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SYNTHESIS OF CARBOXYLIC ESTERS USING FORMALDEHYDE DIMETHYL DITHIOACETAL S,S-DIOXIDE

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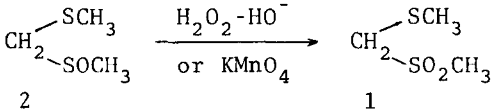
Abstract: Formaldehyde dimethyl dithioacetal S,S-dioxide (1) reacted with an alkyl bromide or a 2-alkenyl bromide (8) under phase-transfer conditions using 50% aq. NaOH to give an alkyl or 2-alkenyl derivative of 1, whereas, in the reaction with 8 in the presence of K_2CO_3*-KI in HMPA, 1 formed a 1-alken-3-yl derivative. Transformation of these products into the corresponding carboxylic esters was also described.*

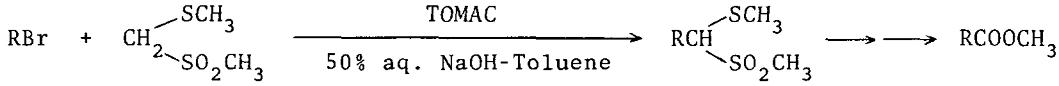
Recently, it was found that formaldehyde dimethyl dithioacetal S,S-dioxide (1) was conveniently prepared by oxidation of the corresponding S-oxide (2)[1] with alkaline hydrogen peroxide or potassium permanganate.[2] The present paper discloses utilization of 1 as a synthetic reagent for regiospecific introduction of methoxycarbonyl group into the 1- or 3-position of a 2-alkenyl halide as well as for conversion of an alkyl halide into the carboxylic ester.



$$CH_2\begin{smallmatrix}SCH_3\\SOCH_3\end{smallmatrix} \xrightarrow[\text{or } KMnO_4]{H_2O_2\text{-}HO^-} CH_2\begin{smallmatrix}SCH_3\\SO_2CH_3\end{smallmatrix}$$

2 1

First, we investigated production of a carboxylic ester (5) from an alkyl halide (3) using 1. This method comprises two parts, *i.e.* (i) formation of a carbon-carbon bond between 1 and 3 to afford an alkylated derivative (4) and (ii) transformation of the dithioacetal S,S-dioxide functional group of 4 into methoxycarbonyl group.



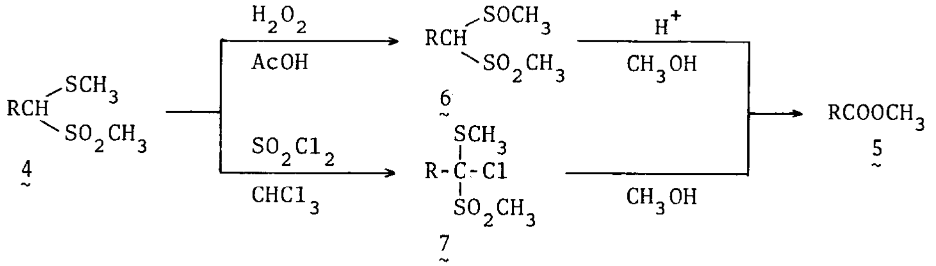
$$RBr + CH_2\begin{smallmatrix}SCH_3\\SO_2CH_3\end{smallmatrix} \xrightarrow[\text{50\% aq. NaOH-Toluene}]{\text{TOMAC}} RCH\begin{smallmatrix}SCH_3\\SO_2CH_3\end{smallmatrix} \longrightarrow\longrightarrow RCOOCH_3$$

3 1 4 5

[a: R = n-$C_{12}H_{25}$ b: R = $PhCH_2$]

Formation of 4 from 1 and 3 can be achieved under phase-transfer conditions using aq. NaOH as a base. This is in striking contrast with the fact that 2 is not alkylated with 3 under the analogous conditions. To a solution containing dodecyl bromide (3a) (5.999 g, 24.1 mmol) and 1 (2.248 g, 16.0 mmol) in toluene (19 ml), were added 50% aq. NaOH (17 ml) and trioctylmethylammonium chloride (TOMAC)[3] (141 mg, 0.35 mmol) and the resulting mixture was magnetically stirred at 60 °C for 30 h. The usual workup and column chromatography on silica gel gave tridecanal dimethyl dithioacetal S,S-dioxide (4a) (4.087 g, 83% yield).[4,5] In a similar manner, the benzylated derivative (4b) of 1 was obtained as shown in Table 1.

