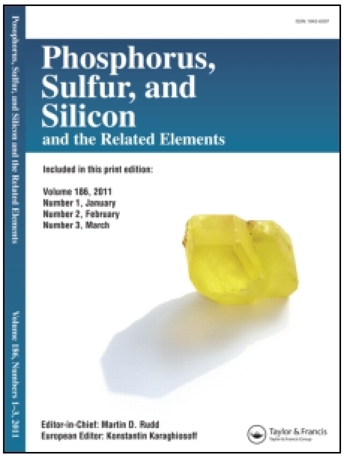

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Synthesis and Studies of Some Ketosulfones, Part I

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Synthesis and Studies of Some Ketosulfones, Part I

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New ketosulfones have been prepared. Their chemical composition and structure were proved by analytical and spectral methods. The kinetics of 1,4-addition of arenesulfinic acids to 1,3-diphenyl-2-nitropropenone and 3-nitro-4-phenyl-3-butene-2-on were studied by LC. The overall reaction is second order, while it is first order regarding each reagent and substrate. On the basis of the experimental results for the dependence of rate constants on the temperature and the influence of the substituents on the rate, a probable mechanism of the nucleophilic addition was suggested.

Keywords Ketosulfones; nucleophilic addition; structure

INTRODUCTION

Studies on methods of obtaining and the chemical behavior of chalkones date back to the second half of the last century when these compounds became known as chemotherapeutical agents. H. Gilman and L. Cason synthesized a great mumber of ketosulfones by the 1,4-addition of sulfinic acids to chalkones, thus contributing to the development of the chemistry of conjugated systems.[1] Publications describing in detail the mechanism and kinetics of the isomerization of cis-chalkones are also available.[2–4] A. C. Jain and A. K. Prosad studied the interaction of α-bromo- and α-methoxychalkones with urea resulting in derivatives of thiazine.[5] Recently, scientists have been aiming at extracting cytotoxic chalkones from *Calytbropsis aurea* (Myrtaceae).[6,7] The present study on the reactivity of nitrochalkones when interacting with arenesulfinic acids is a natural continuation of our work on the chemistry of heteroconjugated alkenes. The systematic study of nucleophilic additions

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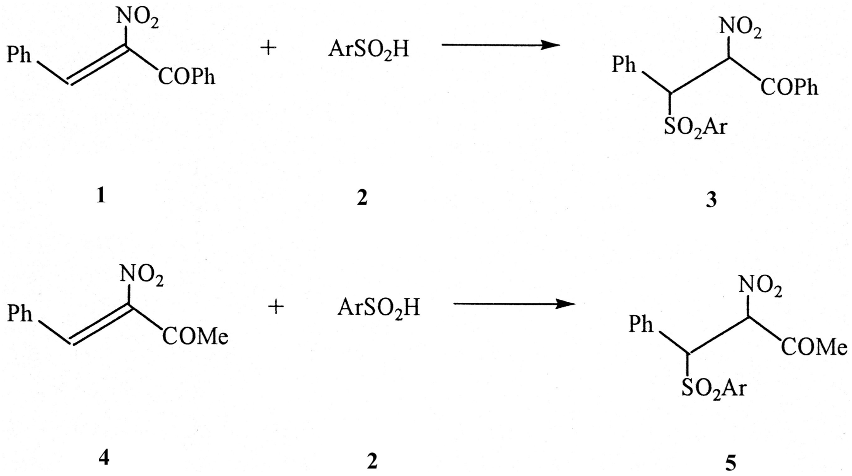
makes it possible to estimate the change in the activity of the double bond regarding the nucleophilic reagents in the presence of different substituents linked directly to the carbon atoms.

RESULTS AND DISCUSSION

Synthesis

The interaction of 1,3-diphenyl-2-nitropropenone and 3-nitro-4-phenyl-3-butene-2-on with sulfinic acids takes place by Scheme 1:



SCHEME 1 Ar = Ph (**2a**, **3a**, **5a**); Ar = 4-MeC$_6$H$_4$(**2b**, **3b**, **5b**); Ar = 4-CIC$_6$H$_4$ (**2c**, **3c**, **5c**).

3-arylsulfonyl-2-nitro-1,3-diphenylpropanones (**3a–c**) and 4-arylsulfonyl-3-nitro-4-phenyl-3-butene-2-ones (**5a–c**) were synthesized by mixing equimolar quantities of the corresponding reagents in ethanol at 18–20°C for 48 h. These compounds are colorless, crystalline substances and are very soluble in chloroform, acetone, and dioxane. They are stable in long storage and melt without decomposing. The compounds obtained were identified by TLC. Their compositions were determined by elemental analysis, and their structures were studied by spectral methods (Tables I and II).

