Tetrahedron Letters,Vol.26,No.23,pp 2787-2788,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

ALKYLATION OF AROMATIC COMPOUNDS WITH PUMMERER REARRANGEMENT INTERMEDIATES. APPLICATION TO THE PREPARATION OF METHYL-ARYL COMPOUNDS

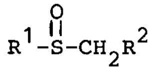
Ioannis K. Stamos

The National Hellenic Research Foundation, 48 V. Konstantinou Ave.,
Athens 11635, Greece.

Abstract: Pummerer intermediates generated from dimethylsulfoxide reacted with aromatic compounds in the presence of tin(IV) chloride to give methylthiomethylaryl products which were in turn desulfurized to methylaryl compounds with Raney-Ni.

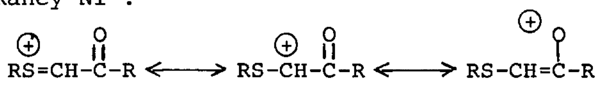
We have recently reported a mild reaction of Pummerer rearrangement intermediates (2), generated from sulfoxides which were activated in the α-position by a carbonyl or cyano-group (1), with aromatic compounds in the presence of Lewis acids[1]. We have now extented this reaction further[2] to cover such simple sulfoxides as the dimethylsulfoxide, $R^1=CH_3$, $R^2=H$, which is devoid the synergetic effect of a carbonyl group to the acidity of its hydrogens as well as the contribution of structure 2c to the stability of the Pummerer intermediates[3]. Alkyl or alkylaryl sulfoxide derivatives have been used for alkylations under Pummerer reaction conditions with limited success, but they have been exploited nicely in intramolecular cases toward the total synthesis of indole alkaloids. Whereas the substrates in these reactions were somewhat activated the reaction conditions were rather vigorous[4].

In this attempt we have used either $(COCl)_2$, Me_3SiCl, or $(CF_3CO)_2O$ as the sulfoxide "activator" in combination with either $Et_2O.BF_3$, $TiCl_4$, or $SnCl_4$ as the Lewis acid and phenanthrene as the aromatic substrate with mixed results. Among the above the combination of $(CF_3CO)_2O$ with $SnCl_4$ is the best choice[5,6]. Consequently these conditions were applied on the other substrates used, and the results are summarized in the table. The sulfides were desulfurized to arylmethyl compounds with Raney-Ni[7].



$R^1\text{-}\overset{O}{\overset{||}{S}}\text{-}CH_2R^2$

(1)

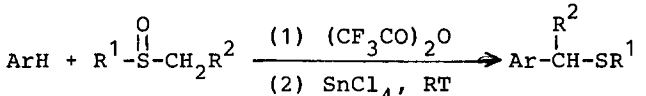


$R\overset{\oplus}{S}=CH\text{-}\overset{O}{\overset{||}{C}}\text{-}R \longleftrightarrow R\overset{\oplus}{S}\text{-}CH\text{-}\overset{O}{\overset{||}{C}}\text{-}R \longleftrightarrow RS\text{-}CH=\overset{\overset{\oplus}{O}}{C}\text{-}R$

(2a) (2b) (2c)

R^1=alkyl, R^2=carbonyl, CN

It would be of interest to see the described reaction applicable to the



$$\underset{(3)}{ArH} + \underset{(1)}{R^1-\overset{O}{\overset{\|}{S}}-CH_2R^2} \xrightarrow[(2)\ SnCl_4,\ RT]{(1)\ (CF_3CO)_2O} \underset{(4)}{Ar-\overset{R^2}{\overset{|}{C}}H-SR^1}$$

R^1=Me, R^2=H

TABLE

AROMATIC COMPOUND	SOLVENT	REACTION TIME, Hr	ARYLMETHYL METHYL SULFIDE (4), Ar	YIELD %
1. Phenanthrene	CH_2Cl_2	10.5	9-Phenanthryl	80
2. Benzene	Benzene	10.5	Phenyl	62
3. Naphthalene	CH_2Cl_2	10	1-Naphthyl	74
4. Toluene	Toluene	8	4-Methylphenyl	62
5. Isobutylbenzene	CH_2Cl_2	12	4-Isobutylphenyl	64
6. 1,3-Diisopropylbenzene	CH_2Cl_2	12	3,5-Diisopropylphenyl	58
7. Ethylbenzene	$C_6H_5-C_2H_5$	11	4-Ethylphenyl	67
8. t-Butylbenzene	CH_2Cl_2	4	4-t-Butylphenyl	62
9. p-Xylene	CH_2Cl_2	9.5	2,5-Dimethylphenyl	60
10. Ethyl Benzoate	CH_2Cl_2	10	Carbethoxyphenyl	0

sulfoxides of β-lactam antibiotics and to the family of thiazepine sulfoxides. We are investigating this possibility[8].

Typical experiment: To a solution of the aromatic compound (10 mmol) and the dry DMSO 1.01 g (13 mmol) in 20-30 ml of dry CH_2Cl_2 under argon, cooled in an ice-water bath, was added dropwise with a syringe 1.84 ml (13 mmol) of $(CF_3CO)_2O$. After about an hour 1.3 ml (11 mmol) of $SnCl_4$ was added dropwise with a syringe. The cooling bath was removed, and after completion of the reaction, the mixture was quenched with $H_2O-CHCl_3$ or $H_2O-C_6H_6$ and then basified with Na_2CO_3. The organic layer was washed with water, dried (Na_2SO_4), filtered through short column of silica gel, and the solvent removed. The product was purified by chromatography on silica gel (n-hexane or n-hexane-benzene mixtures) or distilled under vacuum (water pump).

REFERENCES AND NOTES

1. Ioannis K.Stamos, Tetrahedron Letters 26, 477(1985).
2. The reaction of Pummerer intermediates generated from α-halosulfoxides and methyl methylsulfinylmethyl sulfide will be reported elsewhere.
3. X.Creary, Acc.Chem.Res., 18, 3(1985) and references cited therein.
4. P.Magnus, T.Gallagher, P.Brown, and P.Pappalardo, Acc.Chem.Res., 17, 35(1984) and references cited therein. R.McCrindle, A.J.McAlees, and D.K.Stephenson, J.C.S.Perkin I, 3070(1981). D.K.Bates, J.Org.Chem., 42, 3452 (1977).
5. When methylphenylsulfoxide was used instead, the reaction failed. In an attempt to generate the reactant $C_6H_5SCH_2OSiMe_3$ (E.Vedejs and M.Mullins, Tetrahedron Letters, 2017 (1975)), using excess of LDA and of Me_3SiCl, in a solution of methylphenylsulfoxide in THF, the reaction led to formation of species assigned tentatively as the $C_6H_5SCSiMe_3(OSiMe_3)Li$ which decomposes. These results warrant further investigation.
6. The reaction mixture turns from faint yellow to pale pink and eventually to pale red during the reaction time. When the mixture turns to red shortly after the addition of $SnCl_4$ and then red-brown, the yield drops to 62%.
7. R.E.Ireland J.A.Marshall, J.Org.Chem., 27, 1615(1962). L.N.Mander and P.H.C. Mundill, Synthesis, 620(1981). R.Mozingo, Org.Synth., Coll.Vol.III, 181(1955).
8. G.A.Koppel and L.J.McShane, J.Am.Chem.Soc., 100, 288(1978). C.U.Kim, et.al., J. Med.Chem., 27, 1226(1984). R.D.G.Cooper, G.A.Koppel in "Chemistry and Biology of β-Lactam Antibiotics", Vol. I, edited by R.B.Morin and M.Gorman, Academic Press, 1982.

(Received in UK 11 April 1985)