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Vicarious Nucleophilic Substitution of Hydrogen versus Bis - Annulation in the Reaction of Chloromethyl Aryl Sulfone Carbanion with Electrophilic Arenes #,1)

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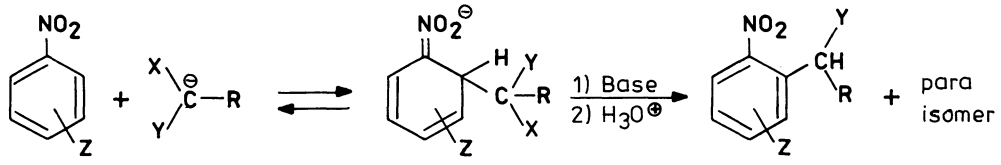
The carbanion of chloromethyl aryl sulfone reacts with 1-cyanonaphthalene to form a bis-annulated product whereas with 1-nitronaphthalene vicarious nucleophilic substitution of hydrogen takes place. This result and the bis--annulation of quinoxalines and naphthyridines which was reported earlier are rationalized in terms of the negative charge delocalization in the intermediate σ-adducts.

The vicarious nucleophilic substitution of hydrogen (VNS) in nitroarenes is a general reaction between carbanions containing leaving groups X and a variety of nitroaromatic molecules. It proceeds via addition of the carbanions to the nitroarenes to form anionic σ-adducts followed by base-induced β-elimination of HX,[2,3]



In our search for further expansion of this process, the reaction between 1-cyanonaphthalene and the carbanion of chloromethyl p-tolyl sulfone 1 was attempted.

It resulted, however, not in the VNS of hydrogen but in an unprecedented bis-annulation of the naphthalene ring giving rise to the bis-cyclopropane derivative 2 (Table). We have already observed a similar bis-annulation in the reaction of 1 with quinoxalines and naphthyridines.[4]

The structure of the bis-annulated product 2 and its stereochemistry (all trans) were established on the basis of the ^{1}H NMR spectrum

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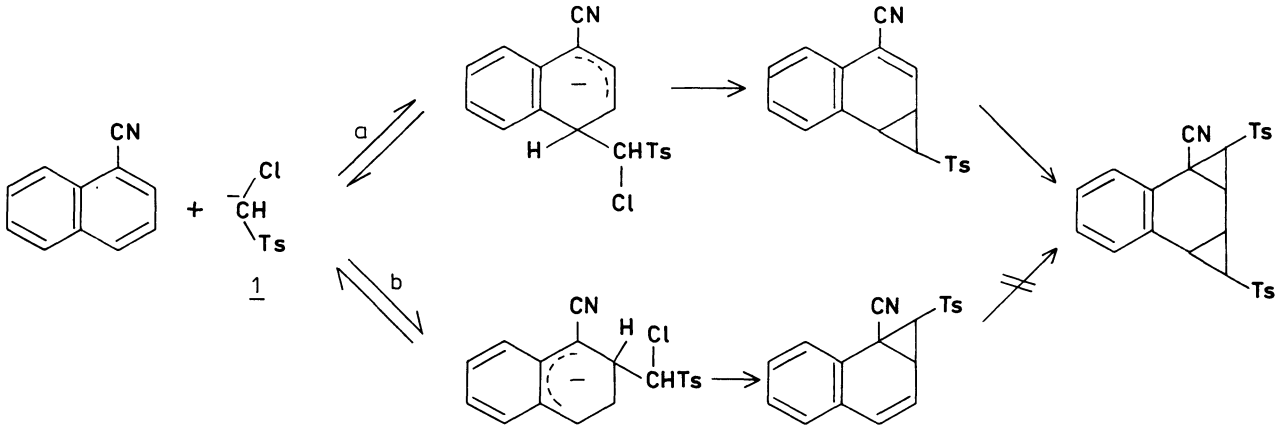
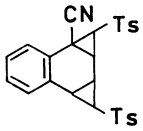
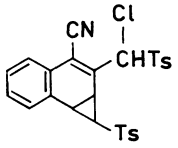
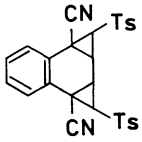
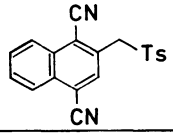
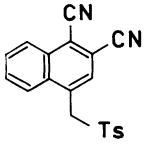
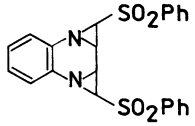
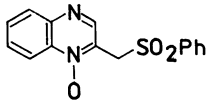
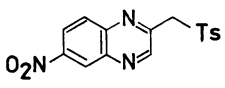
Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.



