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MILD REACTION OF PUMMERER REARRANGEMENT PRODUCTS WITH AROMATIC COMPOUNDS IN THE PRESENCE OF LEWIS ACIDS. APPLICATION TO THE PREPARATION OF ARYLMETHYLENE KETONES,[22] ARYLACETOESTERS, AND ARYLACETONITRILES.

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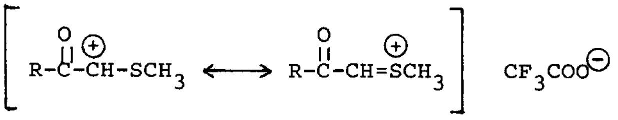
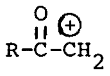
Abstract: Pummerer intermediates generated from precursors (3), (4) and (5) reacted mildly with aromatic compounds in the presence of Lewis acids to give the corresponding sulfides which in turn desulfurized to arylmethylene ketones, arylacetoesters, and arylacetonitriles.

Pummerer rearrangement products such as (1) the equivalent of (2) from β-ketosulfoxides have been involved in a variety of preparations in recent years. They have been exploited mostly in intramolecular reactions with aromatic and olefinic π-bonds[1-6]. Their use though to initiate intermolecular reactions has been limited to olefinic π-bonds[7-8], and only under refluxing conditions and continuous removal of separated water brought about an intermolecular aromatic substitution of ethyl α-(methylsulfinyl)acetate in the presence of p-toluenesulfonic acid[9]. Also analogous precursors had to be heated at 140°C to initiate aromatic substitution, if they initiated at all[10].



$$\left[R-\overset{O}{\overset{\|}{C}}-\overset{\oplus}{C}H-SCH_3 \longleftrightarrow R-\overset{O}{\overset{\|}{C}}-CH=\overset{\oplus}{S}CH_3 \right] CF_3COO^{\ominus}$$

(1)

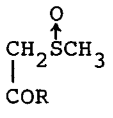


$$R-\overset{O}{\overset{\|}{C}}-\overset{\oplus}{C}H_2$$

(2)

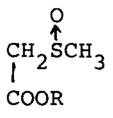
We wish to report herein that these Pummerer intermediates generated in situ from the representative precursors depicted by (3), (4), and (5) react with a variety of aromatic compounds at 0°C or below in the presence of Lewis acids such as $TiCl_4$ and $SnCl_4$ to give high yields of sulfides such as (7). The $BF_3.OEt_2$ gave poor yields and only the $TiCl_4$ worked well in the case of precursor (5). We have to point out here that the reaction is quite sensitive to

(3)



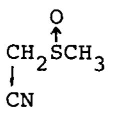
$$\underset{COR}{\underset{|}{CH_2}}\overset{O}{\overset{\uparrow}{S}}CH_3$$

(4)

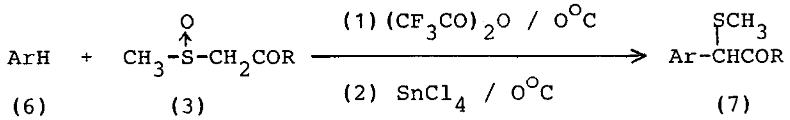


$$\underset{COOR}{\underset{|}{CH_2}}\overset{O}{\overset{\uparrow}{S}}CH_3$$

(5)



$$\underset{CN}{\underset{|}{CH_2}}\overset{O}{\overset{\uparrow}{S}}CH_3$$



$$\underset{(6)}{ArH} + \underset{(3)}{CH_3\overset{\overset{O}{\uparrow}}{S}CH_2COR} \xrightarrow[(2)\ SnCl_4\ /\ 0^{o}C]{(1)\ (CF_3CO)_2O\ /\ 0^{o}C} \underset{(7)}{Ar\text{-}\overset{\overset{SCH_3}{|}}{C}HCOR}$$

the rate of addition of Lewis acids at least at the temperature of $0^{o}C$[15]. The best results we obtained was when the Lewis acid was added dropwise through the needle of a syringe.