Spectroscopic Study

In the IR spectra of the ketosulfones obtained, there are intensive absorption bands corresponding to asymmetric and symmetric valence

TABLE I Analytical Data for Compounds 3–5

Compound no.	Yield %	M.p. °C	Formula mol. wt.	Analysis (%) found (calcd.) C	H	N	S
3a	85	177	$C_{21}H_{17}NO_5S$	63.81	4.30	28.22	8.11
			395.30	(63.45)	(4.12)	(27.55)	(7.80)
3b	78	160	$C_{22}H_{19}NO_5S$	64.46	4.64	3.42	7.83
			409.31	(63.95)	(4.50)	(3.50)	(7.75)
3c	83	181	$C_{21}H_{16}NO_5SCl$	58.69	3.72	3.26	7.46
			429.75	(58.25)	(3.35)	(3.11)	(7.52)
5a	89	134	$C_{16}H_{15}NO_5S$	57.69	4.50	4.20	9.62
			333.24	(57.30)	(4.15)	(4.12)	(9.45)
5b	91	137	$C_{17}H_{17}NO_5S$	58.80	4.90	4.03	9.23
			347.25	(58.45)	(4.60)	(3.75)	(9.28)
5c	90	140	$C_{16}H_{14}NO_5SCl$	52.26	3.81	3.81	8.72
			367.70	(52.05)	(3.60)	(3.83)	(8.57)

vibrations of a nitro- and sulfonyl group at 1560–1550, 1385–1345, 1310–1300, and 1150–1140 cm^{-1}. An absorption band corresponding to a keto group can be seen at 1730–1690 cm^{-1}. The skeleton vibration of the aromatic nucleus is characterized by an absorption band at 1640–1460 cm^{-1}. The off-plane deformation C—H aryl vibrations at 830–800 cm^{-1} prove the presence of substituted benzenes. Characteristic

TABLE II The Spectral Data of Compounds 3–5

Compound no.	IR (ν, cm^{-1}) KBr	UV/VIS λ max (nm) (lgε)	^{1}H NMR ($CDCl_3$, δ, ppm)
3a	1690 (CO-Ph); 1560–1385 (NO_2); 1300–1140 (SO_2)	209 (3.06); 252 (3.41); 333 (2.29)	7.24–7.78 (m, 15H); 5.13 (d, CH); 6.20 (d, CH)
3b	1690 (CO-Ph); 1560–1350 (NO_2); 1310–1145 (SO_2)	225 (2.93); 252 (3.21); 295 (3.14)	7.22–7.75 (m, 14H); 5.12 (d, CH); 6.21 (d, CH), 2.40 (S, CH_3)
3c	1695 (CO-Ph); 1565–1345 (NO_2); 1300–1140 (SO_2)	225 (3.12); 252 (3.12); 295 (3.12)	7.28–7.80 (m, 14H); 5.15 (d, CH); 6.20 (d, CH)
5a	1715 (CO); 1550–1345 (NO_2); 1310–1145 (SO_2)	220 (2.91); 248 (3.21); 284 (3.21)	7.26–7.80 (m, 10H); 5.15 (d, CH); 6.21 (d, CH), 2.40 (S, CH_3)
5b	1725 (CO); 1550–1365 (NO_2); 1300–1150 (SO_2)	226 (3.07); 251 (3.14); 306 (3.21)	7.28–7.79 (m, 9H); 5.12 (d, CH); 6.18 (d, CH), 2.40 (S, CH_3)
5c	1730 (CO); 1565–1350 (NO_2; 1305–1145 (SO_2)	223 (3.09); 245 (3.11); 291 (3.20)	7.26–7.76 (m, 9H); 5.19 (d, CH); 6.18 (d, CH), 2.42 (S, CH_3)

TABLE III Experimental Proof of the Benzenesulfinic Acids Addition Order to 1.3-Diphenyl-2-Nitropropenone by the Methods of Van't Hoff and Half-Time in the Concentration Range 0.01–10 M, T = 298 K

Concentration range C, M	0.01–0.1	0.1–1	1–5	5–10
Order value by the Van't Hoff method	1.64	1.66	1.66	1.69
Order value by the half-time method	1.65	1.62	1.63	1.62

absorption maximum at 1370–1340 and 1170–1150 cm^{-1} shows that the compounds under study contain aryl-sulfonyl groups.

In their ^{1}H NMR spectra there are aromatic multiplets in the interval 7.20–7.80 ppm. Two doublets are centered at 5.11–5.20 and 6.22–6.27 ppm, and the integral data show that each doublet corresponds to one proton.

