REACTION OF 5-NITROFURFURYLTRICHLOROMETHYL SULFONE WITH ALIPHATIC ALDEHYDES. THE SYNTHESIS OF CYCLOPROPANES DERIVED FROM 5-NITROFURAN*

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5-Nitrofurfuryltrichloromethyl sulfone (*I*) reacts with aliphatic aldehydes under catalysis of piperidine in dioxane at 80—100°C to give 1-(5-nitro-2-furyl)-1-trichloromethylsulfonyl-2-(5-nitro-2-furyl)-3-R-cyclopropanes (R=H, CH_3, C_2H_5 and C_3H_7). 1-(5-Nitro-2-furyl)-1-trichloromethylsulfonyl-2-methylethylene (*II*) was synthesized by condensation of *I* with ethanal. The mechanism of formation of cyclopropanes is suggested and the effect of the bulkiness of substituents on the stereospecificity leading to final products is discussed. The spectra (^{1}H-NMR, IR, UV and mass) of cyclopropanes *III*—*VI* are interpreted.

Condensation reactions of 5-nitrofurfuryl sulfones of general formula 5-NO_2—C_4H_2O—CH_2—SO_2—R (R=CH_3, $CHCl_2$, C_6H_5) with aryl, heteroaryl and arylfurylaldehydes furnish α,β-unsaturated sulfones[1-3]. Aliphatic aldehydes were found not to react with these sulfones. A suitable substrate for condensation-reactions with aryl, heteroaryl and arylfuryl, as well as with aliphatic aldehydes was obtained only after replacement of R in the sulfonyl group by trichloromethyl[4]. So far, little attention has been paid to direct condensation of aliphatic aldehydes with sulfones; esters of alkylsulfonylacetic acid were reported[5] to react under conditions of Cope reaction with butanal and 2-methylpropanal, but similar condensations published by other authors resulted in failure[6]. Trihalogenomethyl sulfones were found to condense with aromatic aldehydes to yield the corresponding ethylenes, whereas the aliphatic aldehydes gave a complex mixture of products from which the corresponding alcohols were isolated in low yields[7]. Condensation reaction of benzyltrifluoromethyl sulfone with methanal and piperidine as a catalyst afforded the product of Mannich reaction, which was thermically transformed into an unsaturated sulfone[8]. Like reactions of trichloromethyl sulfones were not studied as yet.

This paper deals with the synthesis of bis-(5-nitro-2-furyl) derivatives of cyclopropane *III*—*VI* prepared by reacting 5-nitrofurfuryltrichloromethyl sulfone (*I*) (ref.[4]) with aliphatic aldehydes (Scheme 1).

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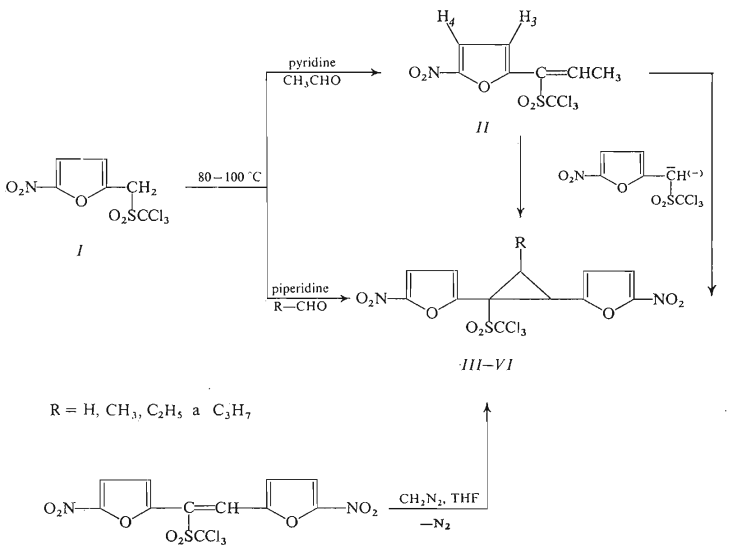
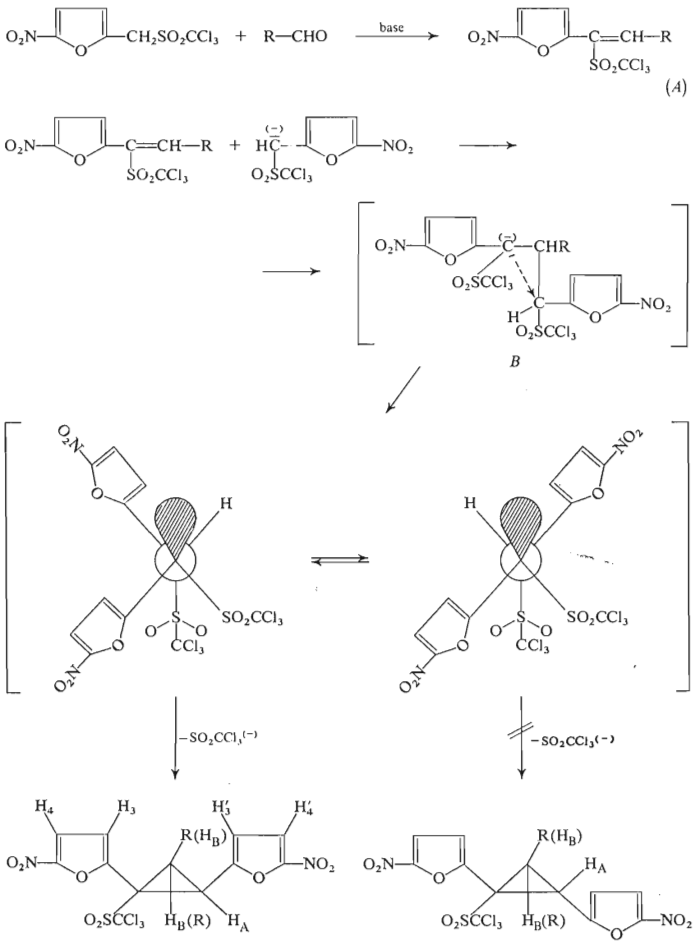
The formation of substituted cyclopropanes proceeds as follows: a strongly polarized α,β-unsaturated sulfone *A*, originating in the first step, reacts with the anion of sulfone *I* to afford an unstable anion *B*. During cyclization an elimination of the strongly polar SO_2CCl_3 group takes place due to the existence of a lone electron pair acting as an internal nucleophile (Scheme 2). This mechanism accords with that involving the formation of cyclopropanes in other systems[9–11]. The configuration of the final product depends on the steric and energetic conditions in the anion being formed in the transition state. Scheme 2 illustrates the distribution of substituents in the direction of the C—C bond formation in cyclopropanes employing Newman projection (*C* and *D*).



