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α-PHOSPHORYL SULPHOXIDES AND SULPHONES: NEW CATALYSTS IN TWO-PHASE ALKYLATION OF KETONES

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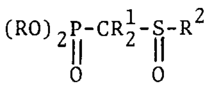
Aqueous organic two-phase reactions catalyzed by either onium salts[1] or crown ethers[1] and cryptands[3] are of great synthetic value. The Horner-Wittig reaction of α-phosphoryl sulphoxides, sulphones and sulphides can successfully be performed in such a way in the presence of the above mentioned catalysts[4]. However, the presence of the catalyst has recently been shown[5] to be unnecessary for the reaction to proceed, and this prompted us to investigate the use of α-phosphoryl sulphoxides, sulphones and sulphides I - IV as catalysts in other anion promoted reactions in two-phase systems. The use of α-disulphoxides and bisphosphonates, which have a structure comparable to that of α-phosphoryl sulphoxides, was also studied.



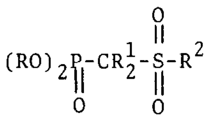
$(RO)_2\underset{O}{\underset{\|}{P}}-CR^1_2-\underset{O}{\underset{\|}{S}}-R^2$

Ia, $R=Et$, $R^1=H$, $R^2=Ph$

Ib, $R=Et$, $R^1=H$, $R^2=Me$

Ic, $R=Me$, $R^1=H$, $R^2=Ph$

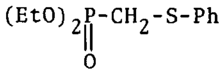
Id, $R=Me$, $R^1=H$, $R^2=Me$



$(RO)_2\underset{O}{\underset{\|}{P}}-CR^1_2-\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}-R^2$

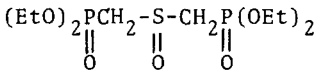
IIa, $R=Et$, $R^1=H$, $R^2=Ph$

IIb, $R=Et$, $R^1=Me$, $R^2=Ph$



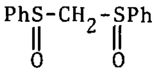
$(\mathrm{EtO})_2\underset{\overset{\|}{\mathrm{O}}}{\mathrm{P}}-\mathrm{CH}_2-\mathrm{S}-\mathrm{Ph}$

III



$(\mathrm{EtO})_2\underset{\overset{\|}{\mathrm{O}}}{\mathrm{P}}\mathrm{CH}_2-\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}-\mathrm{CH}_2\underset{\overset{\|}{\mathrm{O}}}{\mathrm{P}}(\mathrm{OEt})_2$

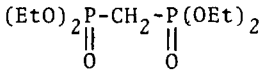
IV



$\mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}-\mathrm{CH}_2-\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{Ph}$

Va, meso form

Vb, dl form



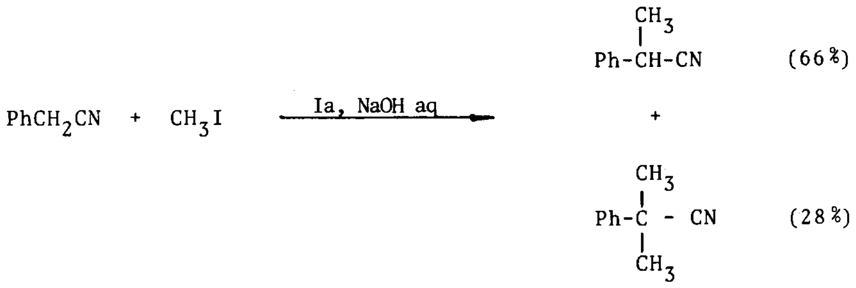
$(\mathrm{EtO})_2\underset{\overset{\|}{\mathrm{O}}}{\mathrm{P}}-\mathrm{CH}_2-\underset{\overset{\|}{\mathrm{O}}}{\mathrm{P}}(\mathrm{OEt})_2$

VI

We have found that compounds I, II, IV, V, VI are effective catalysts in the alkylation of ketones by alkyl halides in the presence of aqueous 50% (w./w.) NaOH. Among the α-phosphoryl sulphoxides used, compound Ia, the most organophilic, is the best catalyst, so that sulphones IIa and IIb, of analogous structure, were chosen for a comparison[6]. However, sulphide III is not effective in promoting the reaction. The results of alkylation of benzyl methyl ketone are reported in Table.

