Non-regiospecific Additions of Enamines to αβ-Unsaturated Sulphones

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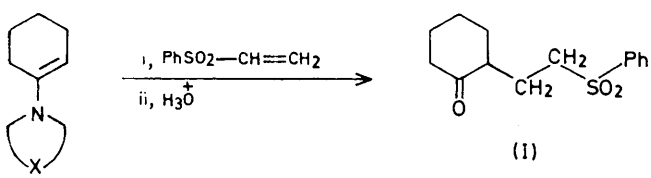
αβ-Unsaturated sulphones react with 1-pyrrolidino-cyclopentene and -cyclohexene to give, after hydrolysis, the corresponding 2-(sulphonylalkyl)cycloalkanones. When the vinyl sulphone system carries no substituents or only a β-methyl group, only the expected normal product, derived from nucleophilic attack of the enamine on the β-position of the olefin, is obtained, *i.e.* the reaction is regiospecific. In contrast, sulphones bearing a β-phenyl group afford two isomeric 2-(sulphonylalkyl)cycloalkanones, in which C-2 is linked to either the β- or the α-carbon atom of the starting sulphone.

It has been shown previously that phenyl vinyl sulphone reacts with cyclohexanone enamines to afford adducts,



(I)

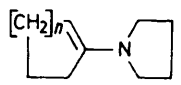
X = $CH_2{\cdot}O{\cdot}CH_2$, $[CH_2]_3$, or $[CH_2]_2$

hydrolysis of which gives 2-(2-phenylsulphonylethyl)-cyclohexanone (I).[1,2] On the basis of this single result, it seems that αβ-unsaturated sulphones behave like αβ-unsaturated ketones,[3] nitro-derivatives,[4,5] and other electrophilic olefins[6] in reactions with enamines. In order to obtain further information about the chemical behaviour of sulphones of this kind, we have now investigated the reactions of 1-pyrrolidino-cyclopentene (II) and -cyclohexene (III) with the sulphones R^1-CH=CH-SO_2R^2 (R^1 = H, Me, or Ph; R^2 = Me or Ph).

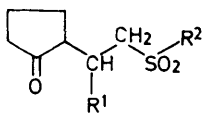
Single products are formed in the reactions of cycloalkanone enamines with electrophilic olefins such as RCH=CHX (X = COPh or NO_2) whatever the nature of the substituent R.[3-5] We have obtained analogous results from the reactions of the enamine (II) with αβ-unsaturated sulphones when R^1 is H or Me. Only

[1] A. Risaliti, S. Fatutta, and M. Forchiassin, *Tetrahedron*, 1967, **23**, 1451.
[2] A. Risaliti, S. Fatutta, M. Forchiassin, and C. Russo, *Ricerca Sci.*, 1968, **38**, 827.
[3] F. P. Colonna, S. Fatutta, A. Risaliti, and C. Russo, *J. Chem. Soc.* (*C*), 1970, 2377.
[4] A. Risaliti, L. Marchetti, and M. Forchiassin, *Ann. Chim.* (*Italy*), 1966, **56**, 317.
[5] A. Risaliti, M. Forchiassin, and E. Valentin, *Tetrahedron*, 1968, **24**, 1889.
[6] A. G. Cook, 'Enamines: Synthesis, Structure and Reactions,' Dekker, New York and London, 1969, p. 359.

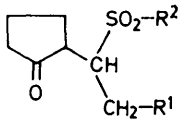
products of type (IVA) were obtained, the structures of which are consistent with their ^{1}H n.m.r. spectra, which are similar to the spectrum of the ketone (I).



(II) $n = 1$
(III) $n = 2$



(IVA)



(VA)

a; R^1 = H, R^2 = Me
b; R^1 = Me, R^2 = Ph
c; R^1 = Ph, R^2 = Me

The spectrum of the ketone (I) exhibits an ill-resolved two-proton multiplet of (CH_2·SO_2) at τ 6·35—7·08. The spectrum of the ketone (IVAa) shows in the same range (τ 6·5—7·3) an analogous multiplet, which however overlaps the methyl singlet giving a complex five-proton signal. Compound (IVAb) was expected to be a mixture of *threo*- and *erythro*-isomers, in accord with the presence of chiral centres at C-2 of the ring and C-1 of the side chain. Although this product gave only one spot on t.l.c. and we were unable to separate the two diastereoisomers, their presence was shown by the ^{1}H n.m.r. spectrum, which exhibits an ill-resolved two-proton multiplet (CH_2·SO_2) at τ 6·30—7·32 and two methyl doublets (total 3H) at τ 8·70—9·25.