I *II* *III–VI*

SCHEME 1

The α,β-unsaturated sulfones undergo in the stage of their formation in the presence of strongly basic catalyst (piperidine, K_2CO_3, alkoxides, NaH *etc.*) and an enhanced



SCHEME 2

temperature a cyclization leading to cyclopropyl derivatives of 5-nitrofuran. A condensation reaction of sulfone *I* with ethanal under the same reaction conditions in the presence of less basic pyridine afforded 1-(5-nitro-2-furyl)-1-trichloromethylsulfonyl-2-methylethylene (*II*). The latter reacts with the anion of sulfone *I* to give the cyclopropane identic with *IV*, which was synthesized from sulfone *I* and ethanal under catalysis of piperidine (Scheme 1).

As evident, the formation of the final product depends on the basicity and bulkiness of the catalyst employed. The more basic piperidine (pK_a 11·12) favourizes the formation of cyclopropanes *III* – *VI*, whereas pyridine (pK_a 5·19) the formation of an α,β-unsaturated sulfone *II*. This fact might be rationalized by the concentration of the anion of sulfone *I* in the reaction medium. If the concentration of the sulfone anion is too low (the catalysis with pyridine) a reaction with aliphatic aldehyde occurred and an unsaturated sulfone was formed. Consequently, the formation of the unsaturated sulfone in this reaction is more rapid than the addition of the carbanion to the double bond of the sulfone. The addition of the sulfone anion to the α,β-unsaturated sulfones with an alkyl substituent at the β-carbon proceeds at higher temperatures only (optimum at 80 – 100°C) and is also influenced by the bulkiness of the base used, obviously due to an existence of an ion pair (anion of the sulfone–protonated base). The replacement of piperidine by $N(C_2H_5)_3$ (pK_a 10·78), or $N(C_4H_9)_3$ resulted in virtual absence of cyclopropane derivatives. This fact is further evidenced by the finding that the use of a carbonate anion (pK_a 10·33) leads to the formation of cyclopropane derivatives in almost the same yield. The limiting factor whether

TABLE I

Physical Constants and Elemental Analyses of Cyclopropanes *III* – *VI*

Compound R	M.p., °C (yield, %)	*cis*/*trans* (%)[a]	Mol.formula (mol.weight)	Calculated/Found		
				% Cl	% N	% S
III	214 – 215	–	$C_{12}H_7Cl_3N_2O_8S$	23·87	6·29	7·2
H	(15)		(445·6)	24·1	6·3	7·35
IV	165 – 175	80/20	$C_{13}H_9Cl_3N_2O_8S$	23·14	6·09	6·98
CH_3	(20)		(459·6)	23·34	6·0	7·05
V	132 – 133	100/0	$C_{14}H_{11}Cl_3N_2O_8S$	22·45	5·91	6·77
C_2H_5	(30)		(473·7)	22·3	5·72	6·8
VI	140 – 141·5	100/0	$C_{15}H_{13}Cl_3N_2O_8S$	21·81	5·74	6·58
C_3H_7	(30)		(487·7)	21·8	5·57	6·67

