

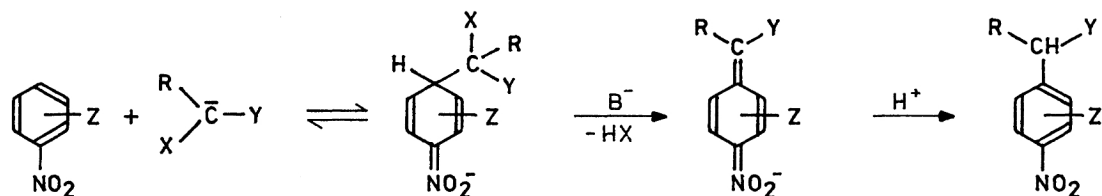
REACTIONS OF CHLOROMETHYL PHENYL SULFONE CARBANION WITH
NITROBENZOPHENONES. THE VICARIOUS SUBSTITUTION OF HYDROGEN
versus THE DARZENS CONDENSATION ¹⁾

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Carbanion of chloromethyl phenyl sulfone replaces hydrogen atoms o'- and p- to the nitro group in o-nitrobenzophenone, whereas with p-nitrobenzophenone it enters the Darzens condensation followed by rearrangement and decarbonylation. Reaction course with m-nitrobenzophenone depends on the conditions (base concentration). When an excess of a base is present the vicarious substitution of hydrogen takes place whereas low concentration of a base favours the Darzens condensation.

The vicarious nucleophilic substitution of hydrogen which proceeds according to Scheme 1 is a process of general character and significant potential value for organic synthesis.²⁻⁴⁾



X-leaving group, Y-carbanion stabilizing group, R-substituent

Scheme 1.

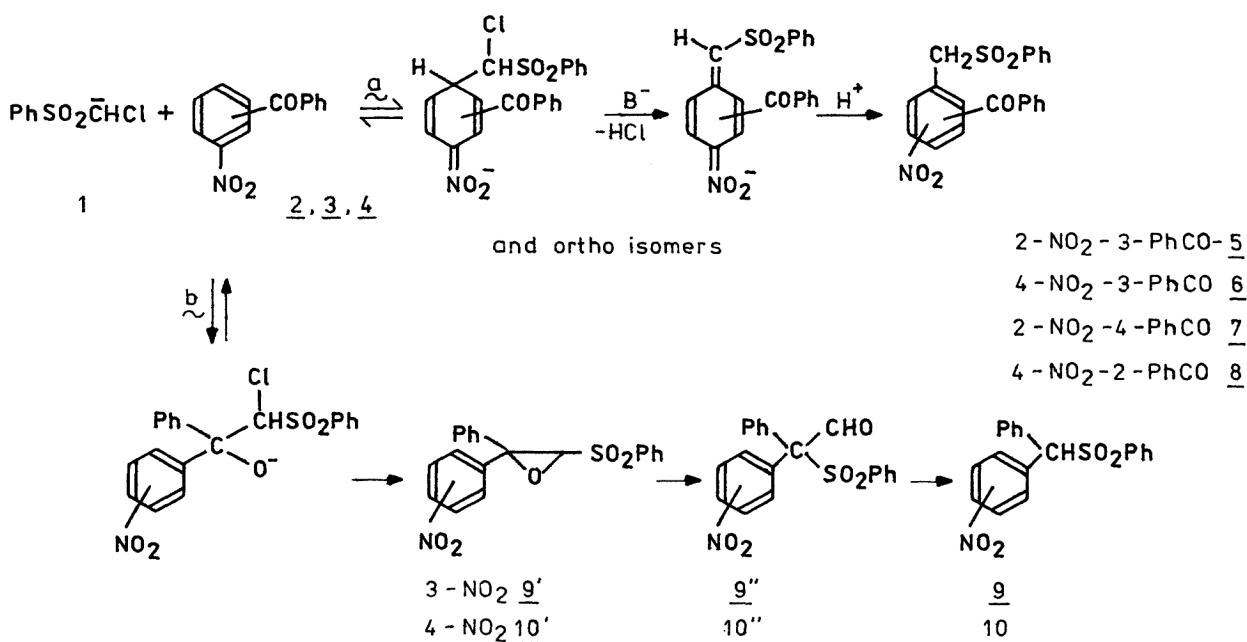
The crucial assumption made in designing this reaction was that in mononitroarenes, similarly to polynitroarenes,⁵⁾ nucleophilic addition at the ortho/para positions occupied with hydrogen is much faster than at those occupied by leaving groups (e.g. halogens).²⁻⁴⁾ This assumption was shown to be correct. As a rule the vicarious nucleophilic substitution of hydrogen with carbanions RCXY^- proceeds faster than substitution of a halogen located in equally activated positions, provided the system contains a sufficient excess of a base. An excess of a base is necessary to promote β -elimination from the intermediate σ -complex.⁶⁾