The reaction of the enamine (II) with the sulphone PhCH=CH-SO_2Me gave the two isomeric ketones

TABLE 1

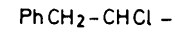
Properties of the 2-substituted cycloalkanones (IV) and (V)

	M.p. (°C)	τ Values: Me	CH_2·SO_2	CH·SO_2
(IVAa)	50—51	7·05	6·50—7·30	
(IVAb)	(Oil) [a]	8·70—9·25 [b]	6·30—7·32	
(IVAc)	58—59	7·45	6·02—6·55	
	72—73	7·55	5·62—6·82	
(VAc)	163	7·42		5·68—6·10 [c]
(IVBa)	72	7·04	6·25—7·20	
(IVBb)	(Oil) [a]	8·85; 8·94	6·40—7·24	
oxime	148	8·90	6·45—7·15	
(IVBc)	116—117	7·45	6·12—6·65	
	143—144	7·60	6·20—6·80	
(IVBd)	113		5·94—6·65	
	134		6·02—6·65	
(VBc)	105 [a]	7·25; 7·40		5·35—5·80 [d]
oxime	133—134	7·35		5·32—5·80 [c]
	148—149	7·42		5·85—6·25 [c]
(VBd)	128 [a]			5·25—6 [d]

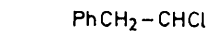
[a] *threo-erythro*-Mixture showing a single spot on t.l.c. [b] Two ill-resolved doublets. [c] Doublet of doublets (1H). [d] Complex signal (1H) due to the overlap of two doublets of doublets.

(IVAc) and (VAc). Each isomer was obtained as a mixture of *threo*- and *erythro*-diastereoisomers. The mixture (IVAc) was separated by column chromatography; the resulting diastereoisomers were each converted into the same equilibrium mixture by treatment with base. Their ^{1}H n.m.r. spectra showed CH_3 and CH_2·SO_2 signals as indicated in Table 1; the latter absorption includes the PhC*H* signal.

Repeated recrystallization of the diastereoisomeric mixture (VAc) furnished a pure compound, m.p. 163°. Its ^{1}H n.m.r. spectrum exhibited a one-proton doublet of doublets (CH·SO_2) at τ 5·68—6·10. On treatment with base the spectrum changed, with the appearance of a further doublet of doublets at τ 5·05—5·44 (0·15H) corresponding to the second diastereoisomer. The assignment of the CH·SO_2 signal of (VAc) (m.p. 163°) follows from comparison with the spectra of the two α-chloro-sulphones (VI) and (VII),[7] which show doublets of doublets (CH·SO_2) at τ 5·05—5·40 and 5·05—5·50, respectively. The spectrum of (VI) approximates to



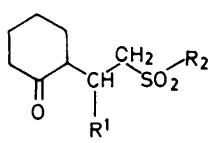
(VI)



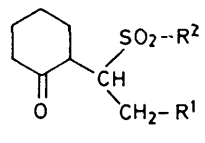
(VII)

that of an AMX system. However the spectrum of (VII) is complicated by overlap of the methyl singlet with the signal of one of the benzylic protons (Figure). Compound (VAc), m.p. 163°, shows an even more complex spectrum in the range above τ 7, because of the overlap of the signals from methyl, benzylic, and ring protons (Figure).

Analogous behaviour was observed in the reactions of 1-pyrrolidinocyclohexene (III) with the same αβ-unsaturated sulphones. In this case also, the sul-



(IVB)



(VB)

a; R^1 = H, R^2 = Me
b; R^1 = Me, R^2 = Ph
c; R^1 = Ph, R^2 = Me
d; R^1 = Ph, R^2 = Ph

phones with R^1 = Ph yielded both isomeric ketones (IV) and (V). The *erythro*- and *threo*-isomers of (IVBc) and (IVBd) were separated by column chromatography. Compounds (IVBb), (VBc), and (VBd) each showed a single spot on t.l.c., but their diastereoisomers were characterized as the corresponding oximes. The ^{1}H n.m.r. spectra of compounds (IVBa—d) and (VBc and d) are similar to those of (IVAa—c) and (VAc), respectively (Table 1).

