REACTION OF 3-ARYL-2-BENZOYLOXIRANES WITH ALKYL THIOCYANATES

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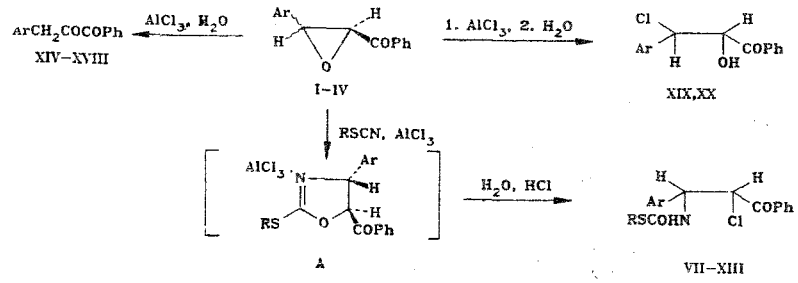
3-Aryl-2-benzoyloxiranes and alkyl thiocyanates in the presence of an equivalent amount of anhydrous $AlCl_3$ form erythro-N-(2-benzoyl-1-aryl-2-chloroethyl)-S-alkyl thiocarbamates and α-diketones. p-Tolyl- and p-anisyl-2-benzoyl-oxiranes do not react with alkyl thiocyanates, but isomerize to the respective α-diketones, and form the threo-chlorohydrins in low yield.

In the reaction of 3-(nitroaryl)-2-benzoyloxiranes with alkyl thiocyanates in the presence of $AlCl_3$, the oxine ring enlarges with a high degree of stereoselectivity to oxazoline, to form the configuration of the benzyl carbon that enters the oxine ring [1, 2].

It was of interest to study the dependence of the direction and stereochemistry of this reaction on the kind of substituent in the aryl segment of the 2-benzoyloxirane.

In the present work we have studied the reaction of alkyl thiocyanates with the trans-3-(p-chlorophenyl)- (I), trans-3-(p-bromophenyl)- (II), trans-3-phenyl- (III), cis-3-phenyl- (IV), trans-3-(p-tolyl)- (V), and trans-3-(p-anisyl)-substituted (VI) 2-benzoyloxirane complexes with $AlCl_3$.

When halosubstituted oxiranes I and II react with methyl, ethyl, and isopropyl isothiocyanates, and when chalcone cis- and trans-epoxides III, IV, react with methyl thiocyanate in the presence of anhydrous $AlCl_3$, the erythro-N-(2-benzoyl-1-aryl-2-chloroethyl)-S-alkyl thiocarbamates VII-XIII form in low yield (Table 1). In addition, oxiranes I-IV isomerize to the respective α-diketones XIV-XVIII. Oxiranes V and VI, which contain electron donor parasubstituents (Me, MeO) do not add methyl thiocyanate; the principal products are the respective α-diketones XVII and XVIII and threo-3-aryl-2-hydroxy-1-phenyl-3-chloropropanones-1 (XIX, XX).



I, VII—IX, XIV Ar=*p*-ClC_6H_4; II, X—XII, XV Ar=*p*-BrC_6H_4; III, IV, XIII, XVI Ar=Ph; V, XVII, XIX Ar=*p*-MeC_6H_4; VI, XVIII, XX Ar=*p*-$MeOC_6H_4$; VII, X, XIII R=Me; VIII, XI R=Et; IX, XII R=*i*-Pr

The IR spectra of thiocarbamates VII-XIII show intense CO bands of the benzoyl and thiocarbamate segments at 1670-1680 cm^{-1}, and a broadened NH at 3400-3410 cm^{-1}.

The structure of thiocarbamates VII-XIII is confirmed by the PMR spectra (Table 2).

In the mass spectra of VII-XIII the [ArCHNHCO—S—R]+ and [ArCHN=C=O]+ ions are evidence for nitrogen bonded to benzyl carbon.

