J.Sci.Soc.Thailand, 23 (1997) 51-55

SHORT REPORTS

HOMO-ALLYLIC REARRANGEMENT OF CYCLOPROPYLKETENE DITHIOACETAL UNDER THE MUKAIYAMA'S HYDROLYSIS CONDITIONS

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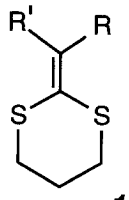
(Received January 8, 1997)

ABSTRACT

Under the Mukaiyama's conditions for hydrolysis of dithioacetal the cyclopropylketene dithioacetal **2** *gave, instead of the ketene* **3**, *the chlorocyclopropyl thioester* **5** *which underwent consecutive ring opening* via *homo-allylic rearrangement to finally give* **7**.

INTRODUCTION

Several convenient syntheses of ketene dithioacetals (*eg.* ***1***) have appeared in the literature,[1] nevertheless such species have not enjoyed popularity as the ketene precursor in organic synthesis. The inhibition to elaborate these intermediates is probably due to the difficulty in hydrolysis, because, although many methods of dithioacetal hydrolysis have been developed,[2] none can as yet be regarded as general for its use in the reaction of ketene dithioacetal counterpart. Meanwhile, the application of some of these methods have resulted in useful and/or mechanistically very interesting products,[3] a new example of which is presented in this communication.



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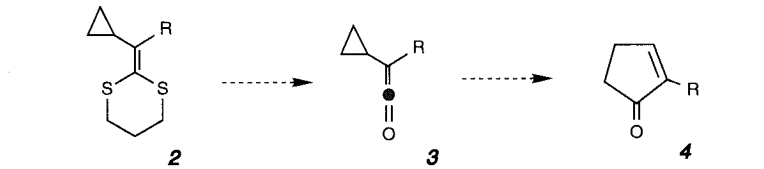
RESULTS AND DISCUSSION

It is well known that vinyl cyclopropane readily rearranges to cyclopentene on heating and the mechanism has thoroughly been studied,[4] hence we regarded the cyclopropylketene dithioacetal ***2*** as a good precusor for substituted cyclopentenone, e.g. ***4*** *via* the ketene intermediate ***3*** as shown below. However, when ***2a*** [5] was subjected to hydrolysis by the various known methods,[2] very complex mixtures resulted. A better situation was encountered

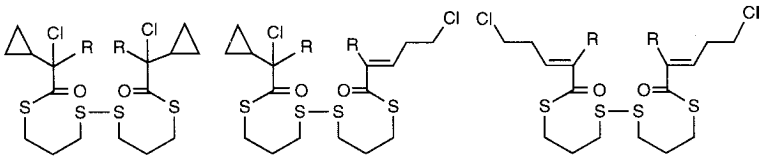
when ***2a*** was heated to reflux for 30 minutes in 2% aqueous acetone in the presence of $CuCl_2$ and CuO (2 and 4 molar equivalents respectively; Mukaiyama's method for the hydrolysis of dithioacetal)[6] when three products ***5a***, ***6a*** and ***7a*** were isolated, albeit in poor yields (6%, 6% and 4% respectively : PLC silica gel, 4% ethyl acetate in hexane as eluent). The spectroscopic data of these products agree well with the proposed structures and the *E*-configurations of the double bonds in ***6a*** and ***7a*** were determined by NOE experiments.[7]



2 ***3*** ***4***

a, R = Me

b, R = Ph

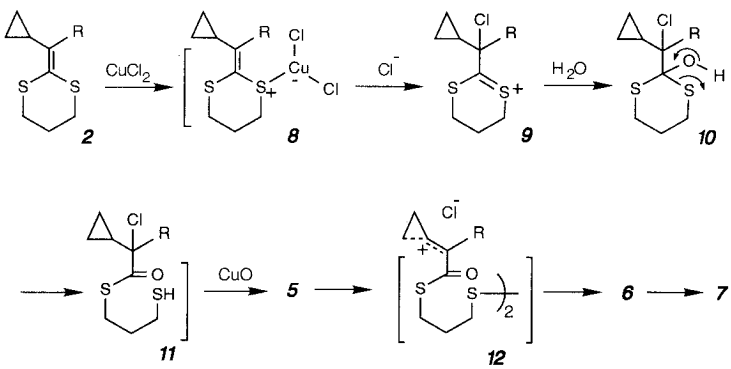


5 ***6*** ***7***

The stepwise cyclopropane ring opening sequence became apparent when the above reaction was monitored by TLC at 5 minutes intervals during which product ***5a*** was observed to be first formed, followed by ***6a***, then finally ***7a***. The starting material ***2a*** was then heated to refulx in aq.acetone-$CuCl_2$-CuO for 5 minutes to yield ***5a***, ***6a*** and ***7a*** in 54%, 6% and 2% respectively together with unchanged starting material 19%. When pure sample of ***5a*** was subjected to the same reaction conditions (refluxing time 15 minutes) ***6a*** (48%) and ***7a*** (19%) were obtained,[8] and, as expected, pure ***6a*** under these conditions gave the final product ***7a*** (62%).

On the other hand the transformation of ***2b*** to ***7b*** (48%) occurred so fast that it was not possible to detect the intermediates (*ie.* ***5b*** or ***6b***) after several attempts under various reaction conditions.

It is quite obvious from the products forms that under these hydrolysis conditions the ketene dithioacetal ***2*** does not give rise to the ketene ***3*** but undergoes reaction of a totally different mechanistic pathway which can be rationalised as follows :



2 ***8*** ***9*** ***10*** ***11*** ***12***

The cyclopropylketene dithioacetal ***2*** forms a complex with $CuCl_2$ which then undergoes inter- or intra-molecular attack by the chloride ion to give the salt ***9***, subsequent hydrolysis of which yields the chlorothiocarboxylate monomer ***11*** which, in the presence of CuO, dimerises to give ***5***. Consecutive cyclopropyl ring openings of ***5*** *via* a homoallylic rearrangement give rise to the unsaturated chloroketones ***6***, and finally ***7***.

The failure to trap the intermediates ***5b*** and ***6b*** can be explained in term of the relative ease in the formation of the homoallylic carbonium ion ***12***, the rate of formation of ***12b*** from ***5b*** (R = Ph) being much faster than that of ***12a*** from ***5a*** (R = Me).

In conclusion, the present work demonstrates yet another example of problems associated with the utilization of ketene dithioacetal as a ketene precursor in organic synthesis. While the hydrolysis of thioacetals have now become routine there is yet no general method for ketene dithioacetal hydrolysis, the existing methods are far from satisfactory due to the unpredictability of the reaction involved and hence the product outcome.[9]

EXPERIMENTAL

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Infrared spectra were recorded on Jasco model A-302 or Perkin Elmer 2000N FT Raman spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on Bruker AM 400 or Bruker 300-DPX instrument. Mass spectra were run on Finnigan MAT INCOS 50 or JMS-DX 300 Jeol mass spectrometer. Elemental analyses were carried out on Perkin Elmer Elemental Analyser 2400 CHN. Silica gel 60 PF_{254} (Merck) was used for preparative layer chromatography. Fluka's anhydrous cupric chloride and cupric oxide were used in the experiments.

HYDROLYSIS OF CYCLOPROPYL METHYLKETENE DITHIOACETAL (*2a*)

A mixture of ***2a*** (930 mg., 5 mmol), cupric chloride (1.34 g., 10 mmol), cupric oxide (1.59 g., 20 mmol) and 2% aqueous acetone (50 ml) was heated to reflux for 5 minutes under nitrogen atmosphere while stirring. The mixture was cooled, filtered and the filtrate evaporated to dryness. The crude mixture was purified by PLC (silica gel, using 4% ethyl acetate in hexane as eluent) to yield ***5a*** (640 mg), ***6a*** (71 mg) and ***7a*** (24 mg) in 54, 6 and 2% respectively.

HYDROLYSES OF *5a* AND *6a*

Hydrolysis of ***5a*** (300 mg., 0.63 mmol), performed according to the procedure described above (reaction time 30 minutes), provided ***6a*** (144 mg, 48 %) and ***7a*** (57 mg, 19%).

Similar reaction of ***6a*** (150 mg, 0.32 mmol) yielded ***7a*** (93 mg, 62%).

HYDROLYSIS OF *2b*

Under the same reaction conditions compound ***2b*** (600 mg, 2.4 mmol) gave ***7b*** (348 mg) in 48% yield.

Compound *5a*

Colourless oil: IR (neat) ; 1675 cm^{-1} : EIMS ; m/e 476(4%), 474(4%), 239(14%), 237(33%), 131(4%), 106(22%), 103(100%) : ^1H NMR ($CDCl_3$) ; δ 0.59-0.69(8H, m), 1.39(2H, quintet, J=6.5 Hz), 1.69(6H, s), 2.01(4H, quintet, J=7 Hz), 2.75(4H, t, J=7 Hz), 2.98(4H, t, J=7 Hz): ^{13}C NMR ($CDCl_3$, 75.46 MHz) ; δ 2.74, 2.80, 20.81, 26.94, 28.37, 28.49, 37.33, 53.44, 200.47.

Analysis; Calcd. for $C_{18}H_{28}Cl_2O_2S_4$: C, 45.48; H, 5.89. Found: C, 45.33; H, 5.70 %

Compound *6a*

Colourless oil: IR (neat) ; 1675, 1655 cm^{-1} : EIMS ; m/e 476(4%), 474(5%), 239(9%), 237(21%), 131(100%), 106(50%), 103(50%) : ^1H NMR ($CDCl_3$) ; δ 0.59-0.69(4H, m), 1.39(1H, quintet, J=6.4 Hz), 1.69(3H, s), 1.92(3H, s), 1.98(4H, quintet, J=6.9 Hz), 2.71(2H, t, J=6.9 Hz), 2.75(4H, J=6.9 Hz), 2.98(2H, t, J=6.9 Hz), 3.03(2H, t, J=6.9 Hz), 3.63(2H, t, J=6.9 Hz), 6.71(1H, dt, J=6.9 and 1.5 Hz) : ^{13}C NMR ($CDCl_3$) ; δ 2.74, 2.80, 12.63, 20.81, 26.94, 27.41, 28.37, 28.49, 28.89, 31.67, 37.36, 37.42, 42.52, 53.35, 135.29, 138.28, 193.03, 200.44. Analysis; Calcd. for $C_{18}H_{28}Cl_2O_2S_4$: C, 45.48; H, 5.89. Found: C, 45.52; H, 6.10 %

Compound *7a*

Colourless oil: IR (neat) ; 1655 cm^{-1} : EIMS ; m/e 477(1%), 475(2%), 440(0.5%), 239(4%), 237(10%), 131(100%), 106(25%), 103(11%) : ^1H NMR ($CDCl_3$) ; δ 1.91(6H, s), 2.01(4H, quintet, J=6.9 Hz), 2.71(4H, dt, J=6.9 and 7.2 Hz), 2.75(4H, t, J=6.9 Hz), 3.03(4H, t, J=6.9 Hz), 3.63(4H, t, J=6.9 Hz), 6.71(2H, t, J=7.2 Hz) : ^{13}C NMR ($CDCl_3$) ; δ 12.63, 27.47, 28.96, 31.73, 37.61, 42.49, 135.23, 138.37, 193.03. Analysis; Calcd. for $C_{18}H_{28}Cl_2O_2S_4$: C, 45.48; H, 5.89. Found: C, 45.72; H, 5.60 %

Compound *7b*

Colourless oil: IR (neat) ; 1660 cm^{-1} : EIMS ; m/e 600(0.5%), 598(1%), 302(3%), 300(7%), 195(23%), 193(74%), 165(36%), 157(98%), 129(100%), 128(20%) : ^1H NMR ($CDCl_3$); δ 2.01(4H, quintet, J=7.2 Hz), 2.71(4H, t, J=7.2 Hz), 2.88(4H, dt, J=6.9 and 6.6 Hz), 3.05(4H, t, J=7.2 Hz), 3.66(4H, t, J=6.6 Hz), 6.05(2H, t, J=6.9 Hz), 7.35(10H, s) : ^{13}C NMR ($CDCl_3$); δ 28.06, 28.81, 32.54, 37.45, 43.58, 127.76, 128.39, 131.90, 136.63, 143.26, 193.96. Analysis; Calcd. for $C_{28}H_{32}Cl_2O_2S_4$: C, 56.10; H, 5.34. Found: C, 55.99; H, 5.50 %

ACKNOWLEDGEMENT

Senior Fellowship Award to Y.T. from the National Science and Technology Development Agency (NSTDA) is gratefully acknowledged.

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2. For examples see : a) Noda, Y., Fukaya, T. and Kikuchi, M. (1996) ***Heterocycles*** **43**, 271 ; b) Stowell, M. H. B., Rock, R. S., Rees, D. C. and Chan, S. I. (1996) ***Tetrahedron Lett.*** **37**, 307 ; c) Bulman Page, P. C., McKenzie, M. J. and Buckle, D. R. (1995) ***J. Chem. Soc. Perkin Trans. 1***, 2673 ; d) Howson, W., Osborn, H. M. I. and Sweeney, J. (1995) ***J. Chem. Soc. Perkin Trans.*** **1**, 2439 ; e) Fletcher, M. T. and Kitching, W. (1995) ***Chem. Reviews*** **95**, 798 ; f) Kozikowski, A. P. and Chen, Y. Y. (1980) ***J. Org. Chem.*** **45**, 2236 ; g) Ogura, K., Furukawa, S. and Tsuchihashi, G. (1975) ***Bull. Chem. Soc. Jpn.*** **48**, 2219 ; h) Seebach, D. and Burstinghaus, R. (1975) ***Synthesis***, 461; i) Russell, G. A. and Ochrymowycz, L. A. (1970) ***J. Org. Chem.*** **35**, 764.

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5. Prepared in one-pot by the method described in Ref. 1a.
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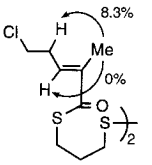
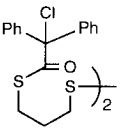
7. Irradiation of the methyl singlet (at δ 1.91) of compound ***7a*** causes an enhancement (8.3%) of the allylic proton but has no effect on the vinylic proton (δ 6.71).



7a

8. It was found that the refluxing time of 15 minutes provided the best yield of ***6a***.
9. That the mode of reaction is not unique to the cyclopropylketene dithioacetals was indicated by a separate result from the hydrolysis of ketene dithioacetal ***1*** (where R = R' = Ph) under the same reaction conditions described in the text. The reaction gave a complex mixture from which two products, tentatively assigned as ***13*** and ***14***, were isolated in poor yields (1.9 and 1.5% yields respectively). However, due to the complexity of the reaction, no serious effort was made neither to properly characterize compounds ***13*** and ***14*** nor to study the reaction in details.



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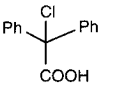

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