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# REGIOSPECIFIC ALLYLATION OF SULFUR SUBSTITUTED ACTIVE METHYLENE COMPOUNDS WITH ALLYLIC BROMIDES

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Allylation of sulfur substituted active methylene compounds such as $RSCH_2Y$ [Y = C(=O)R, COOR, CN] with allylic bromides in the presence of bases gives a mixture of the $S_N2$-product and the apparent $S_N2'$-product. The former product is selectively obtained in alkylation in a nonpolar solvent. Synthetic utility of this regiospecific allylation is demonstrated in the simple synthesis of pellitorine.

Allylation of sulfur substituted enolates with allylic halides gives a mixture of the $S_N2$-product and the apparent $S_N2'$-product.[1,2] For example, the reaction of the enolate of α-(phenylthio)acetophenone with prenyl iodide in THF gives the $S_N2$-product and the apparent $S_N2'$-product in the ratio of 69 : 31,[1] and the apparent $S_N2'$-product predominates in allylation of α-(methylthio)acetophenone.[2] As the allylated products have wide applicability in organic synthesis, a method to get one isomer selectively is highly desired. Ogura et al.[2] recently described a method to get the $S_N2'$-product selectively using a base and solvent system which consists of aqueous potassium carbonate in DMF. In this paper we wish to report a simple method to get the $S_N2$-product selectively in the similar reactions.

Compounds (1a-1d) were alkylated with prenyl bromide under various conditions to give the monoalkylated product which consists of two regioisomers (2 and 3) and the dialkylated product. As the matter of dialkylation has been discussed previously in the alkylation of various active methylene compounds,[3] we focus our attention on regioselectivity of allylation. Results are summarized in Table 1.

$$\underset{\underline{1}}{RSCH_2Y} + Me_2C{=}CHCH_2Br \xrightarrow[\text{at room temp.}]{\text{base}} \underset{\underline{2}}{RSCHY\,(CH_2CH{=}CMe_2)} + \underset{\underline{3}}{RSCHY\,(Me_2CCH{=}CH_2)} \qquad (1)$$

a: R = Me Y = C(=O)Ph, b: R = Ph Y = C(=O)Me, c: R = Ph Y = $COOCMe_3$, d: R = Ph Y = CN

Table 1. Effect of Base and Solvent on the Ratio of 2 to 3 in the Reaction of eq 1

| R | Y | Base | Solvent | Time, h | 2/3 [a] | Isol. yield of 2, % |
|---|---|---|---|---|---|---|
| Me | C(=O)Ph | 50%-NaOH[b] | benzene | 10 | 88/12 | 2a 67 |
| Me | C(=O)Ph | 50%-NaOH[b] | $CH_2Cl_2$ | 10 | 60/40 | |
| Me | C(=O)Ph | 50%-NaOH[b] | $H_2O$ | 10 | 18/82 | |
| Me | C(=O)Ph | t-BuOK[c] | benzene | 10 | 85/15 | |
| Me | C(=O)Ph | t-BuOK | THF | 10 | 40/60 | |
| Ph | C(=O)Me | 50%-NaOH[b] | benzene | 10 | 98/2 | 2b 71 |
| Ph | C(=O)Me | 50%-NaOH[b] | $CH_2Cl_2$ | 10 | 79/21 | |
| Ph | C(=O)Me | 50%-NaOH[b] | $H_2O$ | 10 | 30/70 | |
| Ph | $COOCMe_3$ | 50%-NaOH[b] | benzene | 48 | 100/0 | 2c 62 |
| Ph | $COOCMe_3$ | 50%-NaOH[b] | $H_2O$ | 48 | 75/25 | |
| Ph | CN | 50%-NaOH[b] | benzene | 12 | 100/0 | 2d 70 |
| Ph | CN | 50%-NaOH[b] | $H_2O$ | 12 | 98/2 | |

a) The ratios were determined by GLC and NMR. b) The reaction was carried out in the presence of TEBA as a catalyst. c) The reaction was carried out in the presence of 18-crown-6 as a catalyst.