The spin—spin coupling constants between the vicinal protons of VII-XIII lie in the 8.5-9.5 Hz range, which according to the Karplus equation [3] corresponds to dihedral angles of 150-160°. Analysis of the erythro- and threo-configurations of VII-XIII in Dreiding

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TABLE 1. erythro-N-(2-Benzoyl-1-aryl-2-chloroethyl)-S-alkyl-thiocarbamates VII-XIII.

Compound	mp, °C	Found, %					Empirical formula	Calculated, %					Yield,† %
		C	H	Cl*	N	S		C	H	Cl*	N	S	
VII	172—173	55,6	4,2	19,0	4,0	9,1	$C_{17}H_{15}Cl_2NO_2S$	55,4	4,1	19,3	3,8	8,7	20
VIII	156—157	56,7	4,5	18,5	4,0	8,6	$C_{18}H_{17}Cl_2NO_2S$	56,5	4,5	18,6	3,7	8,4	28
IX	168—169	57,9	5,0	17,6	3,8	7,9	$C_{19}H_{19}Cl_2NO_2S$	57,6	4,8	17,9	3,5	8,1	24
X	166—167	49,6	3,8	27,3	3,7	8,1	$C_{17}H_{15}BrClNO_2S$	49,5	3,6	28,0	3,4	7,8	34
XI	148—149	50,9	4,2	27,7	3,6	7,8	$C_{18}H_{17}BrClNO_2S$	50,6	4,0	27,1	3,3	7,5	30
XII	164—165	51,9	4,3	26,5	3,6	7,6	$C_{19}H_{19}BrClNO_2S$	51,8	4,3	26,2	3,2	7,3	25
XIII	185—186	61,4	4,9	10,3	4,5	9,8	$C_{17}H_{16}ClNO_2S$	61,2	4,8	10,6	4,2	9,6	

*For X-XII, total halogen content is given.
†Yield of XIII from epoxide III 14%, from epoxide IV 12%.

TABLE 2. PMR Spectra of erythro-N-(2-Benzoyl-1-aryl-2-chloroethyl)-S-alkyl Thiocarbamates VII-XIII.

Compound	δ, ppm (J, Hz)			
	R	H_A, d	H_B, t	aromatic protons and NH, m
VII	2,28, s	5,93 (8,5)	5,66 (8,5)	7,17—8,13
VIII	1,10, t; 2,76, q (7)	5,97 (8,5)	5,63 (8,5)	7,17—8,18
IX	1,18, d; 1,20, d; 3,47, m (7)	5,95 (8,5)	5,62 (8,5)	7,17—8,18
X	2,15, s	5,93 (9,5)	5,64 (9,5)	7,45—8,15
XI	1,13, t; 2,75, q (7)	5,94 (9,5)	5,60 (9,5)	7,45—8,14
XII	1,15, d; 1,17, d; 3,45, m (7)	5,90 (9,5)	5,58 (9,5)	7,45—8,17
XIII	2,17, s	5,93 (8,5)	5,66 (8,5)	7,20—8,13

models shows that at such angles only the erythro-carbamates can have an intramolecular hydrogen bond (IMHB) of NH with carbonyl oxygen. The IR spectra of VII-XIII in dilute solution showed that the location of the NH band did not change with decreasing concentration down to $2 \cdot 10^{-3}$ M. Only the low-frequency shoulder of the band, caused by intermoledular association, disappears. These data demonstrate the presence of IMHB in thiocarbamates VII-XIII, so that an erythro configuration of the latter can be presumed. For additional confirmation of the assignment of VII-XIII to the erythro series, IR spectra were obtained of dilute solutions of erythro- and threo-N-2-benzoyl-1-(p-nitophenyl)-2-chloroethyl-S-methyl thiocarbamates [1], and it was shown that only the erythro diastereomer has IMHB.

The α-diketones XIV-XVIII were identified by the melting pints of the respective quinoxalines. The chlorohydrins XIX and XX were identified by means of authentic samples.

