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Ring Enlargement of 2-oxo-1,3-dithiane : Easy Access to 4-substituted-7,8-dihydro-*2H,6H*-1,5-dithiocin-2-one.

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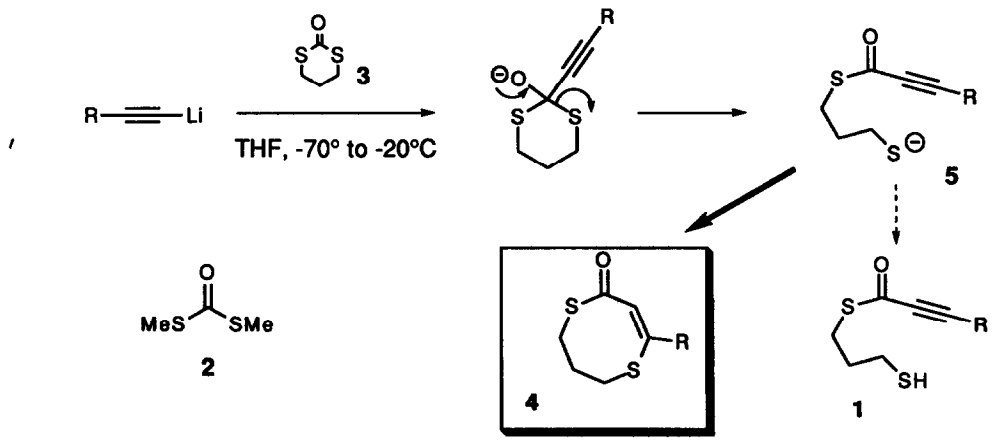
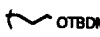
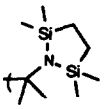
Abstract: : the 2-Oxo-1,3-dithiane reacts with various lithium acetylides to furnish a new class of compounds: the 4-substituted-7,8-dihydro-2H,6H-1,5-dithiocin-2-one derivatives.

Previous results from our group have shown that certain α,α'-difunctionalized acetylenic compounds are inhibitors of enzymes such as aldehyde dehydrogenase and their addition to normal and transformed cells in culture provokes the selective inhibition of the growth of transformed cells [1]. In view of these results we undertook the synthesis of α-acetylenic thiocarboxylic-*S*-esters compounds **1**.

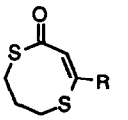
Thiocarboxylic *S*-esters being prepared by reaction of carbon nucleophiles (i.e. ketone enolates) with dimethyl dithiocarbonate **2** [2] we examined the possibility of reaching compounds **1** by the reaction of the cyclic dithiocarbonate 2-oxo-1,3 dithiane **3** [3a] with various lithium acetylides.



None of our attempts led to any trace of acetylenic thioester **1**. In all cases (table) the only isolated product was the hitherto unknown compound **4** [4] coming evidently from the Michaël addition of the thiolate functionality of **5** onto the activated triple bond.

	R	4 (isolated yields*)
a	nBu	73%
b	tBu	61%
c	Ph	41%
d		41%
e		45%
f		42%

Table



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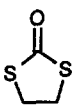
* all products were purified by chromatography on silica gel except 4f on GIII neutral alumina

typical procedure: To a THF solution of hex-1-ynyl-lithium prepared from 2.42 mmol of hex-1-yne and 2.42 mmol of nBuLi(2.6M solution in hexanes) in 6ml of THF was added dropwise at -70°C a solution of 270mg (2.01mmol) of 2-oxo-1,3-dithiane **2** in 4ml of THF. The reaction mixture was reached to -20°C within 2 hours and hydrolyzed by a saturated aqueous NH_4Cl solution. After usual work up, the crude product was purified by chromatography on silica gel (petroleum ether / ethyl acetate = 98/2) to give 315mg (73%) of **4a** [4].

Further attempts at synthesising homologs of **4** starting from 2-oxo-1,3-dithiolane **6** [3b] or γ-thiobutyrolactone **7** failed: when using the lithium acetylide of hex-1-yne under the same conditions or even at room temperature, no reaction occured.



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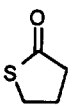

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In conclusion, this work provides an easy access to 4-substituted-7,8 dihydro-*2H,6H*-1,5-dithiocin-2-ones **4**, a new class of heterocyclic compounds [5].

References and notes :

1 a. Ogier, G.; Chantepie, J.; Quash, G.; Doutheau, A.; Goré, J. and Marion C., *Biochem.Pharmacol.*, **1989**, *38*, 1335-1343.
b. Bernard, D. ; Doutheau, A. ; Goré, J. ; Moulinoux, J. ; Quemener, V. ; Chantepie, J. and Quash, G., *Tetrahedron* , **1989**, *45*, 1429-1439.
c. Quemener, V.; Quash, G.; Moulinoux, J.P.; Penpalp, P.; Havouis, R.; Ripoll, H.; Doutheau, A. and Goré, J., *In Vivo* , **1989**, 325-330.

2 Demuynck, C. and Thuillier, A., *Bull.Soc.Chim.Fr.*, **1969** , 2434-2438.

3 a. Satsumabayashi, S. *Synthesis* , **1979** , 184-185.
b. Satsumabayashi, S.; Takahashi, H.; Tanaka, T. and Motoki, S., *J. Org. Chem.*, **1973**, *38*, 3953-3954.

4 **4a** analytical data : IR(neat) : 1620. RMN ^1H ($CDCl_3$, 200MHz) : 0.92 (3H, t, J=7.2, -CH_3), 1.20 to 1.50 (2H, m, -CH_2CH_3), 1.50 to 1.70 (2H, m, -$CH_2CH_2CH_3$), 2.10 to 2.30 (4H, m, vinylic -CH_2- and cyclic -$CH_2CH_2CH_2$-), 3.24 (2H, m, -CH_2-S-), 2.47 (2H, m, -CH_2-S-), 5.90 (1H, s, =CH-). RMN ^{13}C ($CDCl_3$, 50MHz): 13.8(-CH_3), 22.1(-CH_2CH_3), 28.1(-CH_2CH_2S), 30.3(-CH_2S-), 32.2($CH_2CH_2CH_3$), 33.1(-CH_2S-), 40.5(=C(S-)-CH_2-), 119.6(-CH=), 151.3(=C(S-)-), 197.2(C=0). MS: 216($M^{+\cdot}$, 39), 188(15), 114(100), 106(38), 100(72), 85(19), 67(35), 45(38), 41(62). ANAL. : calc. for $C_{10}H_{16}OS_2$: %C 55.30, %H 7.47, %O 7.69, found : %C 55.51, %H 7.45, %O 7.40.

5 for the preparation of vicinal compounds see : Anschütz, R. and Rhodius, E., *Ber. Dtsch. Chem. Ges.*,**1914** , 2733-2735 ; Guise, B.; Ollis, W.D. ; Peacock, J.A.; Stephanidou Stephanatou, J. and Fraser, J. *J. Chem. Soc. Perkin Trans. 1*, **1982** , 1637-1648 ; Steiner,G. *Liebigs Ann. Chem.*,**1978** , 643-657 ; Castells, J., Troin, Y.; Diez, A.; Rubiralta, M.; Grierson, D.S. and Husson, H.P., *Tetrahedron* ,**1991** , *47* , 7911-7924.

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