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A Selenurane Derivative Promotes β-Fragmentation of Carbinolamides Leading to Cyclic Imides

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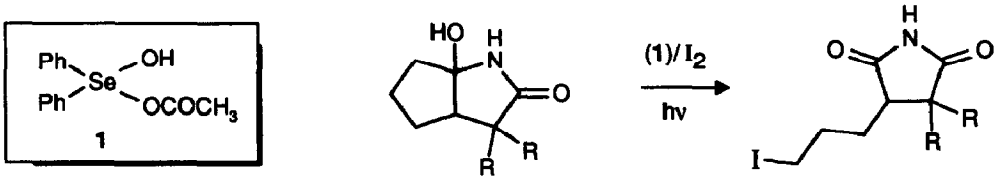
Abstract: The alkoxy radical intermediates generated by reaction of carbinolamides with diphenylselenium hydroxyacetate (1) in the presence of iodine and under irradiation with visible light undergo β-fragmentation to afford 3,4-substituted cyclic imides in good yields.

Although tetravalent organoselenium compounds have been known for many years,[1] their chemical properties have been little investigated.[2] In a previous communication we have introduced the diphenylselenium hydroxyacetate (**1**)-iodine system as an efficient reagent to generate alkoxy radicals.[3] Alkoxy free radicals are able to undergo a wide variety of synthetically useful intramolecular hydrogen abstraction[4] and β-scission processes.[5] For some years, we have been studying the photolysis of hemiacetals,[6a] lactols[6b] and carbinolamides[6c] in the presence of a hypervalent iodine reagent and iodine, developing novel methodologies which successfully allow the synthesis of lactones, anhydrides and cyclic imides, respectively. These last products are very significant not only as reagents,[7] but also as useful intermediates for the synthesis of pyrrolizidine alkaloids,[8] and the biosynthesis of vitamin B_{12}.[9]

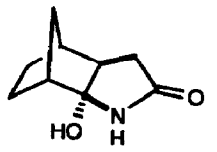
Herein, we describe our observations on the course of alkoxy radical generation by using the selenium (IV) reagent-iodine system. As expected, this method promotes regioselective β-fragmentation of carbinolamides leading to 3,4-substituted cyclic imides cleanly without any by-products (Scheme I, R = H, alkyl).



Scheme I

The procedure was applied to several carbinolamides such as 2-hydroxy-3-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (**2**),[10] bicyclo[3.3.0] derivatives (**6**),[11] (**8**),[12] (**10**)[6c] and the steroidal carbinolamide (**13**).[13] All these substrates were obtained from the corresponding α,β-unsaturated carbonyl compounds by addition of potassium cyanide and hydrolysis of the nitrile intermediates.[13]

A typical procedure is as follows: a mixture of carbinolamide (**2**) (0.30 mmol) in carbon tetrachloride (10 ml) containing diphenylselenium hydroxyacetate (0.45 mmol) and iodine (0.33 mmol) was irradiated with two 100 W tungsten-filament lamps for 40 min at 80 °C. The reaction mixture was then poured into



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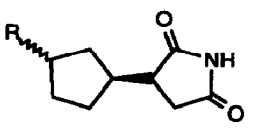
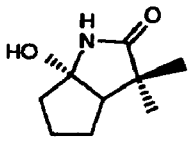


3 R = α-I
4 R = β-I
5 R = H



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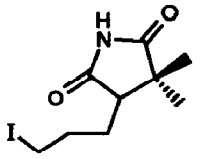

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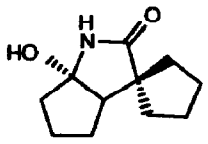

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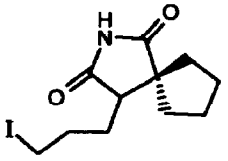

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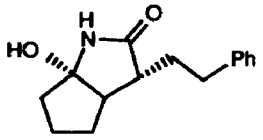

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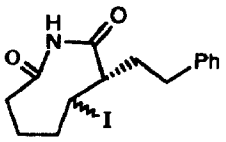

