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THIOUREA, A CONVENIENT REAGENT FOR THE REDUCTIVE CLEAVAGE OF OLEFIN OZONOLYSIS PRODUCTS+

DEEPA GUPTA, RAGHAVAN SOMAN and SUKH DEV*

Malti-Chem Research Centre, Nandesari, Vadodara, India

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Abstract — A convenient procedure for the preparation of aldehydes, in good to excellent yields, from suitable olefins by ozonolysis in methanol, followed by exposure of the resulting products to thiourea, is described.

An important route[1] to aldehydes involves ozonolysis of suitable olefins, and several reagents[1,2] have been employed to effect the reductive cleavage of the ozonide/hydroperoxidic products. The wide spectrum of reducing agents employed include: hydrogen (and catalyst),[3] Zn-AcOH,[4] KI-AcOH,[5] sulphites and bisulphites,[6] phosphites,[7] phosphines[8] and organic sulphides.[9] By far, the most convenient and efficient laboratory procedure, presently available, involves ozonolysis of the olefin in methanol, followed by reduction of the methoxyhydroperoxide[10] with dimethyl sulphide.[9,11] However, dimethyl sulphide is highly volatile (b.p. 37°) and has an obnoxious odour. We now report a new procedure for the reduction of hydroperoxidic products of olefin ozonolysis giving aldehydes in yields comparable to those obtainable by dimethyl sulphide, but by employing thiourea, an odourless and convenient reagent.

Thiourea (1) is quite susceptible to peroxidic reagents. Thus, hydrogen peroxide,[12] peroxy acids[12] readily oxidise it, in good yield, to thiourea S-dioxide (2). Reduction of a cyclic peroxide to the corresponding diol, by thiourea, has also been reported.[13] We now find that hydroperoxides are readily reduced by thiourea.[14] Since, ozonolysis[10] of olefins in methanol generates essentially α-methoxyhydroperoxides or related peroxidic products

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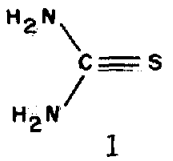
(depending on the olefin structure), thiourea appeared to be a suitable reagent for their reduction to carbonyl end products. Work to be described now, fully borne out our expectations. Since, reductive cleavage is essentially used for the preparation of aldehydes, we have chosen our olefin substrates (Table 1) accordingly.



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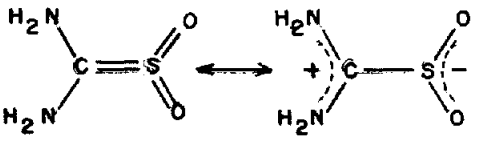

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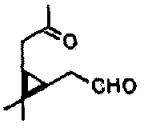
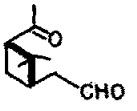
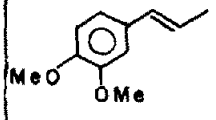
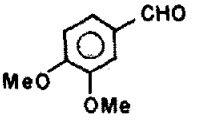
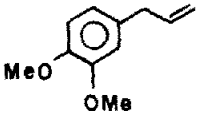
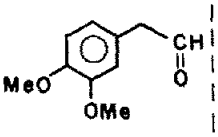
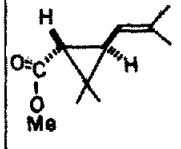
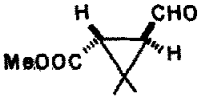
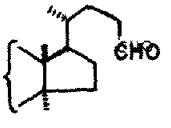
Ozonolysis of the olefin in methanol soln is carried out with ozonized oxygen at -10° to -15° in the usual manner, and the peroxidic soln, thus obtained, is added to a soln of 0.5 mole equivalent of thiourea in methanol at ~0°. Reduction by thiourea is fairly rapid and thiourea S-dioxide starts separating in about 15 min. Suitable work-up affords the desired aldehyde and/or its dimethyl acetal depending on propensity towards acetalization[15] (vide infra). Table 1 summarises the results obtained with a variety of olefins: olefins under entries 1, 3, and 7 have been earlier converted to the corresponding aldehydes by the ozonolysis-dimethyl sulphide sequence, and the yields reported[9] are similar to those obtained by the present procedure.

DISCUSSION

Reduction of α-alkoxyhydroperoxides (e.g. 3) by organic sulphides, such as dimethyl sulphide, has been depicted[16] as shown in Scheme 1. However, this cannot be the sole pathway as more often than not the product of this reaction is an acetal rather than the free aldehyde,[17] and under the reaction conditions such aldehydes do not undergo acetalization (see Experimental). Scheme 2 gives another, mechanistically reasonable, mode for such reductions of α-alkoxyhydroperoxide, which involves solvent-assisted proton transfer.[19] This pathway would generate an hemiacetal (4), which should go over to the acetal, as for the acetalization reaction, the equilibrium is controlled by the nucleophilic addition of the alcohol to the carbonyl function and not by the conversion of the hemiacetal to the acetal.[15,20] It is suggested that preponderance or even exclusion of one pathway over other is dictated by the structure of the expected aldehyde: unhindered saturated aldehydes,[11a] would appear (essentially) as acetals, by way of Scheme 2, while αβ-unsaturated[11b] or aromatic aldehydes may be