Alkylation in a nonpolar solvent such as benzene gives 2 selectively, and alkylation in the more polar solvent gives the mixture of 2 and 3 depending on the polarity of the solvent and the character of R and Y. The method to prepare 2 exclusively is evidently the phase transfer method using 50%-NaOH as base, benzene as a solvent and triethylbenzylammonium chloride (TEBA) as a catalyst, for this is simple in the procedure and also offers high selectivity in the sense of regiospecificity and monoalkylation.

Compounds 1a-1d were allylated with crotyl bromide or 1-bromo-3-octene by the present procedure to give 4 or 5 selectively in good yields, respectively. Results are summarized in table 2. Yields refer to pure and isolated products. Purification was done by distillation or column chromatography.

$$\underset{\text{1a-1d}}{RSCH_2Y} + \underset{\text{(trans)}}{R'CH{=}CHCH_2Br} \xrightarrow[\text{TEBA, benzene at room temp.}]{\text{50\%-NaOH}} \underset{\substack{CH_2CH{=}CHR' \\ \text{(trans)}}}{RSCHY} \qquad (2)$$

R' = Me or $n\text{-}C_5H_{11}$

4: R' = Me

5: R' = $n\text{-}C_5H_{11}$

The allylated products such as 2, 4 or 5 can be transformed into various important compounds.[4] Here a simple synthesis of pellitorine (6)[5] starting from 5c or 5d is described. Oxidation of 5c or 5d with m-chloroperbenzoic acid (m-CPBA)

gave the corresponding sulfoxide in almost quantitative yields. Heating each of them in toluene at about 100°C afforded t-butyl E,E-2,4-decadienoate or 2,4-decadienenitrile (E,E/Z,E = about 1/1), respectively, which is convertible to 6 through E,E-2,4-decadienoic acid.[6] It is rather difficult to prepare 1-bromo-3-octene in pure form which is the requisite allylic bromide to prepare 5c or 5d. However, alkylation of 1c or 1d with the mixture of 1-bromo-3-octene (70%) and 3-bromo-1-octene (30%) gave the desired 5c or 5d, respectively, without contamination of their regioisomers. This bromide was prepared by bromination of 1-octene with N-bromosuccinimide (NBS). Thus pellitorine can be prepared starting from readily available materials by simple procedure as outlined in Scheme 1.

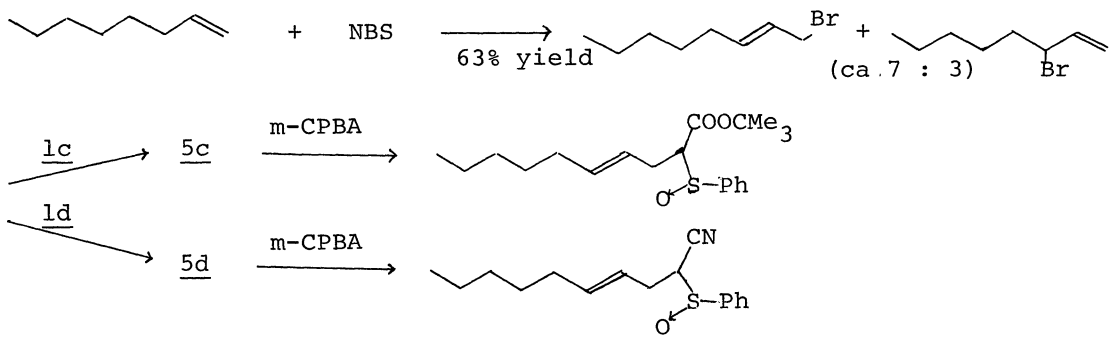
Table 2. Alkylation of $RSCH_2Y$ (1) with $R'CH=CHCH_2Br$ under Phase Trandfer Conditions[a]

