20 cc. of 10% aqueous potassium hydroxide solution was refluxed for 1 hr. Cooling, addition of water, and extraction with ether removed neutral products. Acidification of the aqueous solution, extraction with ether and washing the ether with water until the washings were neutral and evaporation of the solvent gave 3-[2-(2-hydroxy-3,5-xylyl)ethyl]-glutaric acid, m.p. 131–132.5°.

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.3; H, 7.55. Found: C, 64.25; H, 7.56.

Dehydroisocycloheximide. (a) *From isocycloheximide.* A solution of 1.0 g. of isocycloheximide in 20 cc. of acetone was oxidized by the addition of a chromic acid–sulfuric acid mixture.[11] When the mixture retained a brown color for 5 min., 20 cc. of water was added. The mixture was extracted with ether, the ether solution washed with water until the washings were neutral and the extract dried over anhydrous sodium sulfate. Distillation of the solvent and crystallization of the oily residue from aqueous acetone gave 0.81 g. of dehydroisocycloheximide, m.p. 152–154°, $[\alpha]_D^{25}$ −20° (c = 1.0 CH_3OH).

Anal. Calcd. for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.05. Found: C, 64.67; H, 7.30; N, 5.05.

(11) R. Curtis, *J. Chem. Soc.*, 461 (1953).

When a solution of dehydroisocycloheximide in aqueous acetone was added to an excess of aqueous copper acetate a green precipitate of the copper complex formed immediately.

(b) *From dehydrocycloheximide.* To a solution of 1 g. of dehydrocycloheximide[6b] in 20 cc. of pyridine was added 6 cc. of concentrated hydrochloric acid and the mixture was refluxed for 3 hr. Addition of 20 cc. of water to the hot solution followed by cooling gave 0.9 g. of dehydroisocycloheximide, m.p. 151–154°, $[\alpha]_D^{25}$ −23° (c = 1.0 CH_3OH) identified by a mixture melting point (undepressed) and by comparison of the appropriate infrared absorption spectra.

Anal. Calcd. for $C_{15}H_{21}NO_4$: N, 5.05. Found: N, 4.99.

Acknowledgment. The authors wish to express their appreciation to W. A. Struck and associates for microanalyses and rotations, to F. R. Hanson for bioassays, to O. F. Swoap for toxicity determinations, and to Dr. D. J. Cram and Dr. A. K. Bose for helpful discussions.

KALAMAZOO, MICH.

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Cyclic and Acyclic Amides of *cis*-β-(*p*-Bromobenzoyl)-β-methylacrylic Acid

ROBERT E. LUTZ, CARROLL T. CLARK,[2,3] AND JOSEPH P. FEIFER

Received September 9, 1959

Assigned structures of cyclic and acyclic *cis*-β-bromobenzoyl-β-methylacrylic "amides" II–IV, of the cyclic pseudo "acid chloride" V, and of the cyclic and acyclic esters VII–VIII, have been confirmed by ultraviolet and infrared absorption studies. The γ-hydroxylactams show relative pK_a' values of 11.7–11.8, the *cis* acid (the γ-hydroxylactone, Xa) 6.4, the *trans* acid 4.4, and the γ-anilinolactone IIIa 8.4. The anions of the γ-hydroxylactams are cyclic XIII whereas the anions of the acid XIa and the γ-anilinolactone XVI are acyclic. Diazomethane converts the γ-anilinolactone to the acyclic (*cis*) anil-ester XVIII. The cyclic pseudo acid chloride is shown to undergo attack at the chloride group by alcohol and by aromatic amines, but reacts at the lactone carbonyl group with the more basic aliphatic secondary amines.

