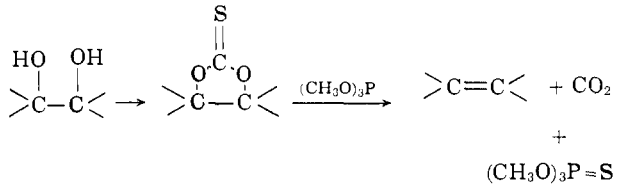
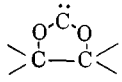
In the present olefin synthesis, a 1,2-diol is converted to a cyclic thionocarbonate derivative which is then transformed into olefin by desulfurization–decarboxylation according to the equation



The first part of the two-step synthesis has been performed in two different ways. Simplest operationally and most efficient is the reaction of a diol with thiocarbonyldiimidazole,[11] in toluene or xylene at reflux for 30 min. This procedure gives the cyclic thionocarbonates directly, in excellent yields, and with essentially complete conversion. Alternatively, diols may be transformed into thionocarbonates by successive treatment in dry tetrahydrofuran solution with 1 equivalent of *n*-butyllithium (Foote Mineral Co., 15% solution in hexane), 1.2 equivalents of carbon disulfide, and 1 equivalent of methyl iodide.[12] Using this procedure, part (*ca.* 50%) of the diol is converted to thionocarbonate and part is recovered unchanged, the separation being accomplished simply by passage through a short column of alumina (Woelm neutral, activity III) in methylene chloride solution.[13]

The elimination reaction which comprises the second step of the olefin synthesis was devised from the hypothesis that a carbene of the type shown might be unstable



relative to olefin and carbon dioxide. Hence, the reagents which have been studied are those that are effective in the removal of sulfur from organic structures. Trimethyl- and triethylphosphite have proved to be both effective and convenient to use and most of our work has been carried out with these reagents.[14] With trimethylphosphite in excess (as solvent) at reflux for 70–80 hr. under nitrogen, cyclic thionocarbonates are converted cleanly to olefins.[15] Specific *cis*-elimination is observed. The stereospecificity and efficiency of the elimination are shown by the following examples (yields of isolated pure product in parentheses).

Thionocarbonate		Olefin
meso-Hydrobenzoin	→	*cis*-Stilbene (92%)
d,l-Hydrobenzoin	→	*trans*-Stilbene (87%)
cis-1,2-Cyclodecanediol	→	*cis*-Cyclodecene (84%)
trans-1,2-Cyclodecanediol	→	*trans*-Cyclodecene (81%)

Even highly substituted olefins can be prepared without difficulty. For example, pinacol was smoothly converted to 2,3-dimethyl-2-butene.

In view of the numerous syntheses of 1,2-diols which are available, often with control of stereochemistry, the thionocarbonate route to olefins is clearly of very broad scope. It constitutes, together with the *trans*-hydroxylation reactions, a general and unambiguous method for the interconversion of *cis* and *trans* olefins; in conjunction with the acyloin reaction it provides a synthesis of *cis* or *trans* cycloolefins in the medium- and large-ring classes.

We are continuing studies of this and other reactions for the synthesis of olefins from 1,2-diols. In addition, other aspects of the chemistry of carbenes from thionocarbonates are being investigated.

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(7) (a) G. Wittig and W. Haag, *Chem. Ber.*, **88**, 1654 (1955); (b) C. B. Scott, *J. Org. Chem.*, **22**, 1118 (1957).

(8) W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 4675 (1952).

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(10) The various syntheses of olefins from acetylenes by addition and from saturated precursors by classical E1, E2, and thermal cyclo-elimination reactions are also subject to a number of limitations which circumscribe their applicability in complex situations.

(11) H. A. Staab and G. Walther, *Ann.*, **657**, 98 (1962).

(12) The carbon disulfide is added *ca.* 5 min. after the lithium reagent and the reaction mixture is kept at 25° for 30 min. and at reflux for 30 min. Then methyl iodide is added and the reaction mixture is again maintained at 25° and at reflux for 30-min. periods.

(13) All the cyclic thionocarbonates which have been prepared to date are nicely crystalline compounds which characteristically exhibit two or more strong bands in the infrared at 7.3-7.9 μ; see R. Mecke, R. Mecke, and A. Lüttringhaus, *Z. Naturforsch.* **10b**, 367 (1955).

(14) Other trivalent phosphorus derivatives with comparable affinity for sulfur may be employed as well. Raney nickel which has been pretreated with acetone at reflux also brings about the elimination to form olefin, but only preliminary studies have been made of this alternative to date.

