tion of 11.3 g (0.053 mole) of sodium metaperiodate in 125 ml of water at 0–5° over a period of 30 min. After stirring for 1 hr, the cold reaction mixture was filtered. The aqueous solution was extracted with 5–30-ml portions of chloroform. The combined chloroform extracts were dried over sodium sulfate. The chloroform was substantially removed by distillation under reduced pressure. The crude product, weighing 2.0 g, possessed an infrared spectrum showing absorption at 1078 cm^{-1} for the S–O bond.[8]

trans-**2-Butene Episulfoxide (II).**—*trans*-2-Butene episulfide, prepared from *trans*-2,3-epoxybutane (99% minimum isomer purity), was distilled at 45–45.5° at 155 mm (lit.[5] bp 43–43.2° at 140 mm) and was found by glpc to be free of the *cis* isomer. *trans*-2-Butene episulfoxide was prepared by oxidation of the episulfide according to the procedure described for the *cis* isomer. The crude product, weighing 0.6 g, showed infrared absorption at 1090 cm^{-1} for the S–O bond.[8]

Pyrolysis of *cis*- and *trans*-2-Butene Episulfoxides.—Samples of each of the isomeric 2-butene episulfoxides were pyrolyzed in the injection port (150°) of an F & M Model 300 glpc instrument. A 30 ft × 1/8 in. column of 30% dimethylsulfolane on Chromosorb P jacketed in an ice bath at 0° was used for separation of the *cis*- and *trans*-2-butenes. Retention times of 31.2 min for *trans*-2-butene and 36.7 min for *cis*-2-butene were determined using known mixtures of the isomeric 2-butenes. Pyrolysis product analyses were determined as peak area per cent of the total column effluent.

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(8) Although isomer purity was established at the episulfide step of the synthesis, it was reconfirmed on the episulfoxides. Using known mixtures of the *cis*- and *trans*-2-butene episulfoxides as infrared standards, it was determined that each isomer possessed a minimum purity of 97%.

The Chemical Shift of the Hydroxyl Proton of Oximes in Dimethyl Sulfoxide

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In the solvents most frequently used in determination of pmr spectra (*i.e.*, $CDCl_3$ or CCl_4) the chemical shift of the OH proton of a hydroxylic substance generally exhibits a very considerable concentration dependence and is therefore not readily correlated with molecular structure; moreover, the OH signal may be quite broad. These phenomena are caused by self-association through hydrogen bonding and by the facile proton exchange among aggregate species catalyzed by the traces of acid almost always present in these solvents. Oximes appear to constitute no exception to this behavior,[1] and this normally precludes the detection of separate OH proton signals due to *syn* and *anti* oxime isomers in mixtures of the two.

We have found that in ≤5 mole % solution in dimethyl sulfoxide most simple oximes and many containing an additional functional group exhibit a hydroxyl proton resonance signal whose chemical-shift value is essentially concentration independent and thus characteristic of the particular oxime. This phenomenon is presumably attributable to the solvent's pronounced tendency to act as a strong hydrogen-bond acceptor which enables it to solvate strongly the oxime monomer. Similar observations have been reported in the case of alcohols[2] and phenols[3] dissolved in this same solvent.

We have now determined the hydroxyl proton chemical shift of some sixty oximes varying widely in type, and have found the signals to range from 8.6 to 13.3 ppm downfield from tetramethylsilane. The data show that the OH proton chemical shift often constitutes a valid basis for assigning *syn*[4] or *anti*[4] configuration to aldoximes and methyl ketoximes and also provides useful information concerning the nature of substituent groups bonded to the oxime trigonal carbon. Other investigators have focused chiefly upon the chemical shift of CH protons in developing criteria for configurational assignment,[5–7] although separate OH proton signals have previously been observed for *syn* and *anti* isomers of isophorone oxime in deuterated dimethyl sulfoxide solution.[8] With few exceptions we have found the OH proton signal rather sharply defined. In no case was splitting of the signal owing to spin–spin coupling detected. More than one oxime OH proton peak invariably signified either (a) the presence of a mixture of *syn* and *anti* isomers or (b) the presence in the molecule of two or more nonequivalent oxime groupings.

Table I summarizes our results with aliphatic aldoximes and methyl ketoximes, two alicyclic ketoximes being included for comparison. In common with other investigators[5–7] we find that most aliphatic oximes isolated and purified by distillation are obtained as mixtures of *syn* and *anti* isomers. In fact the data for all eight isomeric pairs of Table I were obtained from samples containing both geometric isomers. Thus in these instances two separate OH proton signals of unequal intensity were observed. The pure solid *anti* isomer of *n*-heptaldoxime (mp 54–56°) was partially isomerized to the *syn* isomer by heating the neat substance for some time a little above its melting point. This procedure failed entirely to produce detectable amounts of the sterically unfavored and so far unreported *anti* isomers of pivaldoxime and pinacolone oxime from their well-known *syn* isomers.