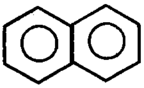
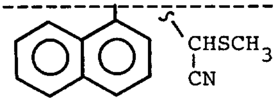
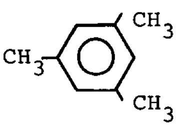
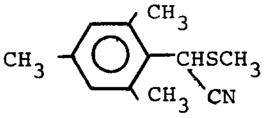
All the sulfides listed on the table were obtained in satisfactory purity for the next step after filtration through a column of silica gel using n-hexane-benzene mixtures. They were desulfurized in high yields using Zn-Cu couple[2]. This method though gave moderate or poor yields of products in the case of sulfides having chloro- and cyano-groups. We have not at present tried to improve these yields using other desulfurized methods which are reported in the literature to give more satisfactory results[11-14,1,4b,5a].

A typical experiment follows: To a stirred solution of the aromatic compound (10 mmol) and the chosen sulfoxide (11 mmol) in 35-40 ml of dry dichloromethane[16] under argon atmosphere, cooled at $0^{o}C$, was added dropwise with a syringe in 5 minutes 1.55 ml (11 mmol) of trifluoroacetic anhydride. After 3 to 5 minutes 1.10 ml (10 mmol) of titanium(IV) chloride[17] was added dropwise through a needle of a syringe in 5 minutes. The coloured reaction mixture was stirred for about 30 minutes, at $0^{o}C$, poured into water and extracted with chloroform or benzene with or without previous neutralization with sodium hydrogen carbonate. The organic layer was washed with dilute sodium hydrogen carbonate solution, dried (Na_2SO_4) and evaporated.

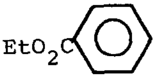
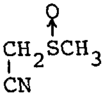
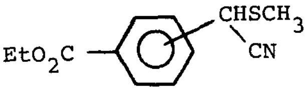
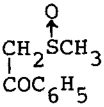
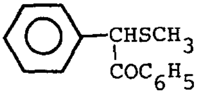
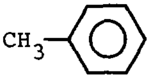
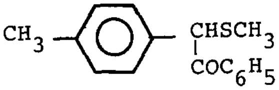
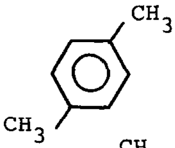
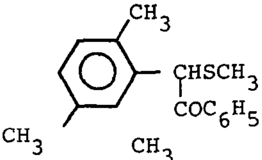
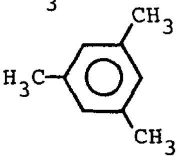
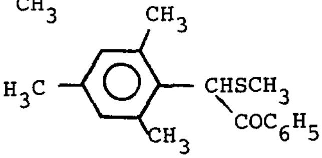
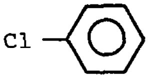
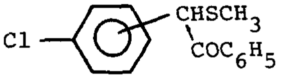
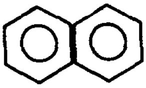
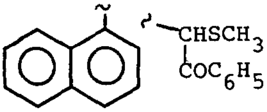
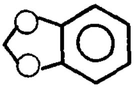
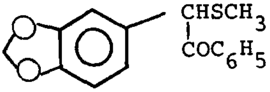
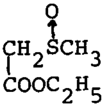
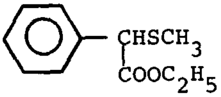
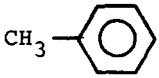
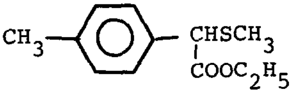
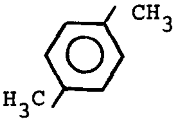
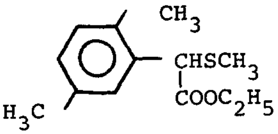
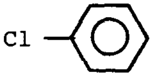
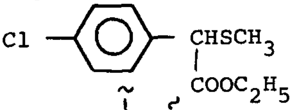
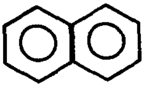
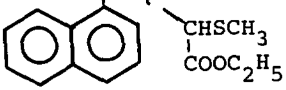
Given the easy access to the precursors of Pummerer products this method appears to be practical and therefore attractive for the preparation of compounds mentioned above. For example, a number of β-ketosulfoxides such as (3) can easily be prepared from an ester and (methylsulfinyl)methyllithium[18].

