CHEMISTRY LETTERS, pp. 1619 - 1622, 1984.

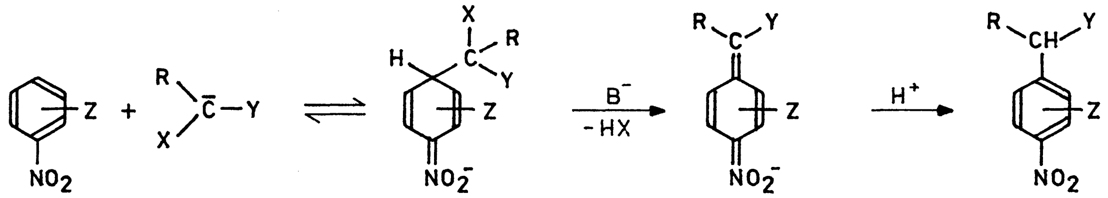
REACTIONS OF CHLOROMETHYL PHENYL SULFONE CARBANION WITH NITROBENZOPHENONES. THE VICARIOUS SUBSTITUTION OF HYDROGEN *versus* THE DARZENS CONDENSATION (1)

Mieczysław MĄKOSZA,* Jerzy GOLIŃSKI, Janusz BARAN,† and Danuta DZIEWOŃSKA-BARAN†

Institute of Organic Chemistry Polish Academy of Sciences, Warsaw, Poland
†Institute of Fundamental Chemistry, Technical University, Szczecin, Poland

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 concetration). 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 significat potential value for organic synthesis.(2-4)



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

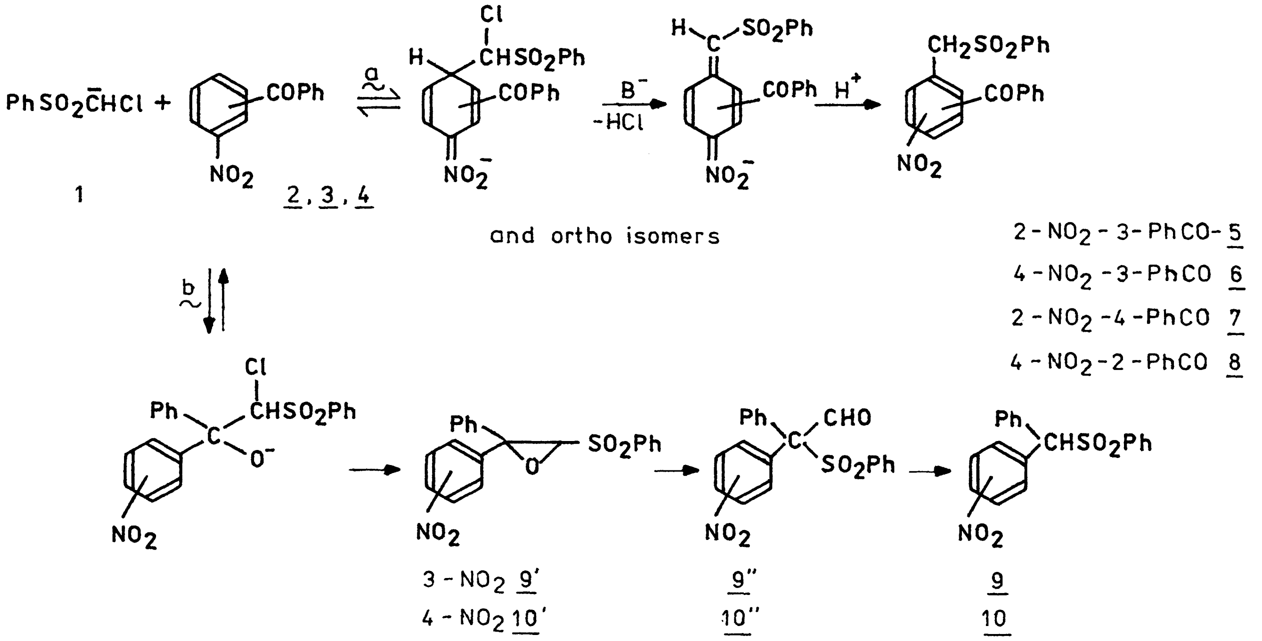
Scheme 1.

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 $R\bar{C}XY$ proceeds faster than substitution of a halogen located in equally activated positions, provided the system contains a sufficient ecess 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 <u>1</u> with o-, m-,and p-nitrobenzophenones 2, 3,and 4 correspondingly are of great interest. Here carbanion $\underline{1}^-$ 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 1^- with 2, 3, and 4 should be a compromise of several factors.