[a] Assignment according to ^{1}H-NMR spectra of the raw product.

or not the cyclopropane derivatives were formed is also the size of the substituent at β-carbon of the unsaturated sulfone. In attempting to add carbanion to trisubstituted α,β-unsaturated sulfones derived from 5-nitrofuran possessing aryl, heteroaryl or arylfuryl at β-carbon, the cyclopropanation did not proceed due to sterical hindrance. The suitable substrate for addition of a carbanion followed by a cyclization was obtained when the substituent at β-carbon was replaced by an alkyl. The limiting factor for addition to sulfones having an alkyl at β-carbon is its branching; thus *e.g.* phenylethanal and 2-methylpropanal did not afford the corresponding cyclopropanes. Yields of cyclopropanes (Table I) vary within 15–30% (calculated on the starting sulfone).

The analogue *II* having a methyl group at β-carbon is, on the basis of ^{1}H-NMR analysis, a single geometric isomer; we propose the *E* configuration for it. This configuration is sterically more favourized for α,β-unsaturated sulfones, since the bulky SO_2CCl_3 group and the substituent at β-carbon are oriented in *trans* direction. Condensation reactions of sulfones derived from 5-nitrofuran with aryl and heteroaryl aldehydes afford always only one geometric isomer, namely the *E* one. This was corroborated by an X-ray analysis[12] of 1-(5-nitro-2-furyl)-1-trichloromethylsulfonyl-2-(5-bromo-2-furyl)ethylene[2,4]. As it follows, the replacement of the more bulky aryl or heteroaryl for a methyl group in the aldehyde did not influence the stereochemical course of the condensation reaction of the sulfone *I*. The ^{1}H-NMR spectra of cyclopropanes under study are surveyed in Table III. As seen, derivatives *III*, *V* and *VI* consist of one isomer and their melting points are sharp; derivative *IV* is a mixture of both isomers and its melting point varies in a broad range (Table I).

TABLE II
IR Spectra (cm^{-1}) of Cyclopropanes *III*–*VI*

Compound	$(NO_2)_{as}$	$(NO_2)_s$	$(SO_2)_{as}$	$(SO_2)_s$	Ring deform.	$(C—H)_{def}$	$(C—H)_{def}$
III	1 540 1 515	1 380	1 357	1 157	1 020	977	850
IV	1 542 1 517	1 380	1 358	1 157	1 025	972	850
V	1 542 1 512	1 384	1 356	1 158	1 026	972	850
VI	1 540 1 510	1 385	1 357	1 156	1 025	972	853

These isomers can readily be distinguished according to the values of coupling constants[13,14] reported for cyclopropane derivatives: the *cis* isomer is characterized by $J = 10{\cdot}7$ Hz, the *trans* one by $J = 7{\cdot}8$ Hz.

Structure *D* can be eliminated (the *trans* arrangement of furan rings) because of a sterically unfavourable system (verified on molecular models – the interaction of 5-nitrofuran ring with the SO_2CCl_3 group). Accordingly, cyclopropanes *III – VI* possess structure *C* (Scheme 2). The fact, that stereoisomer with *trans* interaction of protons is formed only with derivative *IV* (R = CH_3) in a *trans* : *cis* ratio 1 : 4 indicates a sterically crowded system. Replacement of the methyl group by a higher alkyl resulted in formation of a single *cis* stereoisomer (Scheme 2) due to a steric interaction of the more bulky alkyl with the SO_2CCl_3 group. The proposed structure *C* was verified by the identity of cyclopropane *III* with that obtained from 1-(5-nitro--2-furyl)-1-trichloromethylsulfonyl-2-(5-nitro-2-furyl)ethylene[4] and diazomethane[15] (Scheme 1) which, due to the stereospecificity of this reaction, has configuration *C*.