Table 1. Ozonolysis of olefins[a]

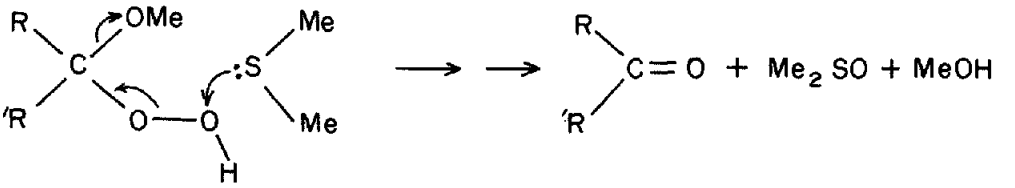
No	Olefin	Product[b] (Aldehyde)	Aldehyde: acetal	^{1}H-NMR {δ,m(J)}[c] HC=O	HC(OMe)$_2$	Yield[d] %
1	n-Oct-1-ene	n-Heptanal	5 : 95	9.69,t(1.5)	4.25,t(5.0)	73
2	10-Undecenoic acid	10-Oxodecanoic acid[21]	24 : 76	9.68,t(1.5)	4.26,t(5.0)	81
3	Cyclohexene[a]	Hexanedial	22 : 78	9.70, s	4.27,t(5.0)	57
4	p-Menth-3-ene	3,7-Dimethyl-6-oxo-octanal[22]	11 : 89	9.71,t(1.5)	4.36,t(5.5)	83
5			11 : 89	9.70,t(1.5)	4.22,t(5.0)	77
6			6 : 94	9.76,t(1.5)	4.19,t(5.5)	75
7	Styrene	Benzaldehyde	67 : 33	9.94, s	3.85, s	81
8			100 : 0	9.73, s	-	88
9			16 : 84	9.58,t(2.0)	4.38,t(6.0)	71
10			42 : 58	9.64,d(3.0)	4.15,d(6.0)	81
11	Cycloartenyl acetate		33 : 67	9.71,t(1.5)	4.23,t(5.0)	90

a) All ozonisations were carried out at -10 to -15°C except for cyclohexene (column 3) in which case ozonisation was done at -70°C

b) Only aldehyde name/structure is given. The actual ratio of aldehyde/acetal produced is indicated in the adjoining column, and is based on ^{1}H-NMR spectral analysis of the product. All aldehydes described herein are known and appropriate reference is given in the column.

c) Multiplicity (m) is indicated by the usual abbreviations (s = singlet, d = doublet, t = triplet), while J value in Hz is given in parenthesis.

d) Figures represent total yield computed as aldehyde.



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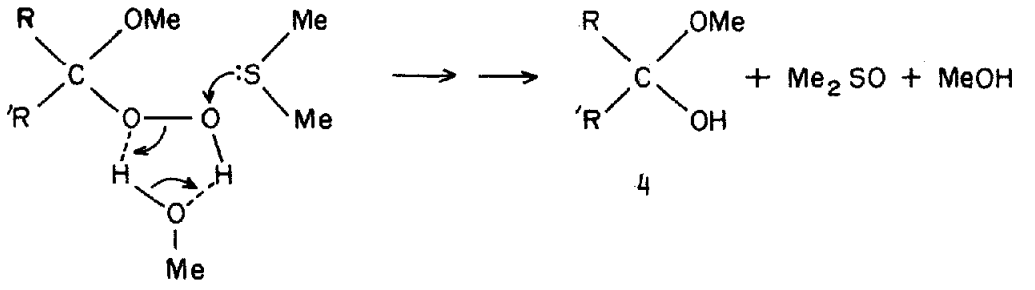
Scheme 1



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Scheme 2

expected to appear largely in the unmasked free state, as in such cases pathway shown in Scheme 1 should become significant, because of conjugation of the resulting carbonyl function with the olefinic/aromatic moiety. It may also be noted that conjugation deactivates the carbonyl function towards acetal formation.[15]

Reduction with thiourea may be expected to proceed along similar lines (Scheme 1 and 2). Data summarized in Table 1 is consistent with the above considerations.

EXPERIMENTAL

All ^{1}H-NMR spectra were taken on 10-15% soln in CCl_4 with TMS as internal reference, using Perkin-Elmer model R32 (90 MHz) NMR spectrometer. Signals are reported in ppm (δ). GLC analyses were carried out on Hewlett-Packard model 5712A gas chromatograph (Al columns, 200.0 x 0.6 cm; support, 60-80 mesh Chromosorb W; carrier gas H_2) using either 10% SE-30 (column A) or 10% Carbowax 20M (column B) as stationary phases.