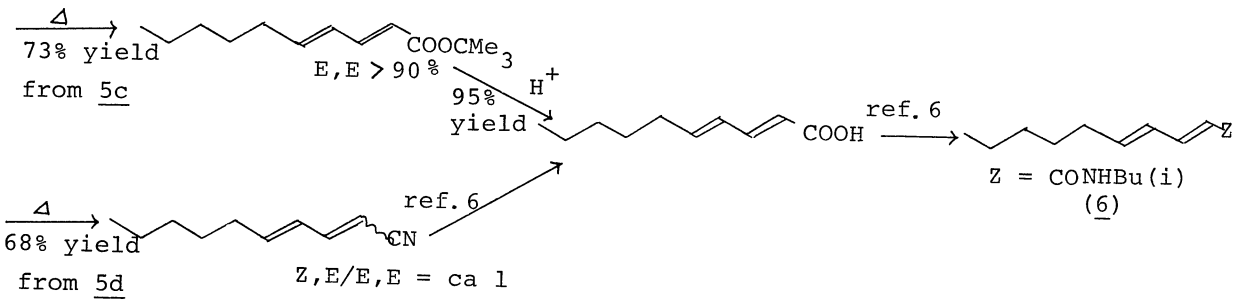
| R | Y | R' | Time, h | Yield of 4 or 5, % | |
|---|---|---|---|---|---|
| Me | C(=O)Ph | Me | 10 | 4a | 60[b] |
| Me | C(=O)Ph | $n\text{-}C_5H_{11}$ | 24 | 5a | 63[b] |
| Ph | C(=O)Me | Me | 10 | 4b | 75 |
| Ph | C(=O)Me | $n\text{-}C_5H_{11}$ | 24 | 5b | 73 |
| Ph | $COOCMe_3$ | Me | 72 | 4c | 54 |
| Ph | $COOCMe_3$ | $n\text{-}C_5H_{11}$ | 72 | 5c | 56 |
| Ph | CN | Me | 10 | 4d | 70 |
| Ph | CN | $n\text{-}C_5H_{11}$ | 24 | 5d | 66 |

a) A mixture of 1 (10 mmol), $R'CH=CHCH_2Br$ (12 mmol), TEBA (100 mg), 50%-NaOH (25 ml) and benzene (20 ml) was stirred vigorously at room temperature for the period listed in the table.

b) About 20% amounts of their regioisomer were included.

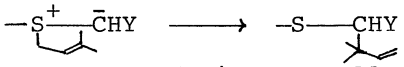
Scheme 1. Synthesis of Pellitorine (6)






References and Notes

1) H. J. Reich and M. L. Cohen, J. Am. Chem. Soc., 101, 1307 (1979).

2) K. Ogura, S. Furukawa, and G. Tsuchihashi, J. Am. Chem. Soc., 102, 2125 (1980). The apparent $S_N2'$-product is formed via [2,3]sigmatropic rearrangement of the sulfur ylide (ref. 1 and 2). 

3) Dialkylation of active methylene compounds is generally suppressed under phase transfer conditions or by alkylation in benzene using DBU as a base. N. Ono, T. Yoshimura, T. Saito, R. Tamura, R. Tanikaga, and A. Kaji, Bull. Chem. Soc. Jpn., 52, 1716 (1979) and references cited therein.

4) Synthetic utility of β-keto sulfides or related compounds has been documented: B. M. Trost, Chem. Rev., 78, 363 (1978), and Acc. Chem. Res., 453 (1978). Recently we have discovered a new method to prepare 4-hydroxycyclopentenones using allylated products of 1b and nitroolefins, which will appear in N. Ono et al., Bull. Chem. Soc. Jpn., No. 11 (1980).

5) Pellitorine (6) is known to be an insecticide, and a number of syntheses of it have been reported. See ref. 6 and references cited therein.

6) T. Mandai, J. Gotoh, J. Otera, and M. Kawada, Chem. Lett., 1980, 313. Thermal elimination of the sulfoxide derived from 5c gave the E,E-olefin stereoselectively, and thermal elimination of the sulfoxide derived from 5d gave the mixture of the E and Z olefins,[4] which can be converted to E,E-2,4-decadienoic acid stereoselectively.

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