

REACTION OF SILYL ENOL ETHERS WITH β -HALOGENOALKYL ARYL SULFIDES - A METHOD OF β -ARYLTHIOALKYLATION OF CARBONYL COMPOUNDS

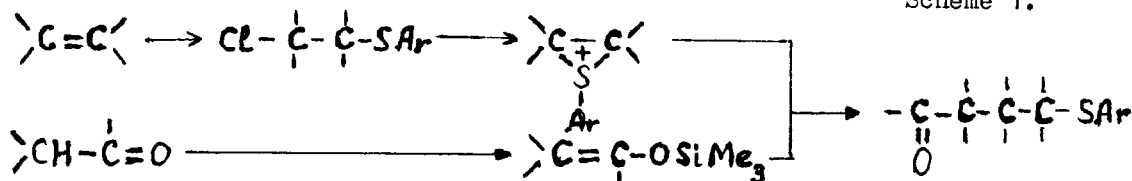
M.A. Ibragimov, W.A. Smit*

N.D. Zelinsky Institute of Organic Chemistry, Leninsky pr. 47, Moscow, USSR

Abstract: Reaction of β -halogenoalkyl aryl sulfides with silyl enol ethers in the presence of Lewis acids produced α -(β '-arylthioalkyl) substituted carbonyl compounds.

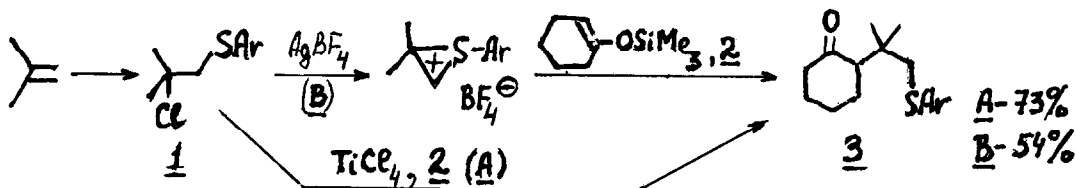
Electrophilic addition to silyl enol ethers has been developed as an efficient method for the regiospecific introduction of various substituents at α -carbon of the parent carbonyl compounds¹. Among potential carbon electrophiles, β -halogenoalkyl aryl sulfides merit special attention since: (i) these compounds are readily available from any alkenes²; (ii) β -halogenoalkyl aryl sulfides could be easily converted into episulfonium ions (ESIs) which are known to reveal carbonium ion-like pattern of reactivity³; (iii) the net result of alkylation of silyl enol ethers with these reagents should correspond to the assembling of complex polyfunctional molecules from simple precursors as shown on the Scheme 1.

Scheme 1.



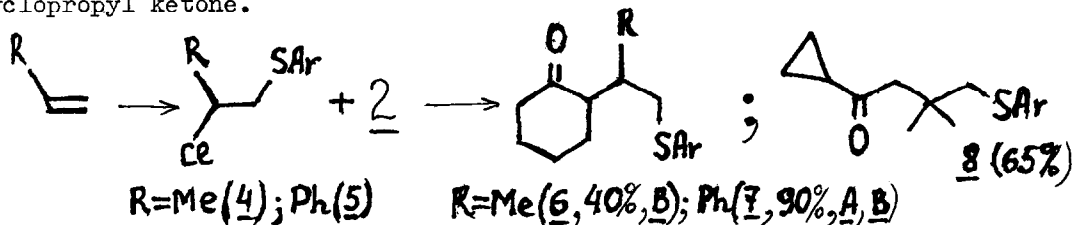
It was shown earlier that the reaction of S-aryl-ESIs with aromatic \mathcal{F} -donors ($\text{Ar}'\text{H}$) proceeds as the β -arylthioalkylation of the parent aromatic substrate⁴. However, this process is also accompanied by the formation of ArSAr' as the by-products arising from the competing attack of $\text{Ar}'\text{H}$ at S-atom of ESI. To the best of our knowledge no data were available on the course of reaction of β -halogenoalkyl aryl sulfides or ESIs with silyl enol ethers and here we present our results bearing to the problem.

For the model study we have chosen the reaction of 2-chloro-2-methyl-1-arylthiopropene, **1**,⁵ with enol ether **2**. It was found, that the interaction of **1** with **2** takes place smoothly at -30°C when the mixture of reagents was treated with TiCl_4 (method A). Alternatively the reaction could be carried out via the formation of ESI⁶ which is further treated with **2** (method B). Both procedures produce the same product α -(1,1-dimethyl-2-arylthio)ethylcyclohexanone, **3**.⁷ The reaction mixture does not contain α -arylthiohexanone in noticeable amounts.