From Table I it can be seen that for simple aliphatic aldoximes the OH proton signals for the *syn* isomers range from δ = 10.25 to 10.31 ppm, while the range for the corresponding *anti* isomers is δ = 10.60 to 10.68 ppm. Formaldoxime constitutes an exception with δ = 11.01 ppm. Thus, owing to magnetic anisotropy effects, the hydroxyl proton is some 0.4 ppm more shielded in *syn*- than in *anti*-aldoximes. Unequivocal assignment of these signals to *syn*- and *anti*-aldoxime isomers was accomplished by correlating each OH signal with the corresponding trigonal CH signal for the same isomer. Phillips[5] and Lustig[6] had earlier demonstrated that the proton attached to the oxime

(1) N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, "NMR Spectra Catalog," Vol. 2, Varian Associates, Palo Alto, Calif., 1963, Spectra No. 373, 420.

(2) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1257 (1964).

(3) R. J. Ouelette, *Can. J. Chem.*, **43**, 707 (1965).

(4) Throughout this communication *syn*-aldoxime means that isomer in which H and OH are *cis* to one another; analogously the *syn*-methyl ketoxime has CH_3 and OH *cis* to one another.

(5) W. D. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 817 (1958).

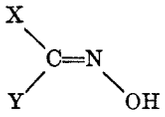
(6) E. Lustig, *J. Phys. Chem.*, **65**, 491 (1961).

(7) (a) G. J. Karabatsos, R. A. Taller, and F. M. Vane, *J. Am. Chem. Soc.*, **85**, 2326 (1963); (b) *ibid.*, **85**, 2327 (1963).

(8) G. Slomp and W. J. Wechter, *Chem. Ind.* (London), 41 (1962).

TABLE I

OH PROTON CHEMICAL SHIFT FOR OXIMES OF ALIPHATIC AND ALICYCLIC KETONES AND ALDEHYDES

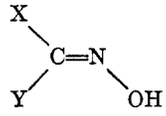


Oxime	X	Y	OH proton shift,[a] δ (ppm)	Oxime	X	Y	OH proton shift,[a] δ (ppm)	$\delta_{OH} - \delta_{CH}$, ppm
1	Cyclohexanone oxime		10.02	12	CH_3	H	10.25	2.95
				13	t-C_4H_9	H	10.26	3.01
2	CH_3	n-C_6H_{13}	10.05	14	C_2H_5	H	10.26	2.96
3	CH_3	C_2H_5	10.06	15	n-C_6H_{13}	H	10.28	2.98
4	CH_3	i-C_3H_7	10.08	16	i-C_3H_7	H	10.28	2.98
5	C_2H_5	C_2H_5	10.10	17	n-C_3H_7	H	10.31	3.01
6	Cyclopentanone oxime		10.10	18	H	i-C_3H_7	10.60	4.16
7	CH_3	CH_3	10.12	19	H	C_2H_5	10.64	4.04
8	n-C_6H_{13}	CH_3	10.12	20	H	n-C_6H_{13}	10.64	4.02
9	i-C_3H_7	CH_3	10.12	21	H	n-C_3H_7	10.66	4.02
10	C_2H_5	CH_3	10.14	22	H	CH_3	10.68	3.96
11	t-C_4H_9	CH_3	10.21	23	H	H	11.01	

[a] All spectral data in this communication were obtained at *ca.* 36° using a Varian Associates A-60 nmr spectrometer. Data are for ≤5 mole % solutions of oxime in dimethyl sulfoxide, whose low-field ^{13}CH satellite at 221 cps was utilized as the internal standard.

TABLE II

OH PROTON CHEMICAL SHIFTS FOR AROMATIC AND HETEROAROMATIC OXIMES



Oxime	X	Y	OH proton shift, δ (ppm)	Oxime	X	Y	OH proton shift, δ (ppm)	$\delta_{OH} - \delta_{CH}$, ppm
24	C_6H_5	CH_3	11.15	28	C_6H_5	H	11.19	3.04
25	C_6H_5	C_6H_5	11.29	29	H	C_6H_5	11.58	3.82
26	C_6H_5	$C_6H_5C(=O)$	11.73	30	2-C_4H_3O	H	11.20	3.18
27	$C_6H_5C(=O)$	C_6H_5	12.44	31	H	2-C_4H_3O	11.74	4.23

trigonal carbon is more deshielded in *syn*- than in *anti*-aldoximes.