Table II lists the IR data of the synthesized cyclopropane derivatives. The characteristic bands of individual groups are approximately equal. Stretching vibrations of the C—H bonds of both furan and cyclopropane rings are in the $3000-3150\ cm^{-1}$ region and the corresponding bending vibrations in the $1017-1020\ cm^{-1}$ region and therefore, the correct assignment was impossible. The UV spectra of *III – VI* are consistent and reveal two absorption maxima at 208 and 309 nm (log ε 4·07 and 4·13, respectively). The ethylene derivative *II* displayed the absorption maximum

TABLE III

^{1}H-NMR Spectra of Cyclopropanes *III – VI* (δ, ppm)

Compound	H_3[a]	H_4[a]	H'_3[a]	H'_4[a]	H_A	H_B	R[b]	
III	6·94	7·28	6·79	7·25	dd, 3·93	m, 2·88	m, H_C, 2·88	
IV	7·06	7·49	6·93	7·44	d, 3·95	m, 3·12	d, 3 H, 1·64	
IV[c]	6·92	7·4	6·85	7·39	d, 3·84	m, 3·05	d, 3 H, 1·86	
V	7·02	7·49	6·93	7·48	d, 3·97	m, 3·06	m, 2 H, 2·07;	t, 3 H, 1·21
VI	7·02	7·48	6·94	7·47	d, 3·97	m, 2·97	m, 4 H, 1·75;	t, 3 H, 0·96

[a] Doublet of protons H_3, H_4, H'_3 and H'_4 of the furan ring, $J_{3,4} = J_{3',4'} = 3{\cdot}8$ Hz; $J_{A,B} = 10{\cdot}7$ Hz, *cis* interaction of protons; $J_{A,B} = 7{\cdot}8$ Hz, *trans* interaction of protons; $J_{B,C} = 7{\cdot}5$ Hz, geminal interaction of protons (*III*); [b] $J_{H,H} = 6{\cdot}7$ Hz, interaction of aliphatic protons of alkyl; [c] *trans* isomer.

at 205 and 315 nm (log ε 4·08 and 4·03, respectively). The K-band of this derivative is by 6 nm bathochromically shifted in relation to the corresponding cyclopropanes *III*–*VI*. The mass spectra showed a peak of molecular ion and characteristic fragmentation pattern $[M - CCl_3]^+$, $[M - OCCl_3]^+$, $[M - SOCCl_3]^+$ and $[M - SO_2CCl_3]^+$.

EXPERIMENTAL

1-(5-Nitro-2-furyl)-1-trichloromethylsulfonyl-2-(5-nitro-2-furyl)-3-alkylcyclopropanes *III*–*VI*

A mixture of the respective aliphatic aldehyde (6 mmol) and piperidine (10 mmol) in dioxane (20 ml) was dropwise added to 5-nitrofurfuryltrichloromethyl sulfone (5 mmol) in dioxane (40 ml) heated at 80–100°C for 3–4 h. After this time the mixture was concentrated at room temperature under reduced pressure, the residue diluted with chloroform, washed with dilute HCl and water and dried with $MgSO_4$ or Na_2SO_4. The product was purified chromatographically using silica gel Brockmann II, 100–250 mesh (column i.d. 30 mm, lenght 200 mm).

1-(5-Nitro-2-furyl)-1-trichloromethylsulfonyl-2-methyl-ethylene (*II*)

A mixture consisting of ethanal (10 mmol) and pyridine (10 mmol) in dioxane (20 ml) was dropwise added to 5-nitrofurfuryltrichloromethyl sulfone (5 mmol) under the same conditions and work-up as above. Yield about 30%, m.p. 123–124°C (chloroform). For $C_8H_6Cl_3NO_5S$ (334·6) calculated: 31·8% Cl, 9·6% S, 4·2% N; found: 31·9% Cl, 9·6% S, 4·3% N. IR (cm^{-1}): $\tilde{\nu}(C{=}C)_{aliph}$ 1636, $\tilde{\nu}(NO_2)_{as}$ 1540, $\tilde{\nu}(NO_2)_s$ overlapped with $\tilde{\nu}(SO_2)_{as}$ 1358, $\tilde{\nu}(SO_2)_s$ 1162, $\tilde{\nu}$ (ring deform.) 1026, $\tilde{\nu}(C{-}H)_{def}$ 965, $\tilde{\nu}(C{-}H)_{def}$ 872. ^{1}H-NMR spectrum (δ, in ppm): 7·19 (d, furan-H_3), 7·6 (d, furan-H_4), $J_{3,4}$ = 3·8 Hz; 7·89 (q, =C—H); 2·35 (d, =C—CH_3), J_{H,CH_3} = 7·2 Hz.

Spectral Measurements

Infrared spectra were recorded with a UR-20 Zeiss, Jena spectrophotometer in ethanol-free chloroform in 0·02–1 mm-NaCl cells as saturated or 0·02M solutions. Electron absorption spectra were measured with a Specord UV VIS apparatus in ethanol at a $3 \cdot 10^{-5}$M concentration in 10 mm-cells; reading accuracy ± 1 nm. The ^{1}H-NMR spectra were taken with a Tesla BS 487-C instrument operating at 80 MHz in deuteriated acetone with tetramethylsilane as internal standard. The mass spectra were measured with an AEI MS-902 S apparatus at 70 eV.

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