The results of the present work and the data of [1, 2] can be explained by starting from the presumption that the nature of the reaction products is determined to a significant extent by the degree of positive charge localization on the benzyl carbon of the epoxy ring of the complexes of epoxy chalcones I-IV with $AlCl_3$.

The presence of a p- or m-nitro group in the aryl substituent promotes significant positive charge localization on the benzyl carbon of the epoxy ring. The loosening of the C_β—O•$AlCl_3$ bond makes frontal nucleophilic attack practically immpossible, so that alkyl thiocyanate adds to the benzyl carbon from the rear simultaneously with scission of the C_β—O•$AlCl_3$ and formation of the configuration of the center to be attacked (the S_N2 model).

On the other hand, electron donor substituents in the aryl radical substantially decrease positive charge localization on the benzyl carbon of the epoxy ring. This promotes loosening of the C_β—O•$AlCl_3$ bond by frontal nucleophilic attack; the extent of which increases with increase in the electron donor properties of the substituents in the sequence Br, Cl < H < Me < MeO. Here one must take account of that significant feature of oxirane—nucleophile reactions, viz., that the leaving group remains at a carbon adjacent to the reaction center. Bond loosening, when the developing vacant p-orbital and the orbital of the leaving

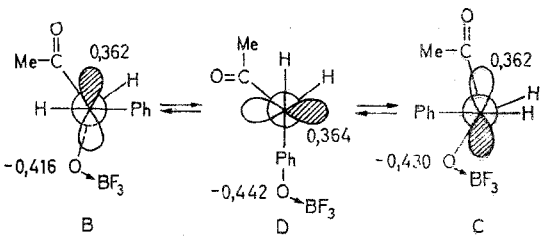
group carrying a negative charge are coplanar, cannot achieve an isolated solvate state, because the maximum distance between the atoms of a dissociated C_β—O•$AlCl_3$ bond, even at a $C_\beta C_\alpha O$ tetrahedral angle, can not exceed the sum of their van der Waals radii [4]. This means that the leaving group should obstruct frontal attack by alkyl thiocyanate, and the primary reaction products should have predominantly the configuration opposite to that of the starting epoxide chalcones (trans-scission). Nevertheless, the isolated chlorothiocarbamates VII-XIII have the erythro configuration; this is possible if the primary intermediate 2-oxazolines have the trans configuration. Formation of trans-2-oxazolines can probably be explained by isomerization of cis-2-oxazoline complex salts (the cis-oxirane IV forms them at once). In this case, in contrast to the cis-2-oxazolines [5], the trans analogs A when isolated from the salt form are quickly converted to erythro-chlorocarbamates VII-XIII.

A definite alternative to such an explanation for the formation of erythro-thiocarbamates VII-XIII can be the presumption that the vacant p-orbital that develops during dissociation of the C_β—O•$AlCl_3$ on the β-carbon of the epoxy ring should, via vibration or rotation around the C_β—C_α bond leave its interaction with the anionoid center of the leaving group, and become accessible to alkyl thiocyanate attack from both sides or from the rear side of the benzyl carbon in the oxirane—Lewis acid complex that has isomerized as a result of rotation.

To verify this assumption, deformed complexes of cis- and trans-3-phenyl-2-acetyloxiranes with BF_3, as model compounds were calculated by the semiempirical MINDO method [6]. All the geometrical parameters were optimized except for Ph and Me(MeCO). The fixed $C_\beta C_\alpha O$ angle was taken as 100°. As a result of the calculation the most stable conformations were found to be the trans complex B (ΔH = -246.9 kcal/mole) and the cis complex C (ΔH = -246.3 kcal/mole). To estimate the rotation barrier between complexes B and C the shielded conformation of the Ph group with the C_β—O•BF_3 bond was calculated analogously (ΔH = -240.7 kcal/mole).