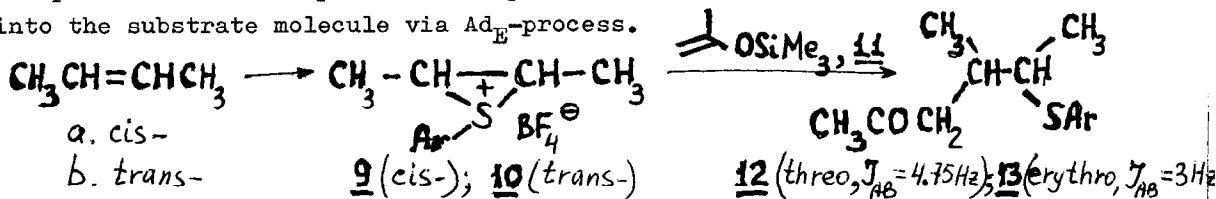
The formation of **3** proceeds evidently as the attack of δ^+ -donor at the more substituted carbon atom of ESI.

Similar regioselectivity was observed for the reaction of **2** with **4** and **5**⁵, as well as for the formation of adduct **8** from **1** and silyl enol ether of methylcyclopropyl ketone.

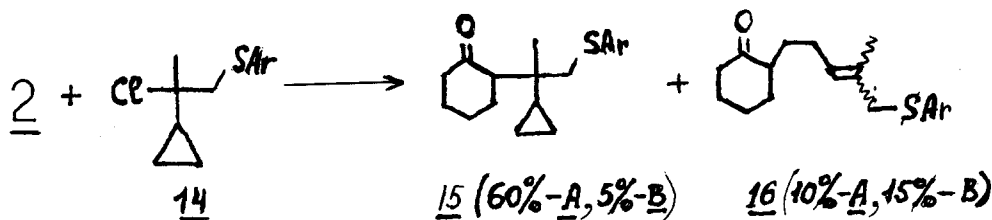


Typical procedures: Method A. A solution of TiCl_4 (1 mmol) in CH_2Cl_2 was added to the stirred mixture of **1** (1 mmol) and **2** (2 mmol) in CH_2Cl_2 at -30° . The mixture was kept 1h at -30°C , warmed up to room temperature, quenched with aq. NaHCO_3 , extracted with CHCl_3 ; the solvent was dried, and removed at reduced pressure. The product **3** was isolated by TLC (SiO_2 , hexane-ether 5:1); yield 0.23g (73%). PMR (CCl_4 , δ , TMS): 0.98 (s, 3H); 1.08 (s, 3H); 1.4-2.2 (m, 9H); 3.1(q, 2H, $J_{AB}=12\text{Hz}$); 7.18(s, 4H). Found: C 64.59, H 7.04 ($\text{C}_{16}\text{H}_{21}\text{ClOS}$) Calc: C 64.74, H 7.13. MW 296 (MS). Method B. A solution of ESI tetrafluoroborate⁶ (1 mmol) in CH_2Cl_2 (5 ml) was added to the solution of **2** (2 mmol) in CH_2Cl_2 (5 ml) at 20° , the mixture was stirred for an hour at 20°C and then treated as described above. Product **3** was isolated with 54% yield.

Stereoisomeric ESIs **9** and **10** (prepared from cis- and trans-butene⁸) afforded upon the reaction with **11** stereochemically pure (GLC and PMR at 250 MHz) adducts **12** and **13** respectively. This reaction seems to constitute the unique example of the stereospecific incorporation of 3-substituted-2-butane moiety into the substrate molecule via Ad_E -process.



Method A has some specific advantages in the case of substrates liable to undergo carbonium ion rearrangements. Thus, the reaction of **2** with **14**⁹ under the conditions of method B yields the mixture of products containing only small amount of the desired **15** and **16**. However, under the conditions of method A the unrearranged product **15** could be cleanly prepared.



Method A proved to be especially rewarding for the alkylation of silyl enol ethers with β -chloro- β -alkoxyalkyl aryl sulfides 19-21¹⁰. This reaction produces smoothly β -alkoxy- γ -aryltiioderivatives of parent carbonyl compounds according to the following generalized Scheme 2 (see also Table 1).

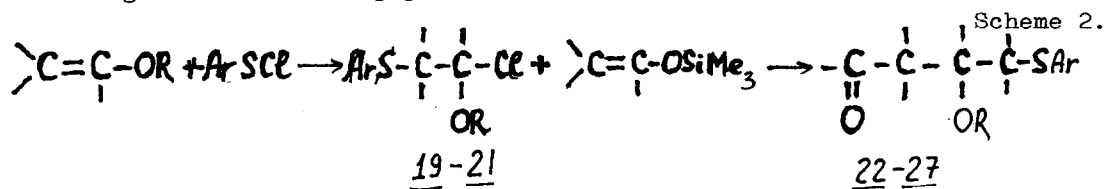
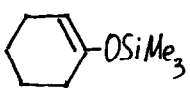
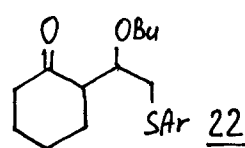
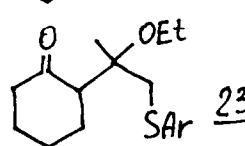
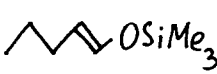
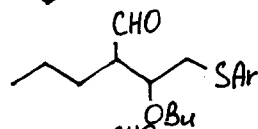
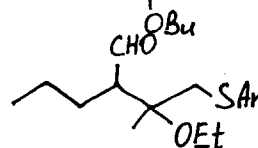
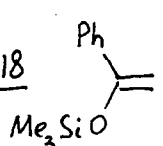
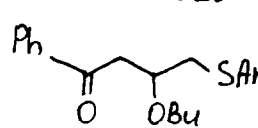
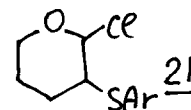
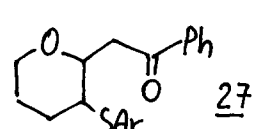
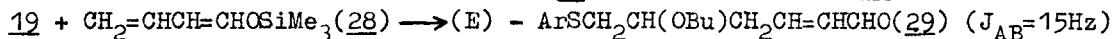