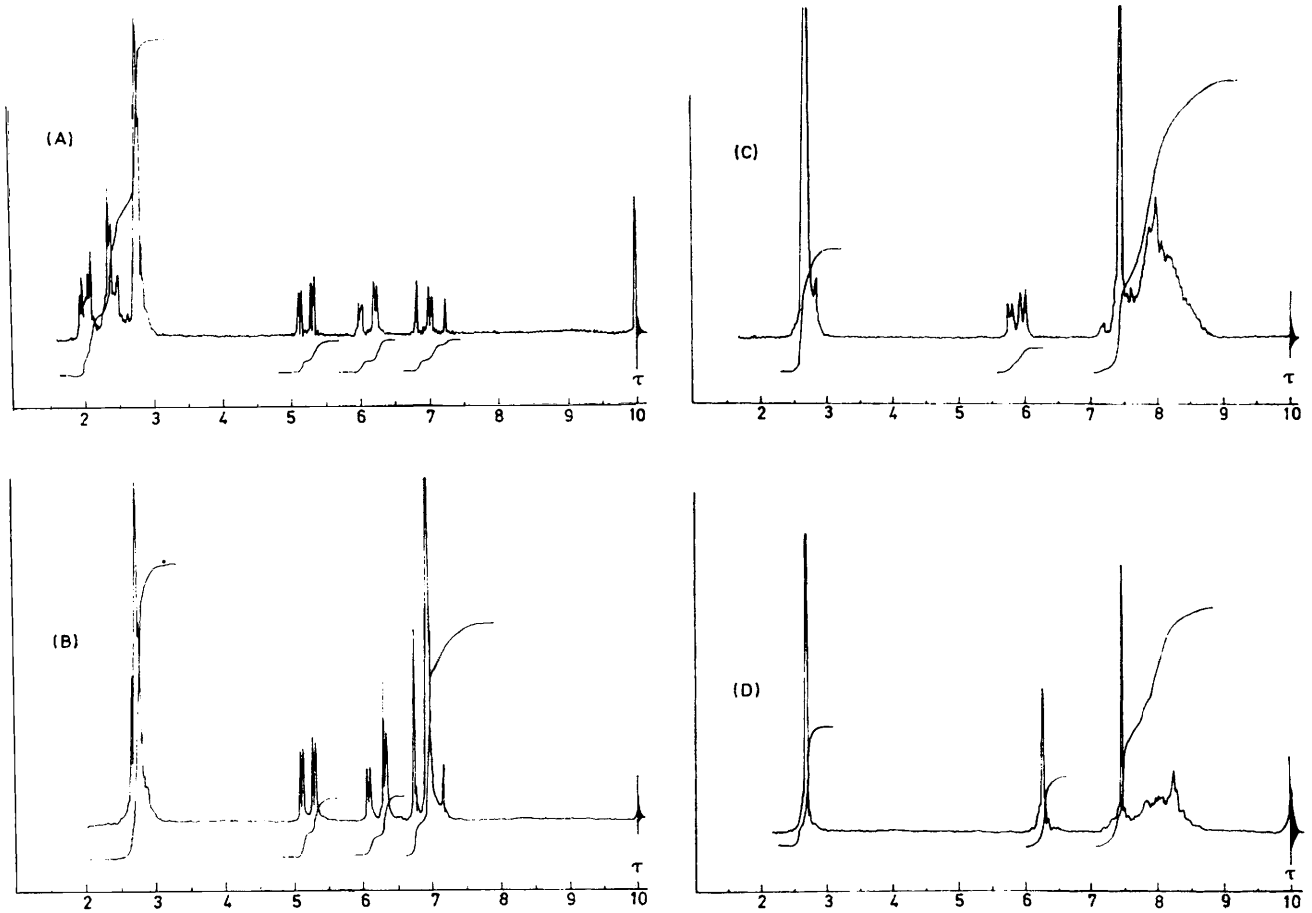
Attempts to synthesize the ketones (V) from the enamines (II) and (III) by alkylation with the chloro-

[7] W. E. Truce, J. J. Breiter, and J. E. Tracy, *J. Org. Chem.*, 1964, **29**, 3009.