It is readily apparent from the data of Table I that replacement of the methyl group of *anti*-acetaldoxime by larger alkyl groups produces a small *upfield* shift of the OH signal (0.02 to 0.08 ppm) while similar replacement in *syn*-acetaldoxime produces a comparable *downfield* shift (0.01 to 0.06 ppm). We have assigned OH signals to individual *syn*- and *anti*-methyl ketoxime isomers (in admixture) on the assumption that similar replacement of *syn*- and *anti*-methyl groups in acetone oxime by larger alkyl groups would produce by analogy a small *upfield* and a small *downfield* shift, respectively. This is the basis for the structural assignments shown in Table I. Thus *syn*-methyl ketoximes exhibit their OH proton signals from δ = 10.12 to 10.21 ppm, while those of the *anti*-methyl ketoximes are found in the range δ = 10.05 to 10.08 ppm. The difference $\delta_{syn} - \delta_{anti}$ is only one-sixth to one-seventh as large as that for the aldoximes, averaging only 0.06 ppm for the three isomeric pairs of methyl ketoximes examined. Nevertheless, the two OH proton peaks are in essence completely resolved when a sweep width of 250 cps is employed in recording the spectra. Our results are consistent with the reasonable assumption of Karabatsos[9] that the sterically favored isomer will likely predominate in mixtures of *syn* and *anti* isomers of this general type. In each instance it is the *syn*-methyl ketoxime which exhibits the more intense OH proton signal.

Table II presents data for a few aromatic and heteroaromatic oximes. These include three pairs of *syn*–*anti* isomers, the benzaldoximes, 2-furaldoximes, and benzil monoximes. Data for *syn*-2-furaldoxime were obtained by partial isomerization of the *anti* isomer, accomplished by heating the neat substance for some time just above its melting point. Here again large differences between OH proton chemical shifts are noted in comparing isomers. In each of these three cases the data show the OH proton to be more deshielded when *cis* to the phenyl or 2-furyl substituent group than when *trans*. This deshielding must be attributed at least partly to the proton's greater proximity to the peripheral paramagnetic effect of the aromatic "ring current." It is of interest to note from the data of both Tables I and II that under our experimental conditions seven *syn*–*anti* pairs of aldoximes show $\delta_{OH} - \delta_{CH} \cong 3$ for the *syn* isomers and $\delta_{OH} - \delta_{CH} \cong 4$ for the *anti* isomers. Durbetaki and Miles[10] first proposed the magnitude of $\delta_{OH} - \delta_{CH}$ as a criterion for assigning aldoxime configuration.

The chemical shift of the OH proton has also been determined for a variety of other compound types containing the oxime group. It has been found that α-

(9) G. J. Karabatsos, J. D. Graham, and F. M. Vane, *J. Am. Chem. Soc.*, **84**, 753 (1962).

(10) A. J. Durbetaki and C. Miles, 148th National Meeting of the American Chemical Society, Chicago, Ill., Aug–Sept 1964, Abstracts A-47.

oximino ketones generally exhibit signals in the range 11.7 to 12.5 ppm; glyoximes, 11.0 to 11.9 ppm; formamidoxime and acetamidoxime, 8.61 and 8.86 ppm (both broad), respectively; ethyl acetohydroximate, 9.25 ppm; acetonitrolic acid, 12.80 ppm; and ethyl α-oximinoacetoacetate, *ca.* 13.1 ppm (very broad). In the case of glyoximes the number of hydroxy proton signals observed is equal to the number of nonequivalent oxime groupings present in the molecule.

Studies are in progress to elucidate more fully the effects of substituent groups upon the OH chemical shift of oximes.

An Example of Sulfur Elimination. The Reaction of Alkyl Isothiocyanates with Anthranilic Acid

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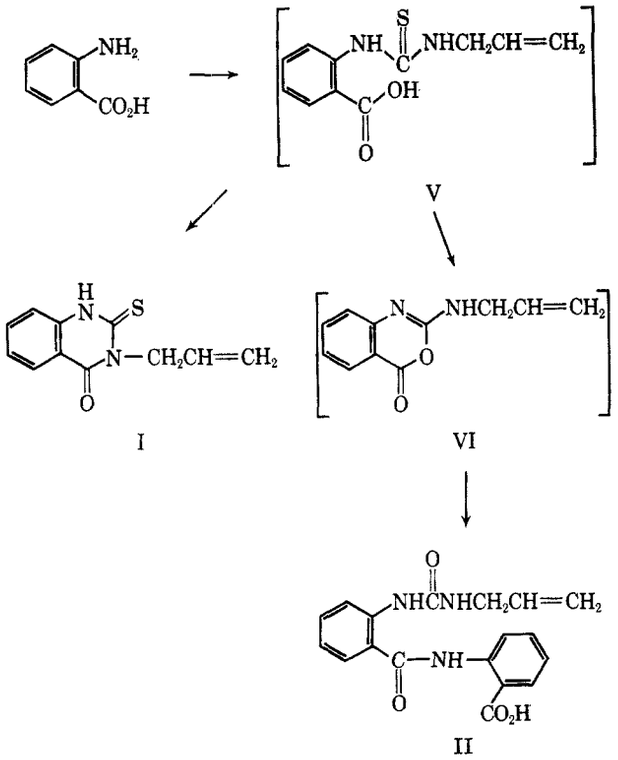
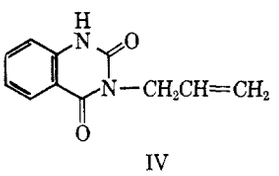
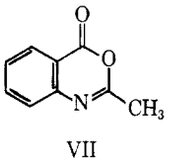
There has been little information available regarding the reaction of isocyanates or isothiocyanates with anthranilic acid. Recently[1] a series of arylureas was prepared from anthranilic acid and aryl isocyanates in refluxing benzene.