We are currently investigating analogous reactions of Pummerer intermediates generated from sulfoxides as simple as the dimethylsulfoxide using trifluoroacetic anhydride as well as other activators with or without the presence of a base[19,20,21].

TABLE

AROMATIC COMPOUND	PUMMERER PRECURSOR	SOLVENT	LEWIS ACID	REACTION TIME, MIN.	TEMPERATURE, C^{O}	SULFIDE	YIELD, %
	$\underset{CN}{\underset{\mid}{C}}H_2\overset{\overset{O}{\uparrow}}{S}CH_3$	$CHCl_3$	$TiCl_4$	120	0		91
	"	"	"	60	0		97

T A B L E (continued)

	 $\underset{CN}{CH_2}\overset{\overset{O}{\uparrow}}{S}CH_3$	$CHCl_3$	$TiCl_4$	120	0		0
	 $\underset{COC_6H_5}{CH_2}\overset{\overset{O}{\uparrow}}{S}CH_3$	$C_6H_6/1$ $CH_2Cl_2/5$	$SnCl_4$	30	0		quant.
	"	CH_2Cl_2	"	30	0		92
	"	"	"	30	0		quant.
	"	"	"	30	0		98
	"	"	"	30--- 0 60--- RT			o:p 1:3 77
	"	"	"	30	0		quant.
	"	"	"	30	T<0		90
	 $\underset{COOC_2H_5}{CH_2}\overset{\overset{O}{\uparrow}}{S}CH_3$	C_6H_6	"	30----0 60----RT			quant.
	"	$C_6H_5CH_3$	"	20--- 0 20--- RT			99
	"	xylene/2 $CH_2Cl_2/1$	"	30--- 0 30--- RT			98
	"	ClC_6H_5	"	120	RT		83
	"	CH_2Cl_2	"	10--- 0 20--- RT			95

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15. In an experiment of (3) $R=C_6H_5$, with phenanthrene the reaction took place even as low as -70°C and completed at -30°C but in longer reaction time (3 hours), gave two products identical with the ones which were obtained when the reaction was run at 0°C, according to TLC.
16. In the experiment with 1,3-benzodioxole the whole reaction mixture solidified, so the amount of dichloromethane was increased to 90 ml.
17. The use of stoichiometric amounts of Lewis acid yielded optimum results.
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21. (a).The reaction described in this communication was first explored during our effort towards the total synthesis of hydroxy-ergot alkaloids and applied successfully in the formation of the C-ring (that is an intramolecular case), enabling us in this way to follow a short cut pathway for the preparation of 4-keto-tricyclic ketones (J.M.Cassady, G.S.Li, E.B. Spitzner, H.G.Floss, and J.A.Clemens, J.Med.Chem.,17, 300(1974)) commencing with the known methoxyindole-3-acetate esters.
   These results as well as the reaction of Pummerer intermediates (see also ref. 19) with O-silylated enolates (I.Paterson and I.Fleming, this Journal 993, 995 (1979); P.Brownbridge, and T-H. Chan, this Journal, 3423(1980))in the presence of sterically hindered trialkylamine base and then Lewis acid will be reported in an other account.

   (b). In preliminary experiments, these generated Pummerer intermediates from α-activated sulfoxides, in the presence of Lewis acid gave us cycloaddition products with olefins and alkynes. By extension, manipulating the use of Lewis acid and of trialkylamine base gave us also cyclization products with conjugated dienes.
22. The Chemical Abstracts use also the name 2-Aryl-ethanones for these ketones.

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