TABLE 2

Reactions of enamines with αβ-unsaturated sulphones

Enamine	Sulphone	Solvent	Reaction time (h)	Relative percentages of products: Recovered *trans*-sulphone	Normal product (IV)	Anomalous product (V)
(II)	CH_2=CH–SO_2Me	MeCN	24		100	
	cis-MeCH=CH–SO_2Ph	MeCN	24		100	
	cis-PhCH=CH–SO_2Me	MeCN	24	40	54	6
(III)	CH_2=CH–SO_2Me	MeCN	24		100	
	cis-MeCH=CH–SO_2Ph	MeCN	24	16	84	
	cis-PhCH=CH–SO_2Me	Dioxan	3	41	41	18
	cis-PhCH=CH–SO_2Me	Dioxan	24	22	34	44
	cis-PhCH=CH–SO_2Me	PhH	24	66	27	7
	cis-PhCH=CH–SO_2Me	MeCN	24	59	19	22
	trans-PhCH=CH–SO_2Me	Dioxan	3	100		
	trans-PhCH=CH–SO_2Me	Dioxan	24	78	22	
	trans-PhCH=CH–SO_2Me	Dioxan	72	45	12	43
	cis-PhCH=CH–SO_2Ph	Dioxan	3	52	34	14
	cis-PhCH=CH–SO_2Ph	PhH	24	29	63	8
	cis-PhCH=CH–SO_2Ph	MeCN	24	23	77	
	trans-PhCH=CH–SO_2Ph	Dioxan	24	71	25	4



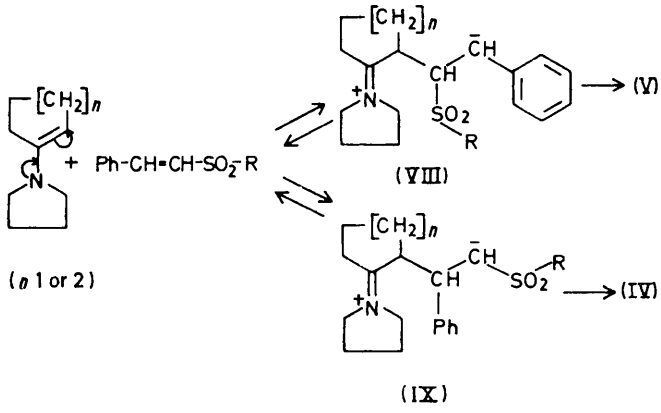
60 MHz ^{1}H N.m.r. spectra ($CDCl_3$) of (A) the chloro-sulphone (VI); (B) the chloro-sulphone (VII); (C) the ketone (VAc), m.p. 163°; and (D) the ketone (IVAc), m.p. 58—59°

sulphones (VI) and (VII) failed, since the chloro-sulphones underwent dehydrohalogenation.

Our results show that, when R^1 is H or Me, the sulphones $R^1CH{=}CH{-}SO_2R^2$ react regiospecifically with the enamines (II) and (III) to give only compounds (IV), which are the expected products derived from attack of the enamine on the β-carbon atom of the sulphone. However, when R is Ph, the reaction is not regiospecific, leading to a mixture of products (IV) and (V). The latter are unexpected products, clearly derived from attack of the enamine at the α-carbon atom of the sulphone.

The formation of the products (V) is difficult to explain. It could be attributed to a small difference in stability between the two intermediates (VIII) and (IX), these being considered as α-phenyl and α-sulphonyl carbanions. Such an explanation would be consistent with a two-step mechanism involving reversible formation of (VIII) and (IX). However, if the stability of the intermediates were a determining factor, styrene and especially *p*-nitrostyrene would be expected to react with enamines. On the contrary, the reactions of these olefins with both (II) and (III) gave only polymerization products.