Kinetic Study

Kinetics of the interaction of sulfinic acids with 1,3-diphenyl-2-nitropropenone and 3-nitro-4-phenyl-3-butene-2-on was studied. Reactions as a whole are second order, but they are first order regarding the substrate and reagents. The overall reaction order was determined by the Van't Hoff method and the half-time method in the concentration interval 0.05–10 M. The calculated overall reaction order of the nucleophilic addition of benzensulfinic acids to 1,3-diphenyl-2-nitropropenone is 1.65 (Table III), and for the reaction between benzenesulfinic acid and 3-nitro-4-phenyl-3-butene-2-on it is 1.66 (Table IV). The linear dependence 1/[chalkone] = f (τ) is another proof of these results. Rate constants for five different temperatures were determined from the resultant slopes of the straight lines illustrating that dependence. The activation energy and the enthalpy of activation were calculated using the Arrhenius equation. Rate constants of the nucleophilic addition of sulfinic acids to nitrochalkones are shown in Table V. The

TABLE IV Experimental Proof of the Benzenesulfinic Acids Addition Order to 3-Nitro-4-phenyl-3-butene-2-on by the Methods of Van't Hoff and Half-Time in the Concentration Range 0.01–10 M, T = 298 K

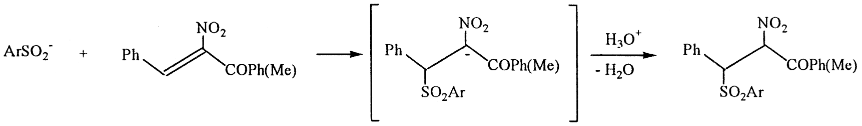
Concentration range C, M	0.01–0.1	0.1–1	1–5	5–10
Order value by the Van't Hoff method	1.69	1.67	1.68	1.69
Order value by the half-time method	1.60	1.65	1.66	1.67

TABLE V Substituent Effect on the Constants and Addition Parameters at Different Temperatures

Nusleophile	Subst. rate	Temp., K	$K \cdot 10^4\ M^{-1} \cdot s^{-1}$	$E\ kJ \cdot mol^{-1}$	$\Delta H \neq kJ \cdot mol^{-1}$
1	**2b**	288	4.83 ± 0.9	37.99	37.75
		293	9.26 ± 1.1		
		298	15.2 ± 1.2		
		303	30.12 ± 0.8		
		308	49.66 ± 1.3		
1	**2c**	288	1.83 ± 0.6	44.28	44.03
		293	3.25 ± 0.5		
		298	4.50 ± 0.9		
		303	7.00 ± 1.0		
		308	10.67 ± 1.2		
4	**2b**	288	5.06 ± 0.7	35.43	33.18
		293	13.6 ± 0.6		
		298	24.44 ± 1.1		
		303	30.37 ± 0.9		
		308	49.61 ± 1.2		
4	**2c**	288	2.03 ± 0.4	42.95	40.70
		293	2.81 ± 0.9		
		298	3.69 ± 0.7		
		303	5.24 ± 0.9		
		308	6.72 ± 0.8		

influence of different substituents in the benzene ring on the nucleophilic activity of the sulfinic acid was studied. On the other hand, depending on the group (Me, Ph) directly linked to the keto group, a change in the activity of the double bond is observed. These results show that the double bond in the molecule of 1,3-diphenyl-2-nitropropenone, due to π,π-conjugation, is less polarized, and, therefore, the nucleophilic addition takes place at a lower rate. The kinetic data obtained for the addition reactions, and the fact that sulfinic acids are strong acids, make it possible to suggest the most probable mechanism of their nucleophilic addition to nitrochalkones.

$$ArSO_2H + H_2O \rightleftharpoons ArSO_2^- + H_3O^+$$



SCHEME 2

CONCLUSIONS

Nucleophilic reactions are some of the most characteristic with the participation of heteroconjugated alkenes. Despite of the substrate nature, the addition starts with a nucleophilic attack at the β-carbon atom of the double bond. A further transformation of the carbanion formed is determined by the nature of the alkene, the nucleophilic agent, the medium, as well as the spatial structure of the intermediate products. All these stipulate the possibility for the nucleophilic reactions to occur by different schemes—addition, addition with rearrangement, addition with substitution, isomerization, and transisomerization.

EXPERIMENTAL

Methods

Melting points were determined on a Melt-Temp apparatus and are uncorrected. Microanalyses were obtained using an elemental Analyzer—1104 (Carlo-Erba). IR and UV spectra were obtained using a Bruker and Specord UV-VIS. ^{1}H NMR (chemical shifts measured in deuterated solvents are given in ppm from TMS) spectra were recorded with a Bruker 350 MHz spectrometer, using $CDCl_3$ solution.

General Procedure for Compounds 3–5

To 2-nitro-1,3-diphenyl-2-propenone (3-nitro-4-phenyl-3-butene-2-on) (0.01 mol) in 95% ethanol sulfinic acid (0.01 mol) was added. The reaction mixture was kept standing at 20°C for 100 h to yield the substituted ketosulfones. The crystals obtained were filtered and recrystallized from toluene.

Rate Measurement

Purified benzenesulfinic acids (0.001 mol) were added to the corresponding nitroketones (0.001 mol) in ethanol (50 mL). Aliquots were taken out at regular intervals of time and diluted with ethanol. Flow concentrations of reagents during the reaction were determined by means of HPLC. Second-order constants, the activation energy, and the enthalpy of activation were calculated according to the literature.

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