This paper elaborates upon earlier studies[4,5] of ring-chain tautomerism of *cis*-β-(*p*-bromobenzoyl)-β-methylacrylic acid (Xa), its "acid chloride" which is believed to have the γ-chlorolactone structure V, and its three types of "amides,"[5] the acyclic (normal or true) amides II, the γ-aminolactones III, and the γ-hydroxylactams IV. Examples of all three of the "amide" types had been obtained by reactions between ammonia or amines and the "acid chloride" V. Ammonia and methylamine produced γ-hydroxylactams IVa and IVb; aniline and methylaniline gave γ-aminolactones IIIa and IIIb; and dimethylamine gave the normal (true) *cis* amide IIa. Stereoisomerization by irradiation of the *trans* tertiary amides, the dimethylamide (Id) and the methylanilide (Ie), gave the normal *cis* amides (IIa and IIb), but the *trans* primary amide (Ia) and two *trans* secondary amides (the methylamide Ib and the anilide Ic) went beyond stereoisomerization with subsequent cyclization to the γ-hydroxylactams IVa–c.

The cyclic structure for the acid chloride V had been assigned because of the low rate of alcoholysis and hydrolysis,[6] and because the ester produced by alcoholysis was cyclic (VII). However, this is not sound evidence because the rate of alcoholysis of an acyl chloride group in an acyclic structure of type VI would depend on the steric hindrance involved in this configuration and on its concentra-

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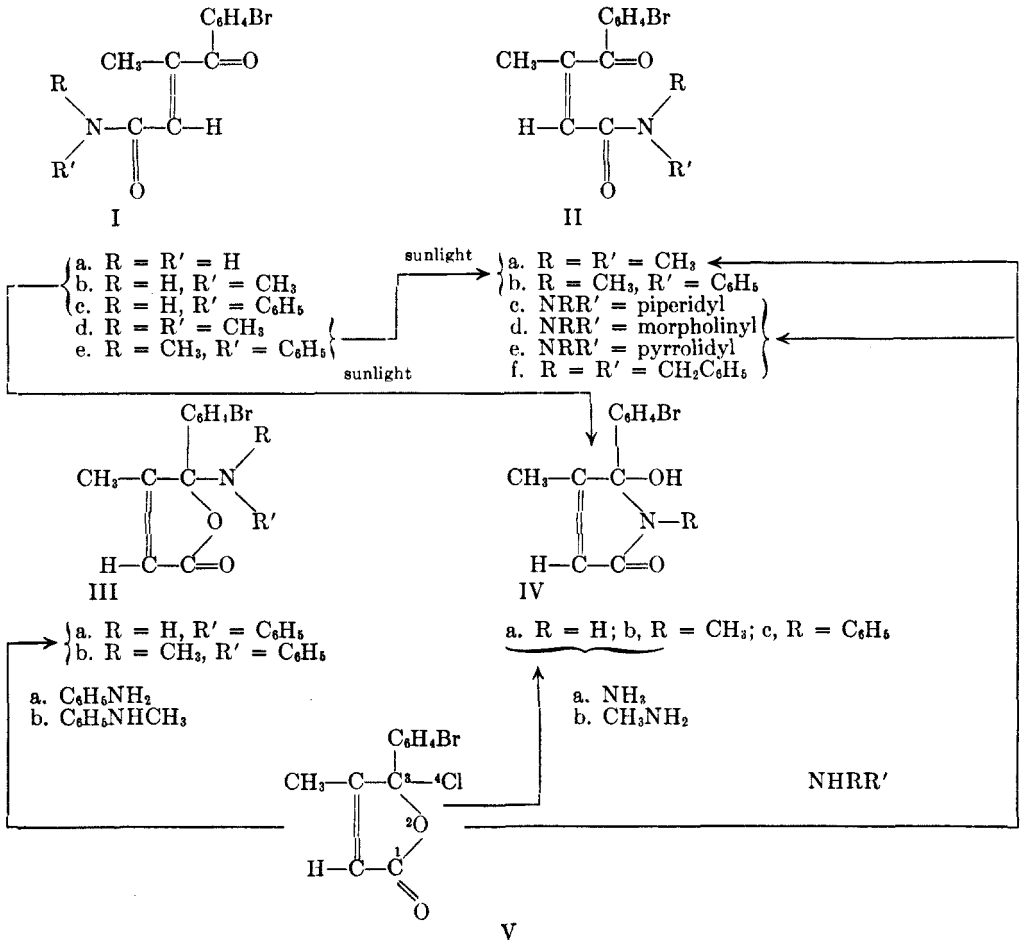
(2) (a) Present address: University of Georgia, Athens, Ga. (b) This paper is based on a dissertation by C.T.C., University of Virginia, 1958. (c) The work was reported at the Atlantic City A.C.S. Meeting, September 1959, abstr. p. 14p. (*Cf.* also ref. 3.)