In this connection reactions of chloromethyl phenyl sulfone 1 with o-, m-, and p-nitrobenzophenones 2, 3, and 4 correspondingly are of great interest. Here carbanion 1⁻ can add to: a. the ortho/para positions to the nitro group resulting in the vicarious substitution of hydrogen, b. the carbonyl group to form the chlorohydrine anion and subsequently the oxirane (the Darzens reaction), c. the carbon atom bearing the nitro group (in the case of 2 and 4) which would result in the

nitro group replacement.⁷⁾ The last reaction was not observed in the present studies. Considering reversibility of both these additions a. and b., and also taking into account that the vicarious substitution of hydrogen proceeds via base induced β -elimination of HCl from the σ complexes the reaction course of $\underline{1}^-$ with $\underline{2}$, $\underline{3}$, and $\underline{4}$ should be a compromise of several factors.

Reaction of $\underline{1}^-$ with $\underline{2}$ (KOH, DMSO) results in the vicarious substitution of hydrogen ortho- and para- to the nitro group giving 3-benzoyl-2-nitrobenzyl and 3-benzoyl-4-nitrobenzyl phenyl sulfones $\underline{5}$ and $\underline{6}$ (path a), on the other hand reaction of $\underline{1}^-$ with $\underline{4}$ (KOH, NH_3 liq.) gave as the main final product 4-nitrobenzhydryl phenyl sulfone $\underline{10}$.⁸⁾ This compound is formed via the addition of $\underline{1}^-$ to the carbonyl group followed by the cyclization to the oxirane $\underline{10}'$ (the Darzens reaction), its subsequent rearrangement to $\underline{10}''$ and decarbonylation giving $\underline{10}$.

Similar transformations of α -arylsulfonyl oxiranes were already reported.⁹⁾



The course of these reactions of $\underline{1}$ with $\underline{2}$ and $\underline{4}$ is not altered when the conditions (solvent and base) are changed, although in the former case the ratio ortho versus para substitution is somewhat changed.

The most interesting case is the reaction of $\underline{1}^-$ with $\underline{3}$, here the vicarious substitution of hydrogen (path a) and the Darzens condensation (path b) compete. In the former process two of the three possible isomeric products $\underline{7}$ and $\underline{8}$ are formed. The ratio between path a and b is strongly affected by the conditions. When an excess of a soluble base is used (MeONa in DMSO) the reaction proceeds practically exclusively along path a, on the other hand in the catalytic two-phase system, where the carbanion of $\underline{1}$ is the only base present in the organic phase¹⁰⁾ the Darzens condensation dominates. Similarly as in the case of the reaction of $\underline{1}^-$ with $\underline{4}$ the oxirane $\underline{9}'$ is rather unstable, it undergoes rearrangement to $\underline{9}''$ and subsequent decarbonylation, so that benzhydryl sulfone $\underline{9}$ is the isolated product. Nevertheless in both these cases (the reaction of $\underline{1}^-$ with $\underline{2}$ and $\underline{4}$) the intermediate formation of $\underline{9}'$, $\underline{10}'$ and $\underline{9}''$ and $\underline{10}''$ is strongly evidenced. Although we have not

