. **8**: ref 20b.

0002-7863/81/1503-4642$01.25/0



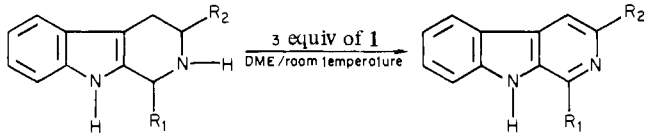
2



3 4

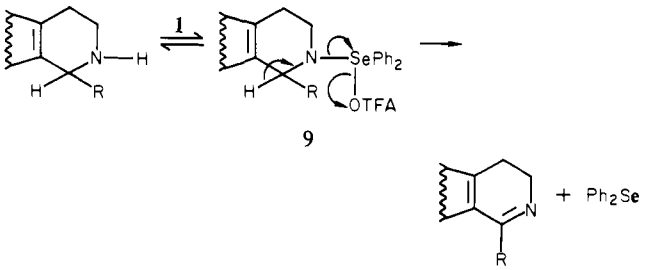
2	1, equiv	yield, % 3	4
a, R_1 = MeO; R_2 = R_3 = H	2	80	0
b, R_1 = MeO; R_2 = Me; R_3 = H	3	81	10
c, R_1 = MeO; R_3 = H; R_2 = 3,4-$(MeO)_2C_6H_3CH_2$	6	85 R_2 = ArCO	10
d, R_1 = MeO; R_2 = COOH; R_3 = H	2	100	
e, R_1 = R_2 = H; R_3 = COOH	3	0	R_1 = R_2 = H; R_3 = CO_2Me, 40 + R_1 = R_2 = R_3 = H, 26%
f, R_1 = R_2 = H; R_3 = CO_2Me	3	0	100

the second oxidation step from the dihydro intermediate.



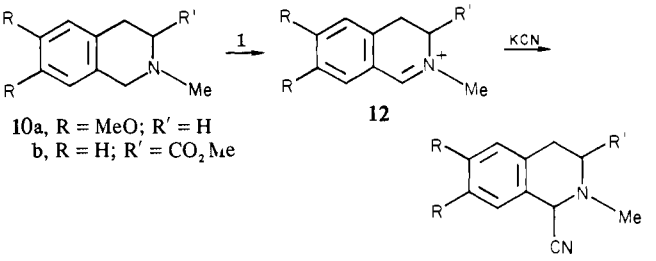
5, R_1 = R_2 = H 7, 61%
6, R_1 = Me; R_2 = CO_2Me 8, 70%

The mechanism for the initial oxidation of the tetrahydropyridine system to its 3,4-dihydro derivative is presumed to involve an aminoselenurane intermediate **9**. The formation of **9** would be expected to occur via the displacement[22] of a trifluoroacetate ligand from reagent **1**. The loss of a benzylic proton from **9** completes the oxidation process to an imine and diphenyl selenide. The reluctance of products **3a–d** to undergo clean oxidation to their isoquinolines reflects the lack of driving force for an 1,2-iminoselenurane to lose a C-4 proton. The facile oxidation of **2f** to its isoquinoline **4f** is thought to proceed via its 1,4-dihydroisoquinoline, which in turn forms a 2,3-iminium selenurane.



9

Having established that secondary amines are readily oxidized by the electrophilic selenurane **1**, we next examined the fate of tertiary amines with reagent **1**. Since the expected oxidation products of the *N*-methyl-1,2,3,4-tetrahydroisoquinolines **10a** and **10b**[23] were the 1,2-iminium species **12**, which are usually difficult to isolate, their reaction mixtures were quenched with an aqueous solution of potassium cyanide. The oxidations of **10a** and **10b** with 3 equiv of selenurane **1** at room temperature proceeded regiospecifically to the 1-cyanotetrahydroisoquinolines **11a**[24] and **11b** in high yields. This overall transformation is an oxidative analogue of the Reissert reaction. Evidently, there was no effect of the carbomethoxy group of **10b** on the regioselectivity of the iminium ion formation. These oxidations are envisaged to involve an ammonium selenurane.