(3) R. E. Lutz and C. T. Clark, *J. Org. Chem.*, in press.

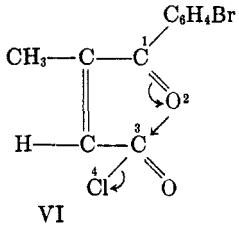
(4) (a) R. E. Lutz, P. S. Bailey, C-K. Dien, and J. W. Rinker, *J. Am. Chem. Soc.*, **75**, 5039 (1953), and references cited therein; (b) J. W. Rinker, Dissertation, University of Virginia, 1955.

(5) (a) R. E. Lutz and F. B. Hill, *J. Org. Chem.*, **6**, 175 (1940); (b) F. B. Hill, Dissertation, University of Virginia, 1940; (c) See references cited in (a) and (b). (d) *Cf.* also polarographic studies by S. Wawzonek, H. A. Laitinen, and S. J. Kwiatkowski, *J. Am. Chem. Soc.*, **66**, 827 (1944).

(6) R. E. Lutz and R. J. Tayler, *J. Am. Chem. Soc.*, **55**, 1168 (1933).



tion if in equilibrium with the cyclic form V, and because of the possibility of a 1,4 reaction mechanism involving a contributing chelate resonance form or transition as indicated in VI.[7]



The ultraviolet absorption spectrum of the acid chloride in isoöctane, or immediately upon solution in methanol before elapse of sufficient time for alcoholysis to occur, showed no *p*-bromobenzoyl type band in the 260–265 mμ region, and this result confirms the postulated cyclic structure V and excludes VI.[9] Infrared absorption of the acid chloride in chloroform solution or in the solid state showed a doublet peak at 5.55–5.64 μ which, although much like that of a conjugated true acid chloride group, must be due rather to the lactone ring carbonyl of the cyclic form V because of the absence of a prominent absorption band at *ca.* 6.00 μ characteristic of the aroyl carbonyl group which would necessarily be present in the acyclic form VI (*cf.* ref. 12). Actually there is a moderately strong 6.04 μ band in this and in spectra of other compounds in this series including IIIa and IIIb which have no bromobenzoyl groups, and it is attributed to the conjugated propylene double bond. Identity of the infrared absorption spectra of the acid chloride in chloroform solution and in the solid state shows that the amount of acyclic form in equilibrium in solution, if any at all, is negligible in amount.

It has been shown previously that the "acid chloride" reacts slowly with alcohol.[6] The ultraviolet absorptivity observed immediately upon solution in ethanol must therefore truly represent the "acid chloride" and not the cyclic ester which

(7) It has been reported that acyclic and cyclic *o*-benzoylbenzoyl chlorides exist and undergo alcoholysis to the acyclic and cyclic esters respectively.[8]

(8) H. Meyer, *Monatsh*, **25**, 475 (1904); **28**, 1211, 1231 (1907).

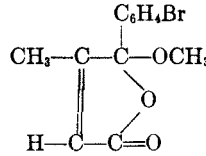
(9) It is assumed that chelation of the type illustrated in VI (2 → 3) would not seriously alter the absorption characteristics of the two carbonyl groups (*cf.* ref. 10, 11).