made attempts to isolate these compound in pure state we have observed that the ^1H NMR spectra of the crude products show presence of signals due to oxirane rings protons (for two geometric isomers of 9' and 10' at $\delta=4.42$, 4.51 and 4.41 and 4.49 ppm correspondingly). These signals disappear rapidly with simultaneous enhancement of the low field signals at $\delta=10.09$ and 10.06 ppm due to 9'' and 10'' correspondingly, characteristic for aldehyde protons. These signals gradually disappeared and so intensity of the benzhydryl protons $\delta=5.46$ and 5.33 ppm of 9 and 10 reached maximum. The results of the reaction of 1 with 2, 3, and 4 shown in Table 1.

Table 1.

Reactions of <u>1</u> with <u>2</u> , <u>3</u> , and <u>4</u>								Properties of products ^{b)}		
Conditions	Total yield ^{a)} %	Products ratio (%) vic. subst.; Darzens;						Mp °C	^1H NMR ^{c)} (ppm)	IR ^{d)} ν/cm^{-1}
<u>2</u> KOH/DMSO	53	<u>5</u>	42	<u>6</u>	58	0	<u>5</u>	160(EtOH)	4.72	1675
KOH/NH ₃ liq	29		60		40	0	<u>6</u>	175(EtOH)	4.40	1670
<u>3</u> KOH/DMSO	51	<u>7</u>	40	<u>8</u>	20	<u>9</u> 40	<u>7</u>	170(C ₆ H ₆)	4.96	1675
KOH/NH ₃ liq	62		27		7	66	<u>8</u>	166(C ₆ H ₆)	4.84	1680
MeONa/DMSO	52		71		29	0		C ₆ H ₁₄)		
CTP ^{e)}	81		13		5	82	<u>9</u>	123(EtOH)	5.46	-
<u>4</u> KOH/NH ₃	46		0		0	<u>10</u> 100	<u>10</u>	117(MeOH)	5.33	-
CTP ^{e)}	55		0		0	100				

^{a)} Yields of isolated products. ^{b)} All compounds gave satisfactory microanalyses. ^{c)} Signals of methylene or methine groups protons. ^{d)} Absorption of the carbonyl group. ^{e)} Catalytic - Two Phase System: 50% NaOH, CH₃CN, Bu₄N⁺HSO₄⁻.

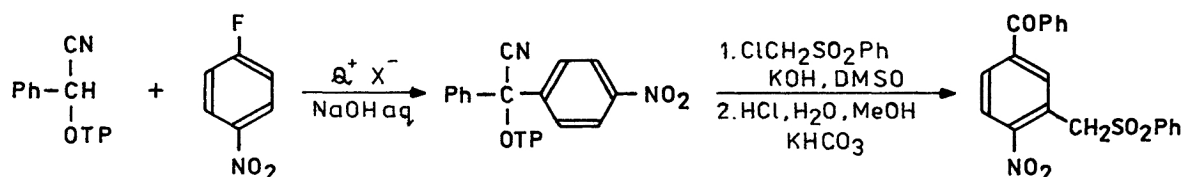
Typical experimental procedures: CTP - To a stirred mixture of 1 (1 mmol) and 3 or 4 (1 mmol), acetonitrile (4 mL) and aq. 50% NaOH (1 mL), tetrabutylammonium hydrogen sulfate (1 mmol) in acetonitrile (4 mL) was added dropwise during 1 h. The mixture was poured into 0.5 M HCl (30 mL), the products extracted with chloroform and purified by chromatography. KOH(MeONa)/DMSO(NH₃ liq)- as described earlier. ^{2,3)}

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- 8) The absence of the vicarious substitution product in the reaction of 1 with 4 was evidenced by the independent synthesis of the product according to the scheme:



TP-tetrahydropyranyl

mp 142 °C (EtOH)

(CH₂)4.92 ppm (CDCl₃)

The product was shown to be stable in the reaction conditions, the ¹H NMR spectrum of the crude mixture after the reaction of 1 with 4 does not contain signal at 4.92 ppm.

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