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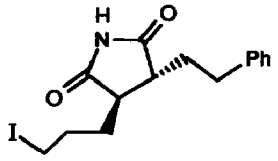

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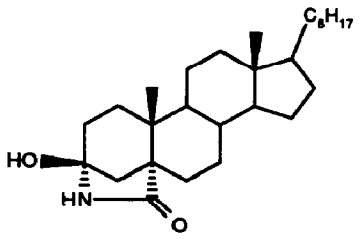

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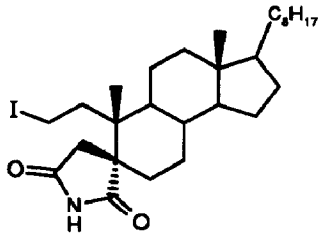

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aqueous sodium thiosulfate solution and extracted with methylene chloride. Rotative chromatography of the crude with EtOAc-*n*-hexane mixtures of increasing polarity gave the isomeric iodoimides (3,[14a] 4,[14b] see Table entry 1) in 78% yield,[15] which by reduction with tributyltin hydride gave a sole product (5)[16] in 86% yield.

When the reaction was performed at temperatures lower than 80 °C the conversion was not complete as occurred with the 4,4-disubstituted bicyclo-derivatives (6) (entry 2) and (8) (entry 3), recovering starting material in both cases. However, conversion of the 4,4-disubstituted bicyclo-derivative (8) maintaining the temperature at 80 °C was complete in 1 hour (entry 4).

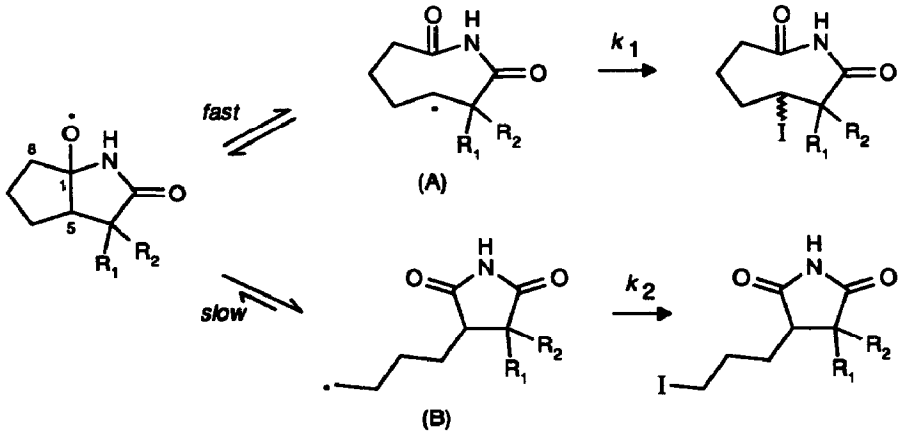
In the case of the 4-monosubstituted carbinolamide (10) ring expansion occurred giving rise to an 8-membered imide (11)[6c] together with the 5-membered imide (12)[6c] (entry 5). Finally, fragmentation of the steroidal carbinolamide (13) gave a sole product (14)[6c] in excellent yield (94%) (entry 6).

Table. β-Fragmentation of Carbinolamides[a] by Diphenylselenium Hydroxyacetate (1).

Entry	Substrate	Reagents[b] (mmol)	Conditions[c] Time (h)	Conditions[c] Temp. (°C)	Products (Yield %)
1	**2**	1.5/1.1	0.6	80	**3** (39), **4** (39)
2	**6**	1.5/1.0	6.5	40	**7** (76)[d]
3	**8**	1.5/1.1	1	60	**9** (72)[d]
4	**8**	1.5/1.1	1	80	**9** (74)
5	**10**	1.5/1.1	1.2	80	**11** (74), **12** (22)
6	**13**	1.5/1.0	1	80	**14** (94)

a) Compounds (**2**), (**6**), (**8**) and (**10**) are racemates; b) Mmoles of diphenylselenium hydroxyacetate/mmoles of iodine per mmol of substrate; c) All the reactions were performed in carbon tetrachloride, 30 ml per mmol of substrate; d) Calculated on transformed product (70%).