(10) R. E. Lutz and C-K. Dien, *J. Org. Chem.*, **23**, 1861 (see p. 1866) (1958).

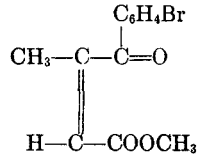
(11) R. E. Lutz and M. G. Reese, *J. Am. Chem. Soc.*, **81**, 127 (1959).

(12) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, 1958.

is ultimately produced from it. This absorptivity, which initially is small in the region characteristic of the aroyl group (ϵ 5,100 at 255 mμ), slowly changes and becomes constant within an hour at a somewhat lower level (ϵ 2,600) close to that of the cyclic ester VII and strikingly different from that of the acyclic ester VIII which absorbs strongly at *ca.* 268 mμ. In a separate experiment under slightly acidic conditions such as would develop during alcoholysis of the acid chloride, the normal ester VIII was shown, by retention of the characteristic ultraviolet absorption of the solution, to be stable and therefore not to be intermediate in the reaction. Thus, it can be said that the "acid chloride" and its alcoholysis product are both cyclic, and that alcoholysis occurs by direct attack at the γ-chloride link (*cf.* ref. 7), presumably by an ionization mechanism.



VII

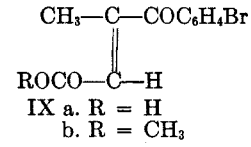


VIII

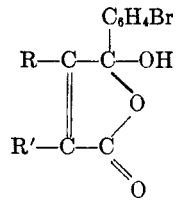
Ultraviolet and infrared absorption determinations confirm the structures previously assigned to the "amides" II–IV on classical chemical grounds. The acyclic types I and II are characterizable by strong 260–265 mμ absorption bands which are due to the aroyl groups necessarily present (*cf.* refs. 13–18), and by overlapping infrared absorption bands at *ca.* 5.9–6.0 μ due respectively to amide and aroyl type carbonyl groups (*cf.* ref. 19). The two cyclic types of "amides," the γ-aminolactones and γ-hydroxylactams III and IV, would show no strong aroyl type ultraviolet absorption and would give rise each to only a single infrared absorption band of *ca.* 5.7 or 5.9 μ respectively.

Specifically the γ-hydroxylactams IVa–c, which were obtained by the action of ammonia and methylamine on the *cis* "acid chloride" V, by ammonolysis of the *cis* esters VII and VIII, and by stereoisomerization of the *trans* anilide, showed no aroyl type ultraviolet absorption at 260–265 mμ as would be required of acyclic compounds of type II.[20] They showed in each case a strong infrared band at 5.8–5.9 μ characterizing the lactam carbonyl group, and a strong 3.0 μ hydroxylic absorption band.

The hydroxyl groups of the γ-hydroxylactams IV, and the N–H group of the γ-anilinolactone IIIa, are significantly though weakly acidic, as is shown by their alkali solubility.[5,22] Putting this to test quantitatively, relative pK_a' values in 50% ethanol were determined for two of the γ-hydroxlyactams, IVa and IVb, for the related largely-cyclic *cis* acid Xa, and for the *trans* acid IXa. The *trans* acid showed the relative pK_a' 4.4, the largely cyclic *cis* acid Xa, 6.4, and the γ-hydroxylactams IVa and IVb, 11.8 and 11.7 respectively. The *cis* α,β-dimethyl acid Xc,[23] which according to absorption spectrum appears to be much closer to completely cyclic at high dilution, showed pK_a' 8.7.

