Tetrahedron Letters,Vol.23,No.37,pp 3747-3750,1982 0040-4039/82/373747-04$03.00/0
Printed in Great Britain 

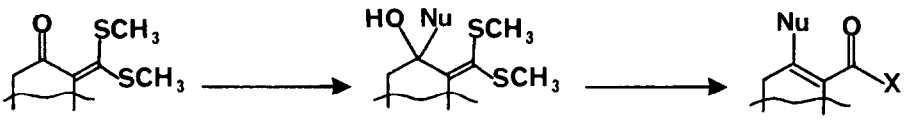
# α-OXOKETENE DITHIOACETALS: VERSATILE SUBSTRATES FOR 1,3-CARBONYL TRANSPOSITIONS

R. Karl Dieter* and Yawares Jenkitkasemwong

Department of Chemistry, Boston University, Boston MA 02215

Abstract: A two step procedure for the conversion of α-oxoketene dithioacetals to β-substituted α,β-unsaturated thioesters or acids is described. The overall transformation represents a 1,3-carbonyl transposition in which the original ketone carbonyl emerges as the carbonyl of an acid or thioester. The resulting thioesters and acids constitute versatile acylating reagents in accord with established procedures.

The ability to transpose a carbonyl functional group constitutes a powerful synthetic strategy for functional group manipulations and regioselective carbon-carbon bond construction. 1,3-Enone transpositions have found wide synthetic utility and several procedures have been developed.[1-3] Recently, we described a simple one pot procedure for the synthesis of conjugated ketene dithioacetals involving the addition of kinetically generated carbon nucleophiles to carbon disulfide.[4] α-Oxoketene dithioacetals, readily prepared by this procedure, were viewed as potential substrates for 1,3-carbonyl transpositions.

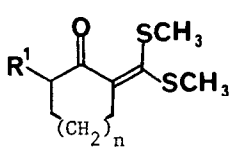



(eq. 1)

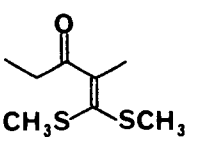
1

2a X = $SCH_3$
2b X = OH

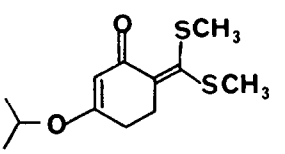
The method required nucleophilic addition to the carbonyl and subsequent hydrolysis of an intermediate α-hydroxyketene dithioacetal (1) (eq. 1). Careful choice of hydrolysis conditions could lead to either a β-substituted α,β-unsaturated thioester (2a) or acid (2b). The transformation (eq. 1) converts a ketone carbonyl to the carbonyl of an acid or thioester and constitutes a versatile complement to vinylogous ester[2] and thioester[3] mediated 1,3-carbonyl transpositions. The α-hydroxyketene dithioacetals (1) proved highly sensitive to acid catalyzed hydrolysis in contrast to the structurally similar γ-hydroxy vinyl sulfides.[3]




3 ($R^1$=H; n=0)
4 ($R^1$=$CH_3$; n=0)
5 ($R^1$=H; n=1)

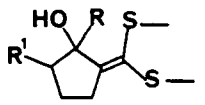
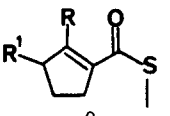
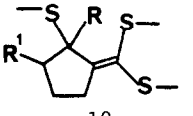
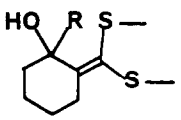
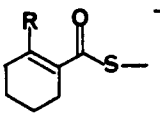
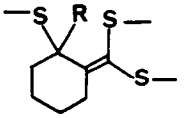
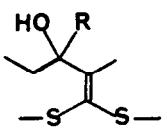
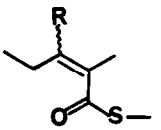
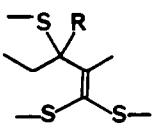
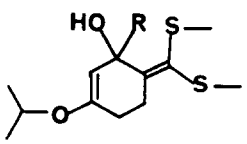
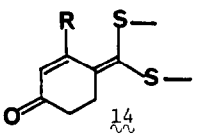