(15) Shorter reaction times can be used with triethylphosphite at reflux temperature, but the reactions are particularly clean with the trimethyl ester. The products can be isolated readily by addition of alkali to hydrolyze the excess phosphoesters and subsequent extraction.

Transition State Differences between Amides and Esters in Chymotrypsin-Catalyzed Hydrolysis[1]

Sir:

We have found that anilides show diametrically opposed responses to changes in charge density at the reaction site when compared to phenol esters. A previous study of substituent effects has shown that electron withdrawal facilitates the acylation of chymotrypsin by O-acyl-substituted phenols.[2]

The pseudo-first-order rate constants for the α-chymotrypsin-catalyzed hydrolysis of a series of three N-benzoyl-L-tyrosine anilides with substituents in the aniline portion of the substrate follow the Hammett equation with a ρ-value of -1.63 at an H_- value of 6.92 as calculated by least squares from the data shown in Table I.

TABLE I

Substrate	$E_0^a \times 10^5$ M	$S_0^b \times 10^3$ M	k/K_s,[c] min.$^{-1}$ M^{-1}
N-Benzoyl-L-tyrosine anilide	5.281	1.402	1483
N-Benzoyl-L-tyrosine-*p*-methoxyanilide	5.127	0.852	3490
N-Benzoyl-L-tyrosine-*m*-methoxyanilide	5.242	1.429	791
N-(*m*-Nitrobenzoyl)-L-tyrosine anilide	6.528	0.264	880
Hydrocinnamamide	4.191	4.872	95
Hydrocinnam-*p*-methoxyanilide	8.636	0.321	5.15
Hydrocinnamanilide	4.241	2.625	0.59

[a] Total enzyme concentration based on an assumed 24.8×10^3 g./mole of active enzyme. [b] Substrate concentration at zero time. [c] Pseudo-first-order rate constants.

The rate constant ratio for hydrogen-substituted to *meta*-nitro-substituted benzoyl of N-benzoyl-L-tyrosine anilide similarly indicates that electron donation from the α-acylamino group aids the catalyzed process. Details may be found in Table I. If the hydrolysis

(1) This research was supported by a National Institutes of Health grant, RG-8476.

(2) M. L. Bender and K. Nakamura, *J. Am. Chem. Soc.*, **84**, 2557 (1962).

mechanism for anilides is analogous to that of esters,[3] the close adherence of anilide hydrolysis rates to a first-order law implies that acylation of chymotrypsin was the reaction studied.

In addition to the amide link, our substrates differ from O-acylphenols in their β-phenyl and α-acylamino groups. That this difference between esters and amides is not due to the α-acylamino group is shown by the facilitating effect of the *p*-methoxy substituent on the chymotrypsin-catalyzed hydrolysis of hydrocinnamanilides (Table I).

Although the observed negative ρ-value for the anilides reflects an increase in electron demand at the reaction site as the transition state is assembled, the rate constants for the chymotrypsin-catalyzed hydrolysis of anilides are much lower than those of O-acylphenols. This difference in rates between O-acylphenols and anilides corresponds to an increase in electron demand when the relative inductive effects of $-NHC_6H_5$ and $-OC_6H_5$ are compared.

The most straightforward way to resolve this dilemma is to assume that the amide nitrogen, but not the phenolic oxygen, is protonated in the transition state. The high rate of chymotrypsin-catalyzed hydrolysis of hydrocinnamamide relative to hydrocinnamanilide (Table I) is in accord with this hypothesis inasmuch as amines are more readily protonated than anilines. Thus the differences in response to polar changes between esters and amides may be reconciled with previous kinetic results.

The amide nitrogen must become much more basic in the transition state. Otherwise amides would be expected to show a much lower pH optimum than esters. The pH profiles for these reactions are now being studied. These experiments and complete experimental details for the work reported here will be submitted in the near future.

The reactions reported here were followed with an automatic, recording pH-Stat. The solvent for these reactions was prepared by mixing one volume of dimethyl sulfoxide with three volumes of an aqueous solution of 0.015 *M* KCl solution which was 0.0015 *M* in $CaCl_2$. α-Chymotrypsin, Worthington Biochemicals Corp., lot No. 6032 was used.