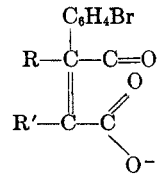


IX a. R = H
b. R = CH_3

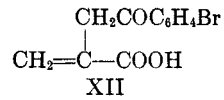


X a. R = CH_3, R′ = H
b. R = H, R′ = CH_3
c. R = R′ = CH_3

The anions of the *cis* acids Xa,[4] Xb,[4] and Xc[17] in solution are shown actually to be acyclic as formulated in XI, by the intense ultraviolet conjugated-aroyl type absorption at *ca.* 260 mμ of strongly basic solutions of these compounds. In one case, Xa, this was demonstrated also in the solid state by using the crystalline sodium salt which gave strong overlapping infrared acid and aroyl type carbonyl bands at 5.8–6.0 μ and no lactone type carbonyl absorption at *ca.* 5.75 μ. On the other hand the acids themselves in the solid state (Xa, Xb, and Xc) are completely cyclic as shown by their strong single infrared carbonyl absorption bands at *ca.* 5.75 μ which characterize the lactone carbonyl group, and by the sharp and intense hydroxyl absorptions at *ca.* 3.0–3.1 μ which are at a somewhat longer wave length than for an ordinary and less acidic alcoholic hydroxyl (the free carboxyl group would not absorb sharply at this point[12]).



XI a. R = CH_3; R′ = H
b. R = H; R′ = CH_3



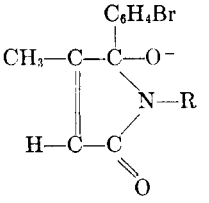
XII

(13) A. Hantzsch and A. Schwiete, *Ber.*, **49**, 213 (1916).
(14) Buu-Hoï and P. Cagniant, *Compt. rend.*, **212**, 268 (1941).
(15) T. Y. Shen and M. C. Whiting, *J. Chem. Soc.*, 1772 (1950).
(16) M. S. Newman and C. W. Muth, *J. Am. Chem. Soc.*, **73**, 4627 (1951).
(17) R. E. Lutz and R. J. Taylor, *J. Am. Chem. Soc.*, **55**, 1593 (1933).
(18) C. L. Browne and R. E. Lutz, *J. Org. Chem.*, **18**, 1638 (1953).
(19) J. F. Grove and A. A. Willis, *J. Chem. Soc.*, 877, 883 (1951).
(20) In all of the anilino compounds the aniline type absorptivity at 235–240 mμ[21] is of course superimposed upon those of the systems being given primary consideration here.
(21) R. A. Friedel and M. Orchin, *Ultraviolet Spectra of Aromatic Compounds*, John Wiley and Sons, Inc., New York, 1951.
(22) *Cf.* also S. Racine, *Ann.*, **239**, 78 (1887).
(23) R. E. Lutz and M. Couper, *J. Org. Chem.*, **6**, 77 (1941).

It should be noted here that the α-methylene isomer of the acid Xb, namely XII, is shown to be completely acyclic in the solid state, as it is in solution,[4] by its lack of hydroxylic infrared absorption band at *ca.* 3.0 μ, by its carboxylic type absorption in the 3.25–3.86 μ region and by the strong bifurcated peak at 5.79–5.84 μ which represents overlapping aroyl and carboxyl carbonyl absorptions.

The existence of the γ-hydroxylactam, apparently completely in the cyclic form IV even at high dilution (5×10^{-5} *M*), is in contrast with the incomplete cyclization at comparable dilution in the case of the more acidic γ-hydroxylactone-*cis*-acid equilibrium (X); in view of the relative pK_a' of 6.4 some observable degree of ionization would be expected. This difference, both in relative stabilities of the cyclic anions and in the facility of cyclization, was predicted from the greater basicity of nitrogen as compared with oxygen.