A plausible mechanism is shown in scheme II; the carbinolamide radical may undergo a fast but reversible β-fragmentation of the C_1-C_5 bond to give the kinetic radical (A), and a slower but essentially irreversible C_1-C_8 cleavage to afford the thermodynamic primary radical (B). The second step rate would be dependent on the efficiency of radical trapping (among other factors). In the hindered carbinolamides (**6**, **8** and **13**) (R_1 = R_2 = alkyl) k_2 must be greater than k_1 and succinimide derivatives are formed exclusively. However, in the less hindered carbinolamide (**10**) (R_1 = H, R_2 = alkyl) k_2 must be smaller or similar than k_1 directing the equilibrium mainly to the formation of the unexpected eight-membered imide (**11**).[17] We were unable to detect the co-formation of any by-products resulting from the C_1-NH fission to give the corresponding amide-radical that eventually can be transformed by amidyl rearrangement into isocyanates.[18]



Scheme II

In view of these results we can conclude that diphenylselenium hydroxyacetate is an interesting alternative to other oxidizing agents, proving to be efficient, mild and selective.

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10. Compound (2): m.p. 206-207 °C (MeOH); IR (KBr) ν_{max} 3354, 3176, 1713, 1650 cm^{-1}; ^{1}HNMR (200 MHz, CD_3OD) δ_H 2.72 (1H, d, *J* 18 Hz), 2.68 (1H, d, *J* 18 Hz), 2.20 (1H, bs, $w_{1/2}$ 8 Hz), 2.00-1.82 (3H, m), 1.65-1.25 (6H, m); ^{13}CNMR (50.3 MHz, CD_3OD) δ_C 180.23 (s), 97.63 (s), 50.34 (d), 47.24 (d), 44.78 (d), 37.49 (t), 35.46 (t), 29.20 (t), 23.51 (t); MS m/z 167.09408 (M^+, 11%).
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14. Compounds 3 and 4 were partially resolved by chromatography. The relative stereochemistries were established by determination of the coupling constants of the iodine geminal proton by the PCMODEL program (Serena Software) and simulation of the signal by the RACOOM program (P.F. Schatz, University of Wisconsin); a) α-Isomer (3) IR ($CHCl_3$) ν_{max} 3403, 1785, 1725 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) δ_H 8.35 (1H, bs, NH), 4.46 (1H, m, $w_{1/2}$ 16 Hz), 2.95-2.80 (3H, m), 2.51-1.33 (8H, m); MS *m/z* 294 (M^++ 1, 3%), 166 (100%); b) β-Isomer (4) IR ($CHCl_3$) ν_{max} 3403, 1785, 1725 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) 8.30 (1H, bs, NH), 4.22 (1H, dddd, J 6, 12, 12, 6 Hz), 3.05-2.82 (3H, m), 2.62-1.29 (8H, m); MS m/z 294 (M^++ 1, 3%), 166.08679 (M^+-I, 100%).
15. Diphenyl selenide was also isolated in all cases. It was characterized by comparison with an authentic sample.
16. Compound (5): m.p. 123.7-124.1 °C (EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3405, 1782, 1724 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) δ_H 8.45 (1H, bs, NH), 2.97-2.74 (2H, m), 2.52-2.27 (2H,m), 1.93-1.56 (6H, m), 1.34-1.21 (2H, m); ^{13}CNMR (50.3 MHz, CD_3OD) δ_C 183.18 (s), 180.54 (s), 46.16 (d), 42.29 (d), 34.65 (t), 31.36 (t), 29.69 (t), 26.30 (t), 25.93 (t); MS m/z 168.10271 (M^++ 1, 3%), 167.09513 (M^+, 1%), 99.11774 (100%).
17. A similar argument has been used by: Beckwith, A.L.J.; Kazlauskas, R.; Syner-Lyons, M.R. *J. Org. Chem.*, **1983**, *48*, 4718 to explain the β-fragmentation of 9-decalinoxyl radicals.
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