This result, along with that reported earlier,[4] give rise to the following questions: (a) which cyclopropane ring is formed first, (b) why is there such a dramatic difference in behaviour of 1-nitronaphthalene reacting exclusively according to the VNS scheme on the one hand, and 1-cyanonaphthalene as well as quinoxalines on the other and (c) how can these reactions be controlled. From general considerations we conclude that the reaction of 1 with 1-cyanonaphthalene proceeds via initial addition of the carbanion to C-4 followed by intramolecular nucleophilic substitution giving the C-4, C-3 monoannulated product. It is an active Michael acceptor so that addition of a second molecule of the carbanion proceeds rapidly, giving rise to the formation of the final bis-annulation product 2 (path a). Path b cannot result in bis-annulation since the eventual intermediate monocyclopropane cannot behave as an electrophile. An additional piece of evidence comes from the reaction of 1 with 2-chloro- and 4-chloro-1--cyanonaphthalenes. In the former case a product of 3-4-monoannulation and 2-Cl replacement 3 was formed, whereas in the latter only nucleophilic replacement of 4-Cl leading to 4 was observed.

In dealing with the second question one should take into account the degree of negative charge delocalization in the σ-adducts of 1 to the electrophilic arenes. In the case of the adduct to 1-nitronaphthalene the highest negative charge density is on the oxygen atoms of the nitro group, hence the ring carbon atoms do not behave as nucleophiles and there is also no difficulty in the ring proton abstraction by the base to give β-elimination leading to the VNS. On the other hand the negative charges in the adducts to 1-cyanonaphthalene and quinoxaline are far less delocalized. The ring carbon and nitrogen atoms have therefore substantial nucleophilicity whereas the base induced β-elimination is hindered. Hence intramolecular nucleophilic substitution dominates over the elimination. One can therefore expect that control of the annulation versus the VNS should be possible via manipulation with substituents affecting the charge delocalization. Simple models demonstrating such control are 1,4-, and particularly 1,2-dicyanonaphthalenes. The addition of 1 to these molecules gives σ-adducts in which the negative charge is more delocalized than in the case of 1-cyanonaphthalene.

Table 1. Reactions of 1 with electrophilic arenes

Starting arenes [a]	Reaction conditions	Products Structure & No	Yield [b] %	Mp [c] °C	^{1}H NMR diagnostic signals [d]
1-CN-N	t-BuOK, DMSO 20 °C, 5 min	 2	48	244	2.66-3.30, m, 5H
1-CN-2-Cl-N	t-BuOK, DMF -40 °C, 20 min	 3	62	230	1.75-1.85, 3.27-3.35 and 3.56-3.64, m, 3H; 5.82, s, 1H
1-CN-4-Cl-N	t-BuOK, DMSO 20 °C, 30 min	 4	18	173	6.58, s, 1H
1,4-Di-CN-N	t-BuOK DMF -35 °C, 20 min	 5	33	297	2.93-3.03 and 3.30-3.40, m (AA'XX'), 4H
		 6	26	244	4.72, s, 2H
1,2-Di-CN-N	t-BuOK, DMF -30 °C, 10 min	 7	47	255	4.83, s, 2H
Q	KOH, DMSO 20 °C, 1 h		66	218	3.43 and 3.64, 2d,4H,J=2.65 Hz [e]
Q-1-oxide	KOH, DMSO 20 °C, 1 h	 8	62	158	5.10, s, 2H
6-NO_2-Q	KOH, DMSO 20 °C, 2 h	 9	73	235	5.35, s, 2H

a) N-stands for naphthalene, Q - for quinoxaline. b) Isolated products.
c) Uncorrected.
d) Recorded on Brucker WP-100 (100 MHz), with TMS as an internal standard. e) Data from ref.[4] All new compounds 2 - 9 gave satisfactory microanalyses.

As a consequence from the 1,4-isomer products of the bis-annulation 5 and of the VNS 6 are formed, whereas the 1,2-isomer reacts exclusively according to the VNS scheme giving 7. Similar control can be effected in the quinoxaline ring. Contrary to quinoxaline and 2-phenylquinoxaline which react with 1 giving bis-annulated products,[4] the reaction with quinoxaline-1-oxide results exclusively in the VNS of 2-H giving 8. In this case the negative charge in the σ-adduct to C-2 is dispersed mainly between the N- and O-atoms so that elimination dominates over cyclization. Introduction of an electron withdrawing group, for example NO_2, in position 6 of the quinoxaline ring results in high negative charge delocalization in the σ-adduct to C-2 and therefore VNS of 2-H to give 9 occurs exclusively.

In this paper the first examples of the bis-annulation of naphthalene ring via nucleophilic addition, and the vicarious substitution of hydrogen in a carbocyclic aromatic ring without a nitro group are reported. The possibility of controlling these two competing reactions is discussed and demonstrated.

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References

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4) J. Goliński, M. Mąkosza, and A. Rykowski, Tetrahedron Lett., 1983, 3279.

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