10a, R = MeO; R′ = H
b, R = H; R′ = CO_2Me

12

11a, 90%
b, 78%

In summary, the oxidations of secondary and tertiary amines by diphenylselenium bis(trifluoroacetate) (**1**) represent a very mild, two-electron process that mimics a number of biological oxidations of amines. We feel that the use of hypervalent selenuranes as oxidants promises to offer more selective and efficient oxidations of heterocarbon functionality. Further work is in progress to explore the synthetic potential of this new class of reagents as well as the mechanism of oxidation.

Acknowledgment. R.D.L. is grateful for a Dow–Britton Fellowship and Chemistry Department Fellowships (Moses Gomberg and Robert Ruthruff) during the course of this work. We also thank Dr. Alan Schwartz for the initial characterization of the selenurane **1**.

(22) The S_N1-like ionization of certain sulfuranes has been postulated for the oxidations of nitrogen compounds: Martin, J. C.; Balthazor, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 152.

(23) **10a**: reference for **2a**. Data for **10b**: **10b**·HCl, mp 192–193 °C; ^1H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 2.5 (s, 3 H), 3.0 (m, 2 H), 3.5 (m, 1 H), 3.6 (s, 3 H), 3.7 (m, 2 H, buried), 7.0 (s, 4 H); MS *m/e* 205 (M^+), 146 (M − 59). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.21; H, 7.38; N, 6.82. Found: C, 70.34; H, 7.38; N, 6.75.

(24) **11a**: Eckhardt, E. *Magy. Kem. Foly.* **1974**, *70*, 295. *Chem. Abstr.* **1974**, *61*, 13355. Data for **11b**: mp 126–128 °C; ^1H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 2.9 (s, 1 H), 3.2 (d, 2 H), 3.8 (t, 1 H, buried), 3.8 (s, 1 H), 5.0 (s, 3 H), 7.3 (m, 4 H); MS *m/e* 230 (M^+), 215 (M^+ − 15), 204 (M^+ − 26), 171 (M^+ − 59), 144 (M − 86). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.80; H, 6.14; N, 12.16. Found: C, 67.65; H, 6.10; N, 12.13.

An Efficient and Stereoselective Synthesis of 2,3-Dihydroindoles via 1,5-Electrocyclization

W. Nico Speckamp,* Siem J. Veenstra, Jan Dijkink, and Rik Fortgens

Laboratory of Organic Chemistry, University of Amsterdam 1018 WS Amsterdam, The Netherlands

Received February 19, 1981

The indole moiety constitutes the central part of a large number of alkaloids. Novel methodology for the general synthesis of varied members of the indole alkaloid family therefore may concentrate on new strategies for the buildup of the indole nucleus.[1] In connection with the development of a general method for alkaloid synthesis on the basis of α-acyliminium intermediates,[2] it became necessary to contrive an efficient dihydroindole synthesis which was also required to possess a high degree of stereocontrol. The

(1) Representative references include the following: R. M. Coates and C. W. Hutchins, *J. Org. Chem.*, **44**, 4742 (1979); R. B. Bard and J. F. Bunnett, *ibid.*, **45**, 1546 (1989); L. S. Hegedus, G. F. Allen, and E. L. Waterman, *J. Am. Chem. Soc.*, **98**, 2674 (1976); J. F. Wolfe, M. C. Sleevi, and R. R. Goehring, *ibid.*, **102**, 3646 (1980); Y. Ito, K. Kobayashi, and T. Saegusa, *ibid.*, **99**, 3532 (1977); H. Person, M. Del Aguila Pardo, and A. Foucaud, *Tetrahedron Lett.*, 281 (1980).

(2) W. N. Speckamp, *Int. Congr. Ser.—Excerpta Med.*, **No. 457**, 50–61 (1979).

0002-7863/81/1503-4643$01.25/0