In an attempt to prepare 3-allyl-2-thio-2,4-(1H,3H)-quinazolinedione (I)[2] the melt procedure of Dhami, *et al.*,[3] was modified by heating anthranilic acid under reflux in toluene with a 10% excess of allylisothiocyanate. The material which resulted had a melting point close to that reported for I. The microanalytical data however indicated that the material formed contained no sulfur and was not the desired I. The microanalytical values, solubility in aqueous base, and spectral data suggested structure II, N-[*o*-(3-allylureido)benzoyl]anthranilic acid, for the compound obtained. Ethyl isothiocyanate similarly gave a material which was found to be N-[*o*-(3-ethylureido)benzoyl]anthranilic acid (III). Independent synthesis confirmed the proposed structures of these anomalous reaction products. Thus ethyl isocyanate was condensed with anthranilic acid in toluene to give N-(ethylcarbamoyl)anthranilic acid.[4] Conversion of the latter into the acid chloride with thionyl chloride in N,N-dimethylformamide at room temperature, followed by treatment with anthranilic acid, gave the desired III identical with the material obtained by the action of ethyl isothiocyanate on anthranilic acid. The reaction of allyl isocyanate with anthranilic acid was more complicated. An initial attempt to form the urea in toluene led only to the isolation of II in poor yield. When the reaction was carried out in ethanol the desired N-(allylcarbamoyl)anthranilic acid[4] was formed in low yield. Treatment of this material with thionyl chloride in N,N-dimethylformamide at 60° and then with anthranilic acid led to ring closure and afforded only a material which appears to be the quinazolinedione IV. This was surprising since Staiger and Wagner[4] reported N-(allylcarbamoyl)anthranilic acid to be resistant to cyclization with mineral acid. Repetition of this procedure at room temperature afforded a product identical (mixture melting point, infrared, ultraviolet) with the material obtained from allyl isothiocyanate and anthranilic acid.





IV



VII

When allyl isothiocyanate and anthranilic acid were heated under reflux in ethanol, the desired quinazolinedione I was obtained without difficulty. Recently a series of 3-aryl derivatives of I was obtained similarly.[5]

The reaction sequence may involve an intermediate containing an activated carbonyl function such as 2-(allylamino)-4H-3,1-benzoxazin-4-one (VI). Such an intermediate could conceivably arise from the thiourea derivative V. Attack by anthranilic acid at the carbonyl function in VI would then give the product II. Similar activated intermediates derived from anthranilic acid have been reported. Thus acetyl anthranilic anhydride VII formed by the action of acetic anhydride on anthranilic acid[6] undergoes nucleophilic attack to give 2-acetamidobenzamides.[7,8] Although compounds similar to VI have recently been reported[9] an attempt to isolate an intermediate of the type VI by treatment of N-(ethylcarbamoyl)anthranilic acid

(1) Netherlands Patent 6,407,915 (1965); *Chem. Abstr.*, **63**, 1742*d* (1965).
(2) This investigation was supported in part by U. S. Army Medical Research and Development Command, Contract DA-49-193-MD-2754.
(3) K. S. Dhami, H. S. Sachdev, and K. S. Narang, *J. Sci. Ind. Res.* (India), **15B**, 690 (1956).
(4) R. P. Staiger and E. C. Wagner, *J. Org. Chem.*, **18**, 1427 (1953).
(5) K. M. Muraveva and M. N. Shchukina, *Biol. Atkiun. Suedin, Akad. Nauk SSSR*, 54 (1965); *Chem. Abstr.*, **63**, 16347*c* (1965).
(6) J. Kacker and S. H. Zaheer, *J. Indian Chem. Soc.*, **28**, 344 (1951).
(7) M. T. Bogert and R. A. Gortner, *J. Am. Chem. Soc.*, **32**, 119 (1910).
(8) Z. Ecsery and I. Kosa, *Chem. Ber.*, **97**, 302 (1964).
(9) M. Kurihara and N. Yoda, *Tetrahedron Letters*, 2597 (1965).