Table 1.

| Enol silyl ether | <u>19-21</u> | Product ¹¹ | Yield, % ⁷ |
|---|---|--|-----------------------|
| <u>2</u>  | $\begin{array}{c} \text{CH}_2\text{-CH-OBu} \\ \quad \\ \text{SAr} \quad \text{CE} \end{array}$ <u>19</u> |  | 89 |
| <u>2</u> | $\begin{array}{c} \text{CH}_2\text{-C-CH}_3 \\ \quad \\ \text{SAr} \quad \text{CE} \end{array}$ <u>20</u> |  | 75 |
| <u>17</u>  | <u>19</u> |  | 95 |
| <u>17</u> | <u>20</u> |  | 90 |
| <u>18</u>  | <u>19</u> |  | 64 |
| <u>18</u> |  |  | 63 |

TMS enol ethers of $\alpha\beta$ -unsaturated carbonyl compound can also be used in this reaction. Thus 28 is alkylated by 19 giving 1,4-adduct 29 exclusively.



These examples clearly demonstrate the scope of the reaction. Thus it is possible to carry out stereoselectively all four types of cross aldol condensation: aldehyde-aldehyde (17+19); aldehyde-ketone (17+20); ketone-aldehyde (18+19); ketone-ketone (2+20).¹² The presence of arylthio group in the adducts opens additional possibilities for their use in the synthesis.

Hence we have shown that the reaction of silyl enol ethers with β -halogenoalkyl aryl sulfides can be used as fairly general method for the transformation of carbonyl compounds and alkenes into polyfunctional molecules (Scheme 1). High regio- and stereospecificity (as regards to alkene precursor) of this process is evidently ensured by the intermediate formation of ESIs or ESI-like species.

REFERENCES

1. For leading references see: E.W.Colvin, *Chem.Soc.Rev.*, 1978, 7, 15.
2. G.H.Schmid "Electrophilic Addition to Carbon-Carbon Bonds", in "The Chemistry of Double Bonded Functional Groups", S.Patai, ed.J.Wiley, 1977, Ch.9.
3. W.A.Smit, N.S.Zefirov, I.V.Bodrikov, M.Z.Krimer. *Acc.Chem.Res.*, 1979, 12, 282.
4. M.A.Ibragimov, W.A.Smit, A.S.Gybin, M.Z.Krimer. *Izv.Acad.Nauk SSSR, ser. chim.*, 1981, 1929.
5. All β -halogenoalkyl aryl sulfides were prepared by Ad_E -reaction of respective alkene with ArSX , $\text{Ar}=4\text{-ClC}_6\text{H}_4$, for all cases except 4,6 ($\text{Ar}=2,4,6\text{-Me}_3\text{C}_6\text{H}_2$) and 5,7 ($\text{Ar}=4\text{-MeC}_6\text{H}_4$).⁶ If necessary the isomerisation of the initial anti-Markovnikov adduct into Markovnikov isomer was carried out as described by A.S.Gybin et al., *Zh.Org.Khim.*, 1979, 15, 1361.
6. For the preparation of this salt and its NMR-data see A.S.Gybin et al., *Izv.Akad.Nauk SSSR, ser.chim.*, 1978, 2156.
7. All yields refer to the purified products. The structures shown are ascertained by spectral (NMR, MS) and analytical data.
8. W.A.Smit, M.Z.Krimer, E.A.Vorob'eva, *Tetrahedron Lett.*, 1975, 2451; *Izv. Akad.Nauk SSSR, ser.chim.*, 1976, 2743.
9. Adduct 14 was prepared according to T.R.Cerksus, V.M.Csizmada, G.H.Schmid, T.T.Tidwell, *Can.J.Chem.*, 1978, 56, 205. These authors point to the easiness of the rearrangement of 14.
10. These adducts are unstable and were used immediately, after preparation from vinyl ethers (cf.data by K.Toyoshima, T.Okuyama, T.Fueno. *J.Org.Chem.*, 1978, 43, 2789).
11. In all cases except 26,27 the products were 1:1 mixture of diastereoisomers.
12. For the use of TMS enol ether in cross aldol condensation see S.Murata, M.Suzuki, R.Noyori, *J.Am.Chem.Soc.*, 1980, 102, 3248 and references given therein.

(Received in UK 6 December 1982)