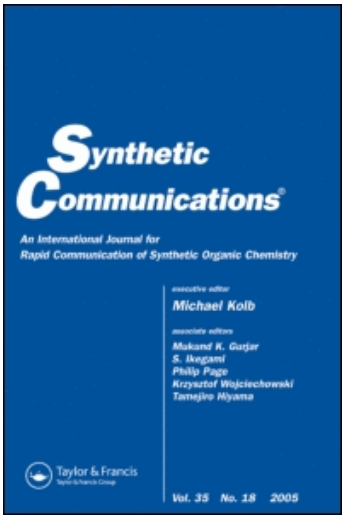

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Reaction of β-Oxodithioesters With Propargylamine: A Facile Entry to Novel 2-(Acylalkylidene)-5-(Methylene)Thiazolidines

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REACTION OF ß-OXODITHIOESTERS WITH PROPARGYLAMINE: A FACILE ENTRY TO NOVEL 2-(ACYLALKYLIDENE)-5-(METHYLENE)THIAZOLIDINES

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Abstract: Reaction of ß-oxodithioesters derived from acyclic and cyclic ketones with propargylamine affords novel 2-(acylalkylidene)-5-(methylene)-thiazolidines in high yields by intramolecular nucleophilic attack of thiocarbonyl sulfur on the triple bond of the ß-oxo-N-propargylthioamide intermediates.

During the course of our studies on acetylenic hetero-Claisen rearrangements[1,2] we wished to synthesize S,N-propargyl acetals **4** for investigating aza-Claisen rearrangement of these intermediates. However,

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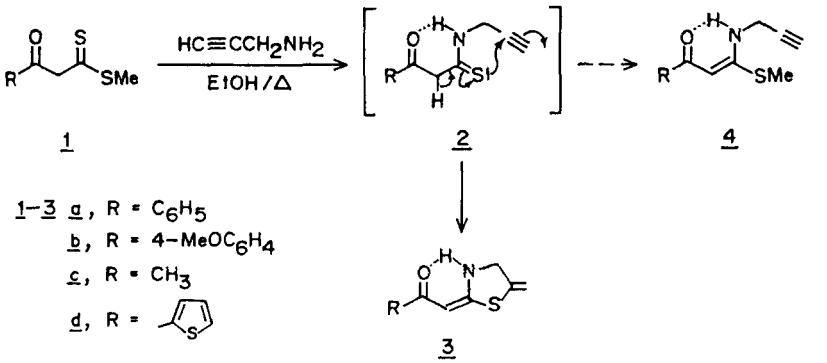
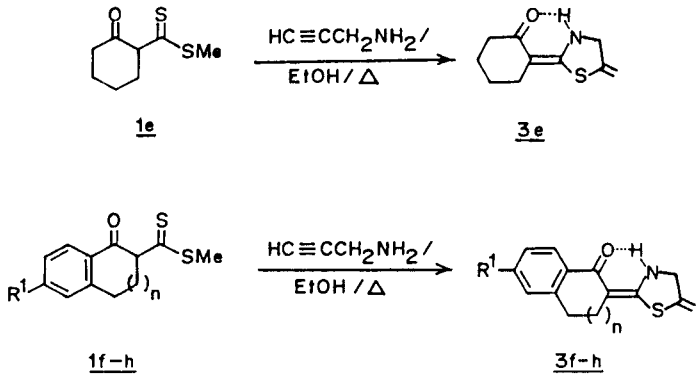


Scheme - 1

direct displacement on α-oxoketene dithioacetals by propargylamine under varying conditions yielded only complex product mixture. We therefore proposed to synthesize these intermediates by S-methylation of ß-oxothioamide intermediates **2** (Scheme-1). However when propargylamine was heated with ß-oxodithioesters[3] **1** in ethanol, the products isolated in high yields were not the desired thioamides **2**, but were found to be novel 2-(acylalkylidene)-5-(methylene)-thiazolidines **3** evidently formed by intramolecular nucleophilic attack of sulfur on the triple bond of the intermediate ß-oxo-N-propargyl thioamides. We report the synthesis of these novel thiazolidines in this communication.

In a typical experiment, when the dithioester **1a** was refluxed with propargylamine in ethanol, work up of the reaction mixture yielded a light yellow solid which was characterized as 2-(benzoylmethylene)-5-(methylene)-thiazolidine **3a** on the basis of its spectral and analytical data. The intramolecular hydrogen bonding in **3a** was confirmed by the presence of low field NH signal at δ 10.60. Similarly the other substituted 2-(acylmethylene) thiazolidines **3b-d** were obtained in overall high yields under identical



1, 3f , n = 1 ; R^1 = H
g , n = 1 ; R^1 = MeO
h , n = 2 ; R^1 = H

Scheme - 2

conditions (Scheme-1). The reaction was found to be general with dithioesters **1e-h** derived from cyclic ketones which afforded the novel 2-(2-oxocycloalkylidene)-5-(methylene)thiazolidines **3e-h** in 83-93% overall yields (Scheme-2). The spectral and analytical data of **3e-h** were in confirmity with the assigned intramolecular hydrogen bonded structures.