When sulphoxide Ia is used as a catalyst, the order of reactivity of alkyl halides is MeI>EtI>n-BuI and n-BuI>n-BuBr>>n-BuCl. In the case of benzyl methyl ketone, mono-alkylation largely predominates over di-alkylation even when the alkyl halide is very reactive. However, when acetophenone is the substrate, reaction with methyl iodide at room temperature in the presence of Ia (0.05 mol for mol of ketone) affords mainly the product of di-alkylation. When two moles of methyl iodide per mol of ketone are used, after 18 h a mixture of iso-propyl phenyl ketone (69%) and ethyl phenyl ketone (13%) is obtained. In the same conditions alkylation of phenyl ethyl ketone by methyl iodide (1:1 molar ratio) affords after 5 h iso-propyl phenyl ketone in 95% yield. Alkylation of simple aliphatic ketones such as di-n-propyl ketone or cyclohexanone is much slower.

α-Phosphoryl sulphoxide Ia is an effective catalyst also in the alkylation of phenyl acetonitrile. Thus, the reaction of phenyl acetonitrile (1 mol) and methyl iodide (1.3 mol) carried out in the presence of Ia (0.05 mol) at room temperature under the two-phase conditions (50% NaOH) afforded after 2 h a mixture of mono- and di-alkylated products in a 3:1 ratio.



$$\mathrm{PhCH_2CN} + \mathrm{CH_3I} \xrightarrow{\text{Ia, NaOH aq}} \mathrm{Ph{-}\overset{CH_3}{CH}{-}CN}\ (66\%) + \mathrm{Ph{-}\underset{CH_3}{\overset{CH_3}{C}}\ {-}\ CN}\ (28\%)$$

TABLE. Alkylation of benzyl methyl ketone by alkyl halides and aqueous NaOH at room temperature

Alkyl Halide	Catalyst [a]	Time/h	Yield [b]
CH_3I	I a	0.1	95 [c]
C_2H_5I	I a	0.25	93
"	VI	0.25	97
"	V a	0.5	100
"	V b	0.5	100
$\underline{n}$-C_4H_9I	I a	1	91
"	IV	1	75
"	II a	1	92
"	II b	1	79
"	V a	3	91
"	V b	3	92
$\underline{n}$-C_4H_9Br	I a	5	91
"	I c	7	86
"	I b	7	78
"	I d	24	69
$\underline{n}$-C_4H_9Cl	I a	8	0

[a] 0.05 mol per mol of ketone [b] yields refer to mono-alkylated product

[c] 5 % of di-alkylated product was detected

On the contrary neither the halogen exchange reaction of n-$C_8H_{17}Br$ with potassium iodide nor the reaction of n-$C_8H_{17}Br$ with cyanide ion are catalyzed by α-phosphoryl sulphoxides.

It must be emphasized that α-phosphoryl sulphoxides and sulphones as well as α-disulphoxides and bisphosphonates represent a new class of catalysts for two-phase reactions, with a structure completely different from that of other catalysts (onium salts, macrocyclic ethers) used up to now. Particularly noticeable is the fact that they have a specific action in alkylation of activated substrates.

Further research on the application and mechanism of the action of the α-phosphoryl derivatives is in progress.

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5. M.Mikolajczyk, S.Grzejszczak, W.Midura and A.Zatorski unpublished results
6. Sulphone IIb was obtained by alkylation of IIa under the two-phase reaction conditions; M.Mikolajczyk, M.Cinquini and S.Grzejszczak unpublished results.