

CYCLOFUNCTIONALIZATION OF UNSATURATED TRITERPENIC ALCOHOLS WITH SELENIUM AND THALLIUM (III) ELECTROPHILES. A COMPARATIVE STUDY.

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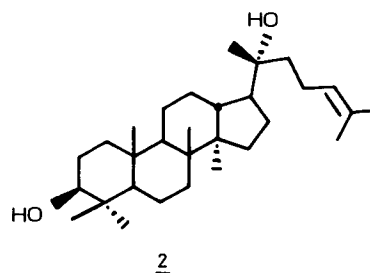
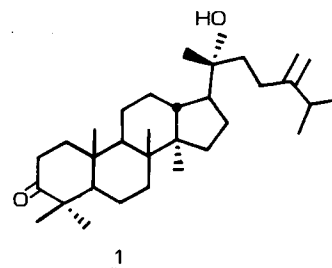
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Abstract: The reaction of triterpenes 1 and 2 with phenylselenenyl chloride leads to tetrahydrofuran derivatives 3 and 4, respectively, in high yields; the same triterpenes react with thallium triacetate to give tetrahydropyran derivatives 6 and 7, in moderate yields, as the major products.

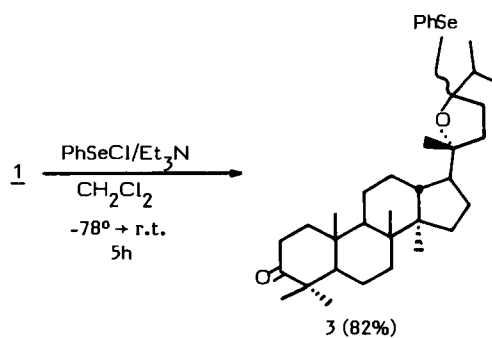
Reactions of an electrophilic reagent with unsaturated substrates possessing an internal nucleophile are long known. These reactions lead to cyclic esters, ethers, sulfides, amines and amides, and are referred to as cyclofunctionalization¹. Among the many electrophilic reagents used for this purpose are the arylselenenyl halides² and the thallium (III) salts³. In view of the easy experimental conditions to perform the selenocyclofunctionalization, as well as the easy removal of selenium from organic substrates, this reaction is presently the method of choice to perform cyclofunctionalizations⁴. Although similar cyclizations using thallium (III) salts are long known⁵ they have not attracted the same attention.

Recently we have reported the utility of thallium triacetate in the synthesis of tetrahydrofuran derivatives of mono and diterpenes⁶. In this work we undertook a comparative study of the reactivity of selenium and thallium (III) electrophiles toward unsaturated substrates. As model compounds we choose the triterpenes vellozone 1⁷ and dammarenediol 2⁸. These compounds are

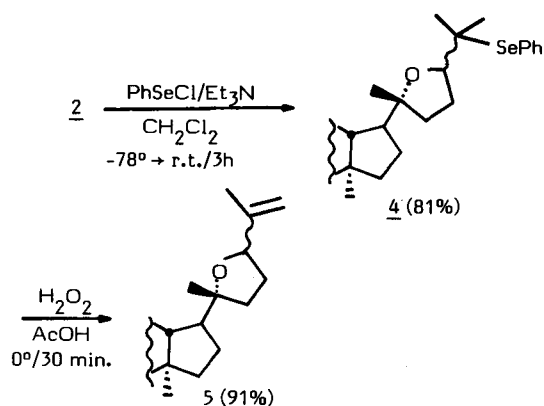
excellent models for a cyclofunctionalization study, since they exhibit double bonds with different substitution patterns. In addition, the position of the hydroxyl group toward the double bond allows the formation of both 5 and 6 membered ring cyclic ethers.



Reaction of 1 with phenylselenenyl chloride, in the presence of triethylamine, gave as only product the tetrahydrofuran derivative 3 in 82% yield, as an 1:1 mixture of epimers at C-24.

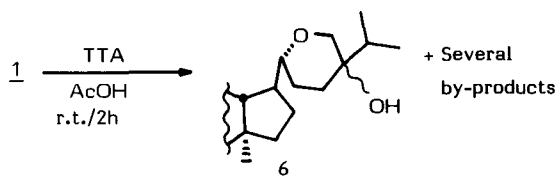


In the same way the triterpene 2 gave the cyclic ether 4 in 81% yield, which upon treatment with hydrogen peroxide led to an 1:1 epimeric mixture of 5 in 91% yield.



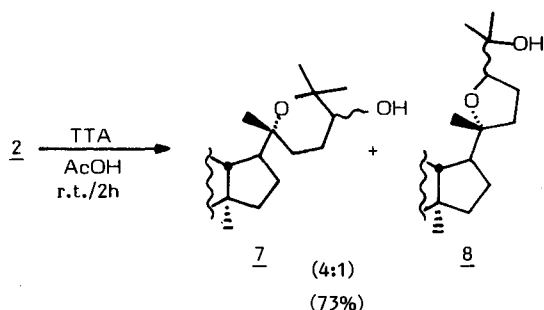
It must be pointed out that in both cases the exclusive formation of the 5 membered ring ether was observed irrespective of the substitution pattern of the double bond. Similar results involving selenium electrophiles have been described⁹.

On the other hand, reaction of **1** with thallium triacetate (TTA) in aqueous acetic acid led to a complex mixture of products, from which it was possible to isolate only the compound **6** by preparative thin layer chromatography.



This result is in accordance with the one obtained by Bartlett et al.¹⁰ in a model study.

Finally, treatment of **2** with TTA, in the same conditions described above, resulted in the preferential formation of the tetrahydropyran derivative **7**, besides a minor amount of the tetrahydrofuran derivative **8** (4:1 by ^1H NMR; 73% total yield).



In conclusion, the phenylselenoclofunctionalization is a good method to construct the tetrahydrofuran ring present in many natural products¹¹. In the particular case of compounds like **2**, the reaction allows the introduction of the isopropenyl moiety into the tetrahydrofuran ring, by selenoxide syn elimination. The cyclization of **2** with thallium triacetate, although less efficient, provides an alternative method to prepare the tetrahydrofuran ring, which is also present in some natural triterpenes.

Experiments designed to investigate further the generality of these reactions are planned.

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REFERENCES

1. D.L.J. Clive et al., *J.Chem.Soc.Chem. Comm.*, 725 (1977).
2. M. de Moura Campos and N. Petragnani, *Chem.Ber.*, **93**, 317 (1960).
3. A. McKillop and E.C. Taylor, in "Comprehensive Organometallic Chemistry", Pergamon Press, vol.7, p. 490 (1982).
4. K.C. Nicolaou, *Tetrahedron* **37**, 4097 (1981).
5. For a review, see: H.M.C. Ferraz, "Aplicações de sais de tálho (III) em síntese orgânica", *Química Nova*, in press.
6. H.M.C. Ferraz, T.J. Brocksom, A.C. Pinto, M.A. Abia and D.H. T. Zocher, *Tetrahedron Lett.* **27**, 811 (1986).
7. A.C. Pinto et al., *Phytochemistry* **19**, 2486 (1980).
8. P.M. Baker, E.J.L. Barreiro and B. Gilbert, *Phytochemistry* **15**, 785 (1976).
9. K.C. Nicolaou and N.A. Petasis, "Selenium in Natural Products Synthesis", Cis, INC., Philadelphia, 208 (1984).
10. J.P. Michael, P.C. Ting and P.A. Bartlett, *J.Org.Chem.* **50**, 2416 (1985).
11. O. Tanaka and S. Yahara, *Phytochemistry* **17**, 1353 (1978).