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A NOVEL ROUTE FROM A CARBOXYLIC ACID TO A CARBALDEHYDE USING METHYLTHIOMETHYL p-TOLYL SULFONE

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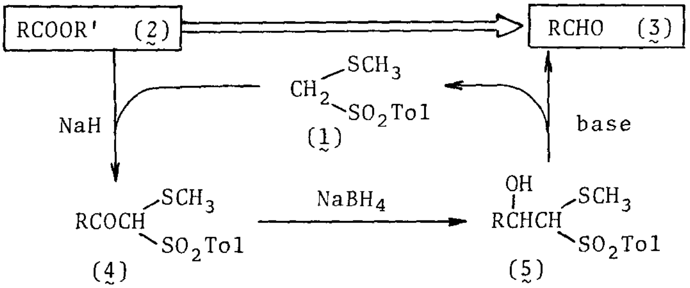
Abstract: A new conversion of a carboxylic ester to a carbaldehyde involing formation and dissociation of a C-C bond at the acyl carbon was accomplished by the use of methylthiomethyl p-tolyl sulfone (1).

Since a carbaldehyde is one of the most valuable intermediates in organic synthesis, various methods for its preparation have been developed. Especially, considerable attention has been paid to reductive conversion of an easily available carboxylic acid to the corresponding carbaldehyde,[1] but a method utilizing formation and dissociation of a C-C bond at the acyl carbon is hitherto unknown for this conversion. Now we wish to report that this can efficiently be realized by employment of methylthiomethyl p-tolyl sulfone (1)[2] as outlined in the following scheme.



The present method comprises a C-C bond formation between 1 and a carboxylic ester (2) to give an acylated derivative (4) and the subsequent reduction of 4 with $NaBH_4$ leading to the corresponding alcohol (5), followed by the base-catalyzed degradation of 5. It is noteworthy that the starting material (1) can be recovered at the final step. Consequently, this process is regarded as a 1-mediated selective reduction of 2 with easily handling $NaBH_4$.

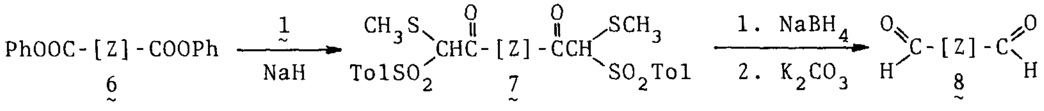
The first transformation of 2 into 4 was achieved by the reaction with 1 in the presence of NaH (2 equiv) in THF. As previously mentioned,[3] an ethyl ester (2; R' = Et) afforded 4 in moderate to good yield. As a result of many efforts, the yield of 4 was improved to be quantitative by employment of a phenyl ester (2: R' = Ph) as shown in Table 1. The thus-obtained 4 was reduced with $NaBH_4$ (1.7 mol-equiv) in methanol at 0 °C to give 5 quantitatively. When the reaction mixture was gradually warmed (r.t./18 h → 40 °C/6 h → reflux/1 h) without any workup, the desired aldehyde (3)[4] was produced along with 1 ("Method A").[5] A higher yield of 3 was attained by the following procedure. After 4 was reduced with $NaBH_4$ (1.0 mol-equiv) in methanol (0 °C/3 h), water was added and the resulting mixture was extracted with CH_2Cl_2. The extract was dried and evaporated. The residual crude 5 was dissolved in 2-propanol and, after addition of K_2CO_3 (1.5 mol-equiv), the mixture was stirred at room temperature for 1.5 h to give 1 and 3[4] in almost quantitative yields ("Method B").[6] The results are summarized in Table 1, which also shows that these conditions are not applicable to the conversion of 5 having an alkyl group as R to the corresponding 3. In this case, it is recommended that the base-catalyzed degradation of 5 is performed with K_2CO_3 in the copresence of 18-Crown-6 in a nonpolar solvent. Thus, the crude 5 ($R = n\text{-}C_{11}H_{23}$), obtained by reduction of 4 ($R = n\text{-}C_{11}H_{23}$) with $NaBH_4$, was stirred together with K_2CO_3 (1.1 mol-equiv) and 18-Crown-6 (0.05 mol-equiv) in benzene-hexane (2 : 1) at 0 °C for 1 h and then at room temperature for 3 h ("Method C"). Addition of water, extraction with diethyl ether, evaporation, and column chromatography on silica gel afforded dodecanal (3; $n\text{-}C_{11}H_{23}$) and 1 in 78% and 85% yields, respectively.