On the other hand, the reversible formation of the dipolar intermediates was confirmed by the fact that from the reaction with *cis*-αβ-unsaturated sulphones the unchanged olefins were recovered as the more stable *trans*-isomers (Table 2). Since no isomerization occurs



between *cis*- and *trans*-αβ-unsaturated sulphones when they are heated in the presence of acids or bases, this result is further evidence for the two-step mechanism of these reactions.[8] Thus little can be said at present about the mechanism of formation of the isomers (V); further investigations are needed.

EXPERIMENTAL

^1H N.m.r. spectra were recorded with a JEOL JNM-C-60 HL spectrometer, with Me_4Si as internal standard for solutions in $CDCl_3$. For analytical t.l.c., plates were coated with Silica Gel G (Merck) and developed with benzene–acetone (85 : 15). For chromatographic columns, extra pure silica (Merck; 70—325 mesh ASTM) was used as stationary phase and benzene and benzene–ethanol (99 : 1) were used as eluants.

The following sulphones were prepared as described in literature: methyl vinyl sulphone,[9] phenyl *cis*-prop-1-enyl sulphone,[10] phenyl *trans*-prop-1-enyl sulphone,[11] methyl *cis*-β-styryl sulphone,[12] methyl *trans*-β-styryl sulphone,[13] phenyl *cis*- and *trans*-β-styryl sulphone.[14]

Reaction between the Enamines (II) *and* (III) *and the Sulphones* $R^1CH{=}CH{-}SO_2R^2$.—A solution of the enamine (II) or (III) (10 mmol) and the sulphone (10 mmol) in anhydrous solvent (80 ml) was refluxed for several hours (Table 2), then concentrated *in vacuo*. The residue was hydrolysed with aqueous 20% acetic acid (30 ml) at room temperature for 10 h. The mixture was extracted with benzene; chromatography of the concentrated extract furnished the unchanged sulphone and the cycloalkanones (IV) and/or (V). The diastereoisomeric pairs corresponding to (IV) and (V) were separated as described in the Discussion section. Analytical data are reported in Table 3.

TABLE 3

Analytical data for the sulphones (IV) and (V)

	M.p. (°)	Formula	Found (%) C	H	N	Required (%) C	H	N
(IVAa)	50—51	$C_9H_{14}O_2S$	50·4	7·5		50·5	7·4	
(IVAb)	(Oil) [a]	$C_{14}H_{18}O_2S$	63·0	6·85		63·15	6·8	
(IVAc)	58—59	$C_{14}H_{18}O_2S$	63·1	6·75		63·15	6·8	
	72—73	$C_{14}H_{18}O_2S$	62·9	6·85		63·15	6·8	
(VAc)	163	$C_{14}H_{18}O_2S$	63·2	6·85		63·15	6·8	
(IVBa)	72	$C_9H_{16}O_2S$	52·75	7·9		53·0	7·9	
(IVBb)	(Oil) [a]	$C_{15}H_{20}O_2S$	64·0	7·25		64·25	7·2	
oxime	148	$C_{15}H_{21}NO_2S$	60·7	7·05	4·7	61·0	7·15	4·75
(IVBc)	116—117	$C_{15}H_{20}O_2S$	64·0	7·25		64·25	7·2	
	143—144	$C_{15}H_{20}O_2S$	64·3	7·25		64·25	7·2	
(IVBd)	113	$C_{20}H_{22}O_2S$	70·3	6·55		70·15	6·5	
	134	$C_{20}H_{22}O_2S$	70·3	6·55		70·15	6·5	
(VBc)	105 [a]	$C_{15}H_{20}O_2S$	64·1	7·15		64·25	7·2	
oxime	133—134	$C_{15}H_{21}NO_2S$	61·2	7·1	4·7	61·0	7·15	4·75
	148—149	$C_{15}H_{21}NO_2S$	61·1	7·1	4·7	61·0	7·15	4·75
(VBd)	128 [a]	$C_{20}H_{22}O_2S$	69·9	6·4		70·15	6·5	

[a] *threo–erythro*-Mixture showing a single spot on t.l.c.

The data summarized in Table 2 show that isomers (IV) are generally the major products, but polar solvents and prolonged heating favour the formation of the isomers (V). Moreover the *cis*-αβ-unsaturated sulphones appeared more reactive than the *trans*-isomers.

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[3/2104 *Received*, 15*th October*, 1973]

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