Reaction of 1^- with 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 5 and 6 (path a), on the other hand reaction of 1^- with 4 (KOH, NH_3 liq.) gave as the main final product 4-nitrobenzhdryl phenyl sulfone 10.8) This compound is formed via the addition of 1^- to the carbonyl group followed by the cyclization to the oxirane 10' (the Darzens reaction), its subsequent rearrangement to 10" and decarbonylation giving 10.

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



The course of these reactions of 1 with 2 and 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 1^- with 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 7 and 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 1 is the only base present in the organic phase10) the Darzens condensation dominates. Similarly as in the case of the reaction of 1^- with 4 the oxirane 9' is rather unstable, it undergoes rearrangement to 9" and subsequent decarbonylation, so that benzhydryl sulfone 9 is the isolated product. Nevertheless in both these cases (the reaction of 1^- with 2 and 4) the intermediate formation of 9', 10' and 9" and 10" is strongly evidenced. Although we have not made attempts to isolate these compound in pure state we have observed that the ^{1}H NMR spectra of the crude products show presence of signals due to oxirane rings protons (for two geometric isomers of 9' and 10' at δ=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 δ=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 δ=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 1 with 2,3, and 4						Properties of products[b]			
	Conditions	Total yield[a] %	Products ratio (%) vic. subst.; o-	p-	Darzens ;		Mp °C	^{1}H NMR[c] (ppm)	IR[d] ν/cm^{-1}
2	KOH/DMSO	53	5 42	6 58	0	5	160(EtOH)	4.72	1675
	KOH/NH$_3$ liq	29	60	40	0	6	175(EtOH)	4.40	1670
3	KOH/DMSO	51	7 40	8 20	9 40	7	170(C_6H_6)	4.96	1675
	KOH/NH$_3$ liq	62	27	7	66	8	166(C_6H_6 C_6H_{14})	4.84	1680
	MeONa/DMSO	52	71	29	0				
	CTP[e]	81	13	5	82	9	123(EtOH)	5.46	-
4	KOH/NH$_3$	46	0	0	10 100	10	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, CH_3CN, $Bu_4N^+HSO_4^-$.

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(NH$_3$ liq)- as described earlier.[2,3)]

This work was supported by the Grant MR-I.12.1.

References

1) Paper 115 of the Series Reactions of Organic Anions, Part 114: M.Mąkosza, T.Glinka, and J.Kinowski, Tetrahedron, 40, 1863 (1984).

2) J.Goliński and M.Mąkosza, Tetrahedron Lett., 1978, 3495.

3) M.Mąkosza and J.Winiarski, J.Org.Chem., 45, 1534 (1980); M.Mąkosza and J. Goliński, Angew.Chem., 94, 468 (1982); M.Makosza, J.Goliński, and J.Pankowski, Synthesis, 1983, 43; M.Mąkosza, J.Goliński, and J.Baran, J.Org.Chem., 49, 1488 (1984).

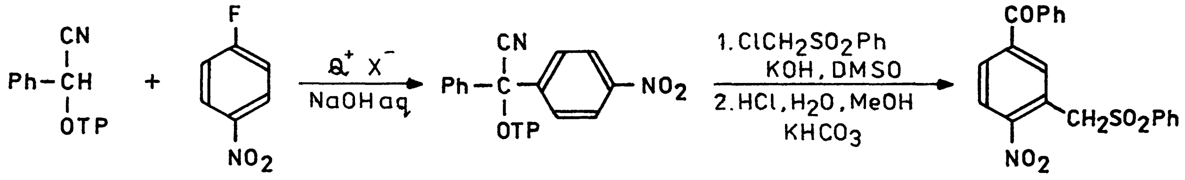
4) M.Mąkosza, "Current Trends in Organic Synthesis," ed by H.Nozaki, Pergamon Press. (1983), p. 401.

5) F.Terrier, Chem.Rev., 82, 77 (1982); G.A.Artamkina, M.P.Egorov, and I.P. Bieletskaya, ibid., 82, 427 (1982).

6) M.Mąkosza and T.Glinka, J.Org.Chem., 48, 3860 (1983).

7) M.Mąkosza and M.Ludwikow, Bull.Acad.Polon.Ser.Sci.Chim., 19, 23 (1971); Roczniki Chem., 45, 851 (1971).

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)
(CH_2) 4.92 ppm $(CDCl_3)$

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.

9) D.F.Tavares, R.E.Estep, and M.Blezard, Tetrahedron Lett., 1970, 2373; T.Durst and K.-C.Tin, ibid., 1970, 2369.

10) M.Mąkosza, "Two-Phase Reactions in Organic Chemistry," in "Survey of Progress in Chemistry," ed by A. Scott, Academic Press (1980), Vol.9, p.1.

(Received May 18, 1984)