For the conversion of 4 to the carboxylic ester (5), it is necessary to increase the oxidation state of the central carbon of the dithioacetal S,S-dioxide group of 4 by one unit and we examined two routes shown in the following.



[a: R = n-$C_{12}H_{25}$ b: R = $PhCH_2$]

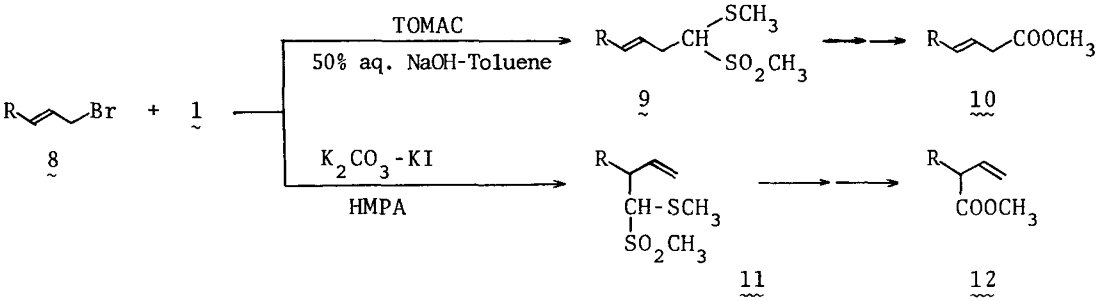
When the S,S,S'-trioxide (6) given by oxidation of 4 with hydrogen peroxide (1 mol-equiv) in acetic acid was treated with hydrogen chloride (1 mol/l) in refluxing methanol, a Pummerer-type rearrangement and methanolysis took place concurrently to afford the expected carboxylic ester (5). Another route passing through a chloro derivative (7) was also found to be effective. The chlorination was carried out by briefly refluxing a solution of 4 and sulfuryl chloride (1.1 mol-equiv) in chloroform. The thus-obtained 7, without any purification, was dissolved in methanol and the resulting solution was refluxed to afford 5 in a high yield. These results are summarized in Table 1.

Table 1. Yield in Transformation of 3 into 5[a]

Bromide (3)	3 → 4		4 → 6	6 → 5	4 → [7] → 5[c]
	3/1 = 1[b]	3/1 = 1.5[b]			
n-$C_{12}H_{25}$Br	68% [60 °C 64 h]	83% [60 °C 30 h]	94% [r.t. 1 d]	81% [refl. 10 h]	87%
$PhCH_2$Br	58% [r.t. 72 h]	80% [r.t. 52 h]	85% [r.t. 1 d]	75%[d] [r.t. 42 h → refl. 20 h]	86%

[a] The values in the bracket show the reaction temperature and the reaction time.
[b] mol-ratio.
[c] A solution containing 4 and sulfuryl chloride (1.1 mol-equiv) in chloroform was refluxed for 1 h and then evaporated. The residue was dissolved in methanol and the resulting solution was refluxed for 1 d.
[d] When sulfuric acid was used instead of hydrogen chloride, the yield was 71%.

When a 2-alkenyl bromide (8) was subjected to the reaction with 1 under the phase-transfer conditions mentioned above, a 2-alken-1-yl derivative (9) was exclusively obtained. Whereas, a 1-alken-3-yl derivative (11) was produced by stirring 1 and 8 (1.5 mol-equiv) together with potassium carbonate (2 mol-equiv) and potassium iodide (0.5 mol-equiv) in HMPA at room temperature → 60 °C, where formation of 9 was not observed. Recently, it was reported that a carbon-carbon bond was formed regiospecifically at the 3-position of 8 by