In the experiments with the N-benzoyl-L-tyrosine anilides, pseudo first-order rate constants were obtained by plotting log $(P_\infty - P_i)$ *vs.* time, t_i, where P_∞ is the titer. Linear plots were obtained to at least 95% completion of the reaction. Most reactions were followed to more than 99% completion to check for side reactions. The rate constants for hydrocinnamoyl derivatives, however, were determined from initial slopes, since the slow hydrolysis rates made it impractical to follow these reactions to completion. The numerical values of the rate constants for the hydrocinnamoyl compounds accordingly should be accepted with some reservation.

The H_- value[4] reported for these experiments was determined by spectrophotometric determination of the ratio of dissociated to undissociated 2-nitrophenol as a function of the e.m.f. between the glass and the reference electrodes of a Leeds and Northrup No. 124138 miniature electrode assembly. The electrodes and conditions were the same as those used for the kinetic experiments. The concentration ratios were determined in the unbuffered solvent described above. The measured value of $d(e.mf.)/d[\log(C_I/C_{HI})]$ was 0.0589 volt; the calculated value of 2.303 RT/F at this temperature is 0.0591 volt. The H_- scale was set using the reported pK_a value of 7.08 for 2-nitrophenol in aqueous solution.[5]

The N-benzoyl-L-tyrosine anilides were formed by treating the corresponding N-benzoyl-L-tyrosine azides with the appropriate aniline in ether solution. The azides were prepared by the action of nitrous acid in the corresponding hydrazides. The hydrocinnamate derivatives were formed by conventional procedures from hydrocinnamoyl chloride and the amine.[6] (Table II).

TABLE II

Compound	M.p.	Lit. m.p.	Ref.
N-Benzoyl-L-tyrosine anilide	208.6–209.6°	208.0–208.5°	(7)
N-Benzoyl-L-tyrosine-*p*-methoxyanilide	205.6–206.6°	...	
N-Benzoyl-L-tyrosine-*m*-methoxyanilide	158.0–159.0°	...	
N-(*m*-Nitrobenzoyl)-L-tyrosine anilide	199.6–200.2°	...	
Hydrocinnamamide	97.2–98.0°	99–100°	(8)
Hydrocinnamanilide	97.5–98.1°	97–98°	(9)
Hydrocinnam-*p*-methoxyanilide	130.2–130.8°	...	

(3) M. L. Bender and B. Zerner, *J. Am. Chem. Soc.*, **84**, 2550 (1962).

(4) L. P. Hammett, "Physical Organic Chemistry," 1st Ed., McGraw-Hill Book Co., New York, N. Y., 1940, p. 269.

(5) M. Rapoport, C. K. Hancock, and E. A. Meyers, *J. Am. Chem. Soc.*, **83**, 3489 (1961).

(6) We are pleased to acknowledge the assistance of Sidney F. Bosen in preparing these compounds.

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Photochemical Cleavage of Aromatic Aldazines

Sir:

In the course of our exhaustive research on reactions of phenyldiazomethane, we observed, when certain photosensitizers[1] were included in photolysis experiments, that whereas the yields of most products remained fairly constant, the yields of benzonitrile increased and the yields of benzalazine decreased correspondingly. Since we could not visualize this as being a direct reaction of phenyldiazomethane, the possibility of forming the nitrile directly from benzalazine[2] was investigated. When benzalazine (1,4-diphenyl-2,3-diazabutadiene-1,3) was photolyzed in quartz[3] with a low pressure mercury arc at room temperature, only about 1% of benzonitrile could be isolated, along with some 17% of *trans*-stilbene. If two equivalent weights of benzophenone were added, however, an 85% yield of benzonitrile was obtained in the same time (3 days, under these conditions). Similar results were obtained with substituted azines; these are summarized in Table I.

Our present thinking leads us to believe that the mechanism of the reaction is not a case of photosensi-

(1) G. S. Hammond, N. F. Turro, and A. Fischer, *J. Am. Chem. Soc.*, **83**, 4674 (1961); K. R. Kopecky, G. S. Hammond, and P. A. Leermakers, *ibid.*, **84**, 1015 (1962).

(2) J. Meisenheimer and F. Heim, *Ann.*, **355**, 269 (1907), reported the formation of benzonitrile from benzalazine on pyrolysis. This reaction was studied briefly (J. E. Hodgkins and D. H. Gibson, unpublished work). The yield of nitrile amounts to *ca.* 30% and is formed from 130 to 250°. The yield is not increased by adding dehydrogenation agents such as selenium or sulfur to the pyrolysis. Some benzonitrile is formed from benzalazine on treatment with strong sulfuric acid.

(3) The reactions proceed in Pyrex equipment but the radiation time must be tripled.