Materials

Except for 10-undecenoic acid and styrene which were from Koch-Light Laboratories, all other olefins used were from our own laboratory and were more than 96% pure (GLC; column B). Cycloartenyl acetate (m.p. 118-120°C) was homogeneous by TLC (solvent: n-hexane-EtOAc, 70:30). Thiourea used was A.R. grade, Koch-Light Laboratories.

General procedure

The following description is typical of the general procedure.

Ozonised oxygen (1.22% w/w O_3 in O_2) was bubbled through a soln of (+)-3-carene (2.74 g, 0.02 mole) in anhydrous MeOH (30 ml) at -10 to -15° till the required quantity of O_3 (0.99 g, 0.02 mole) had been passed (65 min). N_2 was next bubbled (10 min) through the soln to displace any free ozone and the soln added to a soln of thiourea (0.767g, 0.01 mole) in dry MeOH (3 ml) at 0°C under stirring. Thiourea S-dioxide started depositing as white crystals within 15 min. After stirring for another 40 min, the

reaction mixture was filtered to collect the dioxide (0.89 g; one crystallisation from MeOH aq gave pure thiourea S-dioxide, 0.79 g, m.p. 127-28°C; Lit.[29], m.p. 129-130°C. Further identified by comparison (IR, mmp) with an authentic sample prepared[12b] from thiourea and H_2O_2). The filtrate and washings were freed of MeOH under reduced pressure (150 mm), residue taken up in light petroleum (60-80°C, 60 ml), washed with 1% sodium bicarbonate aq (10 ml) and water (10 ml x 3) and dried (Na_2SO_4). Solvent was flashed off and the residue distilled to give 2,2-dimethyl-3-(2'-oxo)-propylcyclopropane-1-acetaldehyde dimethylacetal[18] (3.33g, GLC purity ~90%; column A, 170°. The other component is the free aldehyde, see Table 1), b.p. 95-100°(bath)/0.4 mm, n_D^{25} 1.4475. ^{1}H-NMR (computed for 100% purity): two Me-C-(3H singlets at 0.85 and 1.06 ppm), MeCO (3H, s, 2.04 ppm), CH_2CO (2H, d, 2.23 ppm, J = 6Hz), two OMe (6H, s, 3.2 ppm), CH(OMe)$_2$ (1H, t, 4.22 ppm, J = 5Hz).

When the above product (1.66 g) was stirred with oxalic acid aq (0.1%, 20 ml) at room temp (28-30°), hydrolysis of the acetal was complete (TLC) within 90 min, when usual work-up furnished, after distillation, 2,2-dimethyl-3-(2'-oxo)-propylcyclopropane-1-acetaldehyde[23] (1.32 g), b.p. 90-100° (bath)/0.5 mm, n_D^{25} 1.4570. ^{1}H-NMR: two Me-C- (3H singlets at 0.88 and 1.13 ppm), MeCO (3H, s, 2.06 ppm), CH_2CO (4H, m, 2.1-2.5 ppm), CHO (1H, t, 9.70 ppm, J = 1.5Hz).

Exposure of 2,2-dimethyl-3-(2'-oxo)-propylcyclopropane-1-acetaldehyde to methanol containing dimethyl sulphoxide/thiourea S-dioxide

A soln of the above aldehyde (0.166 g, 0.001 mole) and anhydrous DMSO (0.094g; 0.0012 mole) in anhydrous MeOH (3 ml) was kept at 0°C for 1 hr. Usual work-up furnished only unchanged aldehyde with no trace (GLC) of the corresponding acetal. Similar results were obtained with thiourea S-dioxide.

However, when exposure to MeOH-DMSO was carried out at 25-30° for 15 hr, some 12% of acetal formation was indicated by GLC. Under these conditions thiourea S-dioxide gave <1% of acetal.

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[14]In a test experiment a 10% soln (9.35 g) of t-butyl hydroperoxide in t-butanol was added to a soln of thiourea (0.3247 g; ~0.5 mole equiv.) in MeOH (1 ml) and the mixture stirred at room temp (~25°) for 40 min., when the test for hydroperoxide ($KI-H_2SO_4$ aq) became negative. The separated solid was filtered and recrystallised from aq. MeOH to get a solid (0.38 g; m.p. 127-128° dec.) identified as thiourea S-dioxide.

[15]See e.g.: A.J. Meskens, Synthesis 501 (1981).

[16]P.S. Bailey, Ozonation in Organic Chemistry, Vol. 1, p. 132, Academic Press, New York (1978).

[17]Though, Pappas et al.[9] describe the dimethyl sulphide reduction products of all the α-methoxyperoxidic ozonolysis products investigated as aldehydes, without reference to acetal formation, our own experience (e.g. carene-MeOH/O_3/Me_2S) as well as

that of several others[11a,18] reveals that in many cases acetals are the sole or chief product (vide Discussion).

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