The reaction of ß-oxodithioesters with propargylamine thus provides a facile entry to novel hitherto unreported 5-(methylene)-N-unsubstituted-2-(acylaklylidene)-thiazolidines in high yields. Although a variety of substituted thiazolidines are known in the literature which are synthesized by diverse routes,[4,5] to our knowledge, the corresponding 5-unsubstituted methylene thiazolidines have not been explored and require further investigation.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The IR spectra were recorded on a

Perkin-Elmer-297 spectrophotometer while ^1H NMR spectra were obtained on a Varian EM 390 (90 MHz) spectrometer and the chemical shifts are reported in δ (ppm) relative to TMS. ^{13}C NMR spectra were recorded on Brucker WM-400 spectrometer. Mass spectra were obtained on Jeol D-300 instrument. Microanalyses were performed on Heraeus C,H,N-O-Rapid analyzer. The required ß-oxodithioesters were prepared according to our earlier reported procedure.[3]

General Procedure for the Synthesis of 2-(Acylalkylidene)-5-(methylene)-thiazolidines (3a-h).

A solution of ß-oxodithioester (0.01 mol) and propargylamine (0.0125 mol) in ethanol was refluxed for 1-1.5 hr (monitored by tlc). Ethanol was removed on water bath and the concentrated reaction mixture after cooling was poured into cold water, extracted with chloroform (2x50 ml), washed with water (2x75 ml), dried (Na_2SO_4) and evaporated to afford crude thiazolidines which were crystallized from chloroform/hexane to afford pure samples.

2-(Benzoylmethylene)-5-(methylene)thiazolidine (3a):

Pale yellow crystals; mp 133-134°C ($CHCl_3$-hexane); yield 92%; IR (KBr): 3225, 1625, 1598 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.70 (brs, 2H, NCH_2), 5.14-5.59 (m, 2H, $=CH_2$), 6.00 (s, 1H, =CH), 7.27-7.73(m, 3H, ArH), 7.83-8.30(m, 2H, ArH), 10.60 (brs, 1H, NH, exchangable with D_2O); MS: m/z 217 (M^+, 58%), 140 (19%), 112 (4%); Anal. Calcd. for $C_{12}H_{11}NOS$ (217.29): C, 66.33; H, 5.10; N, 6.45%. Found: C, 66.08; H, 4.90; N, 6.12%.

2-(4-Methoxybenzoylmethylene)-5-(methylene)thiazolidine (3b):

Pale yellow crystals; mp 141-142°C ($CHCl_3$-hexane); yield 94%; IR (KBr): 3227, 1617, 1522 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.84 (s, 3H, OCH_3), 4.63 (brs, 2H, NCH_2), 5.15-5.50 (m, 2H, $=CH_2$), 5.92 (s, 1H, =CH), 6.98 (d, J=9 Hz, 2H, ArH), 7.92 (d, J=9 Hz, 2H, ArH), 10.42 (brs, 1H, NH, exchangable with D_2O); MS: m/z 247 (M^+, 19%); Anal. Calcd. for $C_{13}H_{13}NO_2S$ (247.23): C, 63.16; H, 5.26; N, 5.67%. Found: C, 63.53; H, 5.52; N, 5.36%.

2-(Acetylmethylene)-2-(methylene)thiazolidine (3c):

Pale yellow crystals; mp 110-111°C ($CHCl_3$-hexane); Yield 86%; IR (KBr): 3154, 1602, 1522, 1451, 1320 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.81 (s,3H, CH_3); 4.71 (brs, 2H, NCH_2), 5.12-5.31(m, 2H, $=CH_2$), 5.43 (s, 1H, =CH), 10.32 (brs, 1H, NH, exchangable with D_2O); Anal. Calcd. for C_7H_9NOS (155.22): C, 54.17; H, 5.84; N, 9.02%. Found: C, 53.86; H, 5.56; N, 9.26%.

5(Methylene)-2-(2-thienoylmethylene)thiazolidine (3d):

Pale yellow crystals; mp 138-139°C ($CHCl_3$-hexane); yield 89%; IR (KBr): 3275, 1610, 1495, 1245 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.58 (brs, 2H, NCH_2), 5.15-5.37 (m, 2H, $=CH_2$), 5.75 (s, 1H, =CH), 7.03 (t, 1H, J=7 Hz, H-4), 7.39-7.52 (m, 2H, H-3 & H-5), 10.28 (brs, 1H, NH, exchangable with D_2O); ^{13}C NMR ($CDCl_3$): δ 55.0, 86.5, 105.9, 127.8, 130.0, 138.0, 146.0, 167.2, 179.2; Anal. Calcd. for $C_{10}H_9NOS_2$ (223.32): C, 53.78; H, 4.06; N, 6.27%. Found: C, 53.47; H, 4.33; N, 6.03%.