[a: $R = n\text{-}C_4H_9$ b: $R = n\text{-}C_6H_{13}$ c: $R = n\text{-}C_{10}H_{21}$]

simply stirring along with dimethyl sulfide having such an electron-withdrawing group as acyl or sulfinyl group in the presence of potassium carbonate in water or DMF.[6] Under the conditions using 2 *M* aq. potassium carbonate, the expected 11 was not afforded. When a mixture of 1 and 8a (1.5 mol-equiv) was stirred in the presence of potassium carbonate (2 mol-equiv) and potassium iodide (0.5 mol-equiv)[7] in DMF at 60 °C for 3 d, 11a was produced in a 43% yield. The yield was raised up to 60% by using HMPA as a solvent. In analogous manners, 11b and 11c were obtained in 57% and 43% yields, respectively. 2-Nonenyl chloride could be also employed instead of 8b in the above reaction to give 11b in a comparable yield (59%).

Transformation of the thus-obtained products (9 and 11) into the corresponding β,γ-unsaturated carboxylic esters (10 and 12) was performed successfully by means of oxidation with hydrogen peroxide in acetic acid followed by treatment with hydrogen chloride in refluxing methanol as given in Table 2.[8] It should be noted that the corresponding α,β-unsaturated carboxylic esters were not detected in the reaction mixture by an NMR analysis.

Thus, we have established a method for regiospecific introduction of methoxycarbonyl group into the 1- and 3-positions of a 2-alkenyl bromide (8) by the use of formaldehyde dimethyl dithioacetal S,S-dioxide (1).

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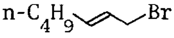
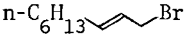
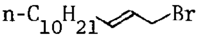
Table 2. Yield in Transformation of 8 into 10 or 12[a]

Bromide (8)	8 → 9[b]	9 → 10		8 → 11	11 → 12	
		Oxidation[c]	Methanolysis[d]		Oxidation[c]	Methanolysis[d]
 n-C_4H_9 Br	75% [r.t. 2 d]	80%(99%)[e] [r.t. 1 d]	51%[f] [refl. 6 h]	60% [r.t. 2 d → 60 °C 2 d]	80%(99%)[e] [r.t. 40 h]	40% [refl. 6 h]
 n-C_6H_{13} Br	77% [r.t. 2 d]	78%(99%)[e] [r.t. 2 d]	54% [refl. 6 h]	57% [r.t. 2 d → 60 °C 2 d]	74%(98%)[e] [r.t. 2 d]	64% [refl. 6 h]
 n-$C_{10}H_{21}$ Br	77% [r.t. 3 d]	77%(96%)[e] [r.t. 2 d]	60% [refl. 6 h]	43% [r.t. 2 d → 60 °C 2 d]	68%(99%)[e] [r.t. 2 d]	78% [refl. 6 h]

[a] The values in the bracket show the reaction temperature and the reaction time.
[b] Stirring 1 and 8 (1.5 mol-equiv) in the presence of potassium carbonate (2 mol-equiv) and potassium iodide (0.5 mol-equiv) in HMPA.
[c] Hydrogen peroxide (1.0 mol-equiv) in acetic acid.
[d] Using hydrogen chloride in methanol (1 mol/l).
[e] The value in the paranthesis is the yield based on the unrecovered 9 or 11.
[f] Using conc. hydrochloric acid in methanol (1 mol/l).

References and Notes

1. The S-oxide (2) is commercially available from Nippon Soda Co. Ltd.
2. K. Ogura, M. Suzuki, and G. Tsuchihashi, *Bull. Chem. Soc. Jpn.*, 53, 1414 (1980).
3. Cetyltrimethylammonium bromide and tetrabutylammonium hydrogensulfate are also effective as phase-transfer catalysts.
4. When this alkylation was carried out in the presence of sodium hydride in THF [60 °C 1 d] or DMF [r.t. 1 d → 60 °C 3 h], 4a was produced in 40% or 71% yield, respectively.
5. All new compounds reported herein were characterized by satisfactory elemental analyses and spectral (IR and NMR) data.
6. K. Ogura, S. Furukawa, and G. Tsuchihashi, *J. Am. Chem. Soc.*, 102, 2125 (1980).
7. In the absence of potassium iodide [60 °C 108 h], the yield of 11a was 4%.
8. Chlorination of 9 or 11 with sulfuryl chloride gave a complex mixture, probably due to attack of chlorine on the carbon-carbon double bond.

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