Table 1. Yields (%) in the Conversion of 2 to 3

R	$2 \longrightarrow 4$		$4 \longrightarrow [5] \longrightarrow 3 + [1]^c$		
	R' = Et[a]	R' = Ph[b]	"Method A"[d]	"Method B"[d]	"Method C"[d]
C_6H_5	71	99	71 [91]	90 [95]	---
$p\text{-}ClC_6H_4$	69	98	69 [86]	96 [99]	---
$p\text{-}MeOC_6H_4$	61	96	86 [91]	95 [99]	---
$p\text{-}MeC_6H_4$	54	97	76 [81]	92 [99]	---
$m\text{-}MeC_6H_4$	68	98	82 [91]	94 [98]	---
$n\text{-}C_{11}H_{23}$	71	95	---	28 [29]	78 [85]

a: see ref. 3. b: a mixture of 1, 3 (1.5 mol-equiv), and NaH (3.0 equiv) in THF was stirred at room temperature for 1-2 d except $R = p\text{-}MeOC_6H_4$ (r.t./1 d → 50 °C/1 d). c: the value in the bracket means the yield of the recovered 1. d: see Text.

Finally, we would like to describe the application of the present method to synthesis of dicarbaldehydes (8). Diphenyl isophthalate (6a) and diphenyl dodecanedioate (6b) were reacted with 1 (3.0 mol-equiv) and in the presence of NaH (6.0 equiv) to give the corresponding diacylated products (7a and 7b) in 93% and 86% yields, respectively. Transformation of these products into isophthalaldehyde (8a; 57%) and dodecanedial (8b; 52%) was accomplished according to the already established methods ("Method B" and "Method C", respectively).



a: [Z] = m-C_6H_4< b: [Z] = $-(CH_2)_{10}-$

Further applications of the present method are being undertaken in our laboratory.

References and Notes

1. E Mosettig and R. Mozingo, *Org. React.*, 4, 362 (1948); E. Mosettig, *Org. React.*, 8, 218 (1954); T. Fujisawa, T. Mori, S. Tsuge, and T. Sato, *Tetrahedron Lett.*, 24, 1543 (1983) and the references cited therein.
2. This reagent (1) can be conveniently synthesized by the reaction of acetoxymethyl methyl sulfide with sodium p-toluenesulfinate: K. Ogura, N. Yahata, J. Watanabe, K. Takahashi, and H. Iida, *Bull. Chem. Soc. Jpn.*, in press. Now 1 is commercially available (from Nissan Chemical Industries Ltd. and Junsei Chemical Co. Ltd.).
3. K. Ogura, N. Yahata, K. Hashizume, K. Tsuyama, K. Takahashi, and H. Iida, *Chem. Lett.*, 1983, 767.
4. trapped as its 2,4-dinitrophenylhydrazone.
5. Since heating a methanolic solution of 5 did not give 3, this conversion (5 → 3) seemed to be initiated by the basic compound(s) derived from $NaBH_4$.
6. The diethyl acetal of 3 (R = Ph) was also obtained in 73% yield by treatment of the crude 5 (R = Ph) with K_2CO_3 in ethanol and the subsequent addition of triethyl orthoformate and sulfuric acid, followed by stirring the resulting mixture at room temperature overnight.

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