The results of the calculation are evidence that rotation around the C_β—C_α bond at 20° is possible [7] (the barrier is ~ 6 kcal/mole). This leads ultimately to parallel formation of cis- and trans-2-oxazolines, the subsequent fate of which is determined by thermodynamic factors and chemical conversions.

To a certain extent this result agrees with the data of [8] on the parallel formation of cis- and trans-2,2-dimethyl-4-benzoyl-1,3-dioxolanes from acetone and chalcone epoxide—BF_3 complexes.



Thus it can be assumed that the isolated chlorothiocarbamates VII-XIII are obtained by a complex parallel-successive process of formation, isomerization, and reaction of the intermediate 2-oxazolines with HCl.

The decrease in yield of VII-XIII down to zero as the electron donor properties of the substituents increase in the sequence Cl, Br < H < Me < MeO is due to the increase in the competing α-diketone formation that is symbatic with the electron donor properties of the substituents. Here, the stronger are the electron donor properties of the substituents, the less is the positive charge localization on the benzyl carbon of the epoxy ring, and therefore the higher is the negative charge on the leaving group; the latter apparently plays the role of a base, intramolecularly detaching a proton from the α-carbon of the chalcone epoxide.

The formation of threo-chlorohydrins XIX and XX from chalcone epoxides V and VI is the result of cis-scission of the epoxy ring in the decomposition of the chalcone epoxide—$AlCl_3$ complex that is produced in aprotic medium, like that described in [9].

EXPERIMENTAL

IR spectra of chloroform solutions (0.1 M) were recorded on UR-20 and 75-IR spectrophotometers. For the study of IMHB we used solutions of chlorothiocarbamates VII-XIII in CCl_4 (0.002 M) at 10 mm layer thickness. PMR spectra of 10% solutions in $CDCl_3$ were obtained in a Varian HA-100 spectrometer, with HMDS internal standard. Mass spectra were obtained on a Varian MAT-311 spectrometer at 70 eV ionization energy. The identities of the compounds were confirmed by TLC on Silufol UV-254 plates, with ether-hexane eluent.

Quantum chemical calculations were carried out on an EC-1035 computer with a standard program.

N-(2-Benzoyl-1-aryl-2-chloroethyl)-S-alkyl Thiocarbamates (VII-XIII) and threo-2-hydroxy-3-aryl-3-chloro-1-phenyl-1-propanones (XIX, XX). To a solution of 1.34 g (0.01 mole) of anhydrous $AlCl_3$ and 0.1 mole of alkyl thiocyanate in 25 ml of CH_2Cl_2 was added 0.01 mole of chalcone epoxide in 15-20 ml of CH_2Cl_2 over 1 h at 10-15°. Then the reaction mixture was treated with 10 ml of saturated aqueous $KHCO_3$. After the solution was evaporated on a rotary filter the crystalline mass was transferred to a Schott filter and washed repeatedly with small portions of cold hexane. The crystalline precipitate is practically pure erthro-chloro-thiocarbamate (in the case of oxiranes I-IV) or threo-chlorohydrin (in the case of oxiranes V, VI). Chlorohydrin XIX, yield 15%, mp 121-122° [8]; chlorohydrin XX, yield 17%, mp 116-118° [9].

1-Phenyl-3-aryl-1,2-propanediones XIV-XVIII. The hexane filtrate obtained in the preceding experiment is evaporated to yield the α-diketone. Yields of XIV and XV are 50-60%; of XVI, 73%; of XVII and XVIII, 80%.

By treatment with o-phenylene diamine without previous purification, diketones XIV-XVIII are converted to the respective quinoxalines. Quinoxaline from XIV, mp 141-142° (EtOH) [10]; from XV, mp 140-141° (EtOH) [10]; from XVI, mp 98-99° (EtOH-H_2O) [11]; from XVII, mp 131-132° (EtOH) [8]; from XVIII, mp 120-121° (EtOH) [9].

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