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NUCLEOPHILIC FORMYLATION OF NITROARENES VIA VICARIOUS SUBSTITUTION OF HYDROGEN WITH TRISPHENYLTHIOMETHANE [1)]

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Carbanion of phenyl trithioorthoformate reacts with nitroarenes according to the vicarious substitution scheme replacing hydrogen in the para position to the nitro group. The reaction offers a new method of nucleophilic formylation of nitroarenes.

The vicarious nucleophilic substitution of hydrogen in nitroarenes was shown to be a general and versatile method of introduction of α-functionalized alkyl substituents into these molecules.[2)]

Direct introduction of formyl functionality or its equivalent into organic molecules is of great interest. Although numerous methods of direct formylation of arenes via electrophilic attack are known, [3)] they can not be applied to nitroarenes. We have therefore attempted to find such possibility for nitroarenes via the vicarious nucleophilic substitution of hydrogen. According to the stoichiometry of this process direct formylation of nitroarenes would require use of a carbanion equivalent of the oxycarbonyl carbanion $-O-\bar{C}=O$.

The most feasible equivalent of this anion seems the carbanion of trisphenylthiomethane $\underline{1}$. It can be easily generated by deprotonation of $\underline{1}$ since its acidity is in a convenient range, $pK_a=22.8$ [4)] and it possesses substituents known as efficient leaving groups.

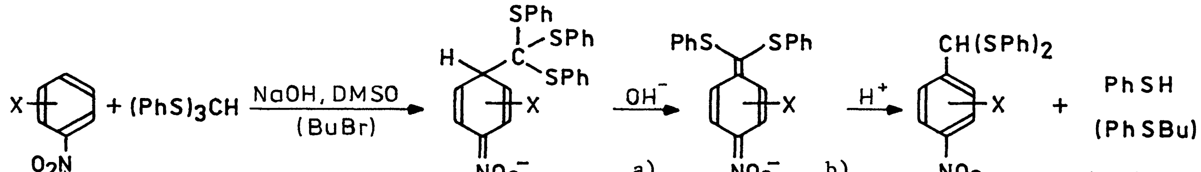
Indeed $\underline{1}$ reacts with nitrobenzene (and some of its derivatives) in the presence of powdered NaOH in DMSO yielding diphenyldithioacetal of p-nitrobenzaldehyde (Table 1).

The carbanion of $\underline{1}$ is extremely bulky so it reacts with nitroarenes exclusively at the para position. When this position is occupied, as for example in p-nitrobiphenyl, the reaction does not take place. The steric demands of $\underline{1}^-$ are so significat that substituents in the meta position to the nitro group - thus ortho to the reaction site - often impede the reaction. As a consequence the reaction proceeds satisfactorily mainly with nitrobenzene and its ortho substituted derivatives and also with 1-nitronaphthalene.

The PhS^- anion produced during the reaction is a powerful nucleophile so o-chloro-, and o-fluoronitrobenzene are converted into dithioacetal of 3-phenylthio-4-nitrobenzaldehyde. In order to eliminate this undesirable process one should remove the PhS^- anions from the reaction mixture. It can be attained by the addition of moderately active alkylating agent e.g. butyl bromide which reacts rapidly with PhS^- giving butyl phenyl sulfide thus preventing thesubstitution of halogen in the nitroaromatic ring.

Typical experimental procedure is as follows: <u>1</u> (3.4 g, 10 mmol), nitroarene (10 mmol), powdered NaOH (4 g, 100 mmol) and (when indicated) butyl bromide (2.7 g, 20 mmol) in DMSO (20 mL) where stirred at the room temp for 6 h. The mixture was poured into ice, acidified and extracted with methylene chloride. The products were purified by recrystallization or column chromatography on silica gel.

Table 1.



	Nitroarene X	Product X	Yield [a)] %	Mp [b)] °C	NMR, $C\underline{H}(SPh)_2$ ppm
1.	H	H	57	98-99.5 [c)]	5.4
2.	2-PhS	2-PhS	65		
3.	2-F	2-PhS	46	120-122	5.1
4.	2-Cl	2-PhS	32		
		2-Cl	22		
5.	2-Cl	2-Cl [d)]	44	61-62.5	5.3
6.	2-F	2-F [d)]	23	77-79	5.3
7.	3-Cl	3-Cl	15	oil	5.9
8.	C_4H_4 [e)]	C_4H_4 [e)]	45	102-104	6.1

[a)] Yields of isolated compounds. [b)] All new compounds gave satisfactory elemental analysis. [c)] Lit. mp 100 °C, Y.Le Floc'h, A.Brault, and M.Kerfanto, C.R.Acad Sci., <u>268</u>, 1718 (1969). [d)] The reaction was carried out in the presence of butyl bromide. [e)] 1-Nitronaphthalene.

The dithioacetals can be easily hydrolyzed to corresponding aldehydes [5)] or converted into nitroaryl ketones. For example alkylation of 4-nitrobenzaldehyde diphenyldithioacetal with an excess of benzyl chloride (K_2CO_3, acetonitrile, $Bu_4N^+Br^-$, reflux) give directly 4-nitrophenylbenzyl ketone, yield 74%.

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References

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