5-(Methylene)-2-(2-oxocyclohexylidene)thiazolidine (3e):

Pale yellow crystals; mp 105-106°C ($CHCl_3$-hexane); yield 83%; IR (KBr): 3155, 1600, 1523, 1453, 1321 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.55-2.05 [m, 4H, $(CH_2)_2$], 2.11-2.68 [m, 4H, $(CH_2)_2$], 4.72 (brs, 2H, NCH_2), 5.21-5.52 (m, 2H, $=CH_2$), 11.22 (brs, 1H, NH, exchangable with D_2O); MS: m/z 195 (M^+, 78%); Anal. Calcd. for $C_{10}H_{13}NOS$ (195.20): C, 61.53; H, 6.67; N, 7.18%. Found: C, 61.20; H, 6.52; N, 7.42%.

5-(Methylene)-2-(1-oxo-1,2,3,4-tetrahydronaphth-2-ylidene)thiazolidine(3f):

Pale yellow crystals; mp 112-113°C ($CHCl_3$-hexane); yield 91%; IR (KBr): 3225, 1608, 1521, 1482, 1445 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.48 (t, 2H, J=7 Hz, CH_2), 2.85 (t, 2H, J=7 Hz, CH_2), 4.67 (brs, 2H, NCH_2), 5.19-5.26 (m, 2H, $=CH_2$), 7.07-7.40(m, 3H, ArH), 7.90-8.00(m, 1H, ArH), 10.90 (brs, 1H, NH, exchangable with D_2O); ^{13}C NMR (Acetone-d_6): δ 27.0, 29.0, 56.0, 97.5, 105.8, 126.0, 126.3, 127.2, 131.0, 134.5, 138.9, 140.9, 166.7, 181.6; Anal. Calcd. for $C_{14}H_{13}NOS$ (243.24): C, 69.13; H, 5.35; N, 5.76%. Found: C, 68.83; H, 5.13; N, 6.02%.

5-(Methylene)-2-(6-methoxy-1-oxo-1,2,3,4-tetrahydronaphth-2-ylidene)-thiazolidine (3g):

Pale yellow crystals; mp 116-117°C ($CHCl_3$-hexane); yield 93%, IR (KBr): 3152, 1602, 1519, 1413, 1260 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.15 (t, 2H, J=7 Hz, CH_2), 2.50 (t, 2H, J=7 Hz, CH_2), 3.46 (s, 3H, OCH_3), 4.33 (brs, 2H, NCH_2), 4.71-5.09(m, 2H, $=CH_2$), 6.14-6.69(m, 2H, ArH), 7.61 (d, J=7 Hz, 1H, ArH), 10.91 (brs, 1H, NH, exchangable with D_2O); Anal. Calcd. for $C_{15}H_{15}NO_2S$ (273.35): C, 65.91; H, 5.53; N, 5.12%. Found: C, 66.25; H, 5.23; N, 4.88%

5-(Methylene)-2-(1-oxobenzocyclohept-2-ylidene)thiazolidine (3h):

Pale yellow crystals; mp 121-122°C ($CHCl_3$-hexane); yield 89%; IR (KBr): 3185, 1600, 1538, 1460, 1420 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.68 (m, 2H, CH_2), 2.63 [t, 4H, J=7 Hz, $(CH_2)_2$], 4.58 (brs, 2H, NCH_2), 5.08-5.31(m, 2H, $=CH_2$), 7.00-7.40 (m, 3H, ArH), 7.47-7.68 (m, 1H,ArH), 10.85 (brs, 1H, NH, exchangable with D_2O); MS: m/z 257 (M^+, 100%); Anal. Calcd. for $C_{15}H_{15}NOS$ (257.36): C, 70.01; H, 5.87; N, 5.44%. Found: C, 70.20; H, 6.02; N, 5.53%.

REFERENCES

1. Bhat, L.N.; Ila, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1749.
2. Gupta, A.K.; Reddy, K.R.; Ila, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1725.
3. Singh, G.; Bhattacharjee, S.S.;Ila, H.; Junjappa, H. *Synthesis* **1982**, 693.
4. Metzger, J.V. in *Comprehensive Heterocyclic Chemistry*, Katritzky, A.R.; Rees, C.W.;Potts, K.T. (Eds.), Vol. 6; Part 4B; Pergamon Press; 1984; p. 316-331.
5. (a) Foglia, T.A.; Gregory, L.M.; Maerker, G.; Osman, S.F. *J. Org. Chem.* **1971**, *36*, 1068; (b) Woodgate, P.D.;Lee, Ho H.; Rutledge, P.S.; Cambie, R.C. *Synthesis* **1977**, 322; (c) Yamamoto, T.; Itoh, M.; Saitoh, N.U.;Muraoka, M.; Takeshima, T. *J. Chem. Soc., Perkin Trans. 1* **1990**,

2459; (d) Bhattacharjee, S.S.; Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis* **1982**, 1062; (e) Eloy, F.; Deryckere, A. *Chim. Ther.* **1973**, *8*, 437; *Chem. Abstr.* **1974**, *81*, 13439x.

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