6




7

Table 2. Hydrolysis of α-Hydroxyketene Dithioacetals

| Entry | Substrate | Hydrolysis Conditions[a] | Product(s)[b] (%Yield)[c] | |
|---|---|---|---|---|
| |  | |  9 |  10 |
| 1 | 8a $R^1$=H; R=$CH_3$ | A | 78 | < 2 |
| 2 | b $R^1$=R=H | A | 50 | 47 |
| 3 | | B | 72 | — |
| 4 | c $R^1$=H; R= $CH_2$=CH | A | 40 | — |
| 5 | d $R^1$=$CH_3$; R=H | A | 44 | 35 |
| 6 | | B | 50 | — |
| 7 | e $R^1$=R=$CH_3$ | A | 52 | 10 |
| |  | |  |  |
| 8 | 11a R=H | A | 58 | 24 |
| 9 | b R=$CH_3$ | A | 72 | < 2 |
| |  | |  |  |
| 10 | 12a R=H | B | 79 | — |
| 11 | b R=$CH_3$ | A | 68 | < 2 |
| |  | |  14 | |
| 12 | 13a R=$CH_3$ | | 87 | |
| 13 | b R=$CH_2CO_2C(CH_3)_3$ | | 75 | |

[a]Procedure A: 10% $HBF_4$, THF, rt. Procedure B: 10% $HBF_4$, THF, 0.50-0.75 equivalents HgO, rt. [b]All final products gave satisfactory C and H combustion analysis. The assigned structures were in accord with infrared, proton nmr, and carbon nmr spectral data. [c]All yields are based upon isolated products purified by column chromatography on silica gel.

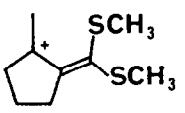
The feasibility of this carbonyl transposition procedure was examined with ketene dithioacetals 3 - 7 and methyllithium and sodium borohydride as two representative nucleophiles. The corresponding adduct allylic alcohols, listed in Table 1, were formed in good to excellent yield. The use of methyllithium generally resulted in recovery of some starting ketone indicating that enolization constituted a minor problem. No attempt was made to minimize the enolization process by judicious choice of solvent mixtures.[5]

Table 1. α-Hydroxyketene Dithioacetals

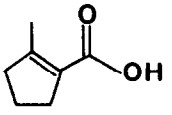
| substrate | Nucleophilic Reagent | Alcohol[a] | (% yield) | substrate | Nucleophilic Reagent | Alcohol[a] | (% yield) |
|---|---|---|---|---|---|---|---|
| 3 | $CH_3Li$ | 8a | 69[b] | 5 | $CH_3Li$ | 11b | 82[b] |
| 3 | $NaBH_4$ | 8b | 98[c] | 6 | $NaBH_4$ | 12a | 96[c] |
| 3 | $CH_2$=CHLi | 8c | 80[b] | 6 | $CH_3Li$ | 12b | 76[b] |
| 4 | $NaBH_4$ | 8d | 98[c] | 7 | $CH_3Li$ | 13a | —— |
| 4 | $CH_3Li$ | 8e | 80[b] | 7 | $LiCH_2CO_2C(CH_3)_3$ | 13b | —— |
| 5 | $NaBH_4$ | 11a | 96[c] | | | | |

[a]Assigned structures were in accord with infrared and 60 MHz proton nmr spectral data.
[b]Yields are based upon isolated products purified by column chromatography on silica gel.
[c]Yields are based upon crude products which were > 95% pure by nmr.

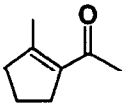
Initially, hydrolysis (10% $H_2SO_4$, THF, 0.5 equivalent HgO, rt.) of α-hydroxyketene dithioacetal 8a afforded low yields of thioester 9a (30%) and methylsulfide 10a (10%). The latter product presumably arises from methanethiol trapping of allylic carbenium ion 15.