The three γ-hydroxylactams (IVa–c) when dissolved in 0.1*N* 50% ethanolic–sodium hydroxide showed no significant change in ultraviolet absorption and there developed no band at 260–265 mμ. Thus, the anions of these compounds are in the cyclic forms XIII and are less active than the normal carbamide (acyclic) anions which are not formed to any observable extent. This is in sharp contrast with the *cis* acid Xa which gives the relatively stable acyclic and true carboxylic type anion XIa.[4]



XIII a. R = H
b. R = CH_3
c. R = C_6H_5

The postulated[5] acyclic structure of the *cis* dimethylamide IIa, the product of condensation of the cyclic acid chloride V with the secondary amine dimethylamine, which is also obtained by stereoisomerization of the necessarily acyclic *trans* dimethylamide Id, is confirmed by the strong ultraviolet absorptivity at 260 mμ which could result only from this form, and by the strong infrared absorptivity at 6.02 μ which is presumed to arise from the similarly absorbing keto and amide carbonyl groups. Four other secondary aliphatic amines also produced similarly absorbing acyclic amides, IIc–f.

The γ-aminolactones IIIa and IIIb obtained by the consistently different reactions of V with the weaker bases, aniline and methylaniline,[5] are distinguished from the only alternative II by the lack of aroyl type ultraviolet and infrared absorptions at *ca.* 260 mμ and 6.0 μ respectively, and by the single infrared absorption band for each at *ca.* 5.7 μ which denotes the lactone carbonyl.

The acyclic *cis* methylanilide IIb made by irradiation of the necessarily acyclic *trans* methylanilide Ie shows the characteristic aroyl ultraviolet and infrared absorptivities as strong bands at 265 mμ and 6.0 μ, the latter a superposition of carbamido- and ethylenic bands. There is no indication of a shorter wave length ring–carbonyl band at *ca.* 5.7 μ. These absorptivities are a repetition of those of the *trans* anilide and *trans* methylanilide, Ic and Ie, the structures of which are certain.

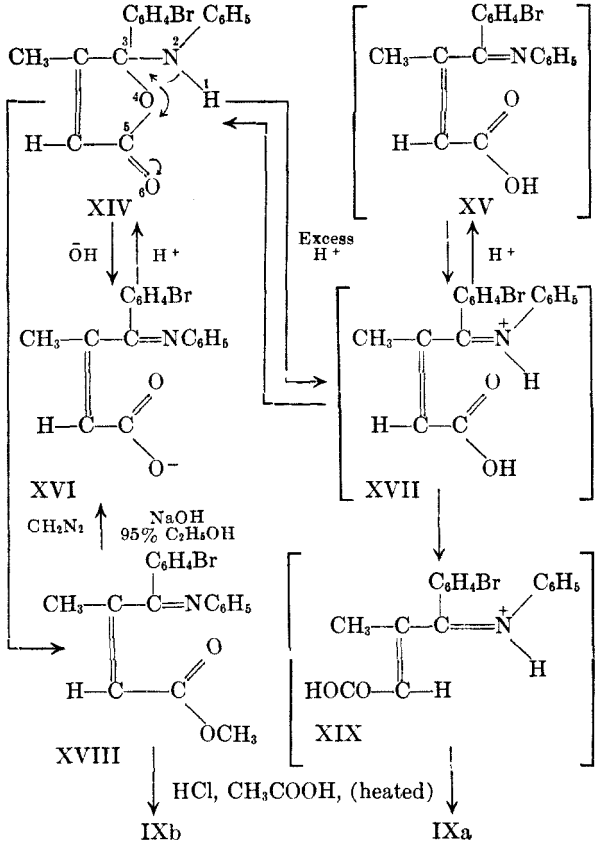
The structure of the *N*-phenyl-γ-hydroxylactam IVc,[5] made from the *trans* anilide Ic under irradiation or acid catalysis, presumably by conversion to and subsequent cyclization of the as yet unknown labile *cis* (acyclic) anilide of type II, is now confirmed by the lack of aroyl type ultraviolet absorptivity at *ca.* 260 mμ, and by the lone infrared lactone-type carbonyl band at 5.78 μ.

To the earlier mechanistic postulates for the reaction by which some of the "amides" I–IV are formed from the cyclic acid chloride V,[5,24] may be added the suggestion that possibly two mechanisms are involved, depending on whether the attacking amine is moderately basic (aliphatic) or weakly basic (aromatic). The active aliphatic amines