15




16




17

Trials of a large number of Lewis and Brönsted acid/solvent couples with or without sulfur complexing agents [e.g. HgO, $Hg(OAc)_2$, CuO, $Cu(OAc)_2$] failed to improve the yield of thioester 9a. Eventually, it was discovered that 10% $HBF_4$ in THF offered good yields of thioester 9a (entry 1, Table 2). Hydrolysis of allylic alcohol 8b under the same conditions afforded a high yield of an equimolar mixture of thioester 9b (50%) and the undesired methyl sulfide 10b (47%) (entry 2), a result revealing the acute sensitivity of the allylic alcohols to substrate structure and hydrolysis conditions. Addition of 0.75 equiv. of HgO (entry 3) to the reaction medium afforded the desired thioester 9b in good yield (72%). These reaction conditions could be extended in a general manner to the allylic alcohols shown in Table 2. The acyclic allylic alcohols [12 (a-b)] (entries 10-11) afforded inseparable mixtures of E and Z diastereomers. Subsequently, it was discovered that treatment of allylic

alcohol 9a with 10% $HBF_4$/THF in the presence of 2.0 equiv. HgO afforded acid 16 in 70% yield. Consequently, the method provides a facile synthesis of either α,β-unsaturated thioesters or acids depending upon the hydrolysis conditions. This provides a versatile opportunity for additional carbon-carbon bond forming processes. Treatment of thioester 9a with lithium dimethylcuprate afforded methyl ketone 17 in 50% yield.[6] Alternatively 17 is potentially available by conversion of 16 to the acid chloride followed by treatment with methylmagnesium iodide in THF at -78 °C.[7] Further, allylic alcohols 13 (a-b) (entries 12-13) could not be isolated and were hydrolyzed to the dienones 14 (a-b) with saturated aqueous ammonium chloride. This result illustrates the superior resonance electron donating capacity of an oxygen vs. sulfur substituent. Finally, ketene dithioacetal 14b provides a potential entry to 3-alkyl substituted analogs of Hagemann's ester.[8]

In summary, a three step procedure for the conversion of ketones to the homologous β-substituted α,β-unsaturated thioesters or acids is available and involves an efficient 1,3-carbonyl transposition methodology. Development of conditions for the hydrolysis of α-hydroxyketene dithioacetals should stimulate further synthetic utilization of α-oxoketene dithioacetals. Investigations into additional synthetic applications of α-oxoketene dithioacetals are in progress in our laboratory.

Acknowledgements: We are pleased to acknowledge the partial support of this investigation by Research Corporation, the donors of the Petroleum Research Fund administered by the American Chemical Society and by Grant #IN-97E (Boston University School of Medicine) from the American Cancer Society.

References

1. (a) D. Liotta and G. Zima, J. Org. Chem., 45, 2551 (1980); and references cited therein. (b) W.G. Dauben and D.M. Michno, J. Org. Chem., 42, 682 (1977); and references cited therein. (c) P. Sundararaman and W. Herz, ibid, 42, 813 (1977). (d) J.H. Babler and M.J. Coghlan, Synth. Commun., 6, 469 (1976).

2. G. Stork and R.L. Danheiser, J. Org. Chem., 38, 1775 (1973); M.L. Quesada and R.H. Schlessinger, Synth. Commun., 6, 555 (1976); E.J. Corey and D.L. Boger, Tetrahedron Lett., 4597 (1978).

3. S. Akiyama, S. Nakatsuji, and T. Hamamura, M. Kataoka, and M Nakagawa, Tetrahedron Lett., 2809 (1979); P.R. Bernstein, ibid, 1015 (1979); R.E. Ireland and J.A. Marshall, J. Org. Chem., 27, 1620 (1962).

4. R.K. Dieter, J. Org. Chem., 46, 5031 (1981).

5. D. Caine in "Carbon-Carbon Bond Formation", R.L. Augustine, Ed., Marcel Dekker, Inc., NY., 1979, Vol. 1, Chapter 2.

6. R.J. Anderson, C.A. Henrick, L.D. Rosenblum, J. Am. Chem. Soc., 96, 3654 (1974).

7. M.K. Eberle and G.G. Kahle, Tetrahedron Lett., 2303 (1980).

8. A.L. Begbie and B.T. Golding, J.C.S. Perkin Trans. I, 602 (1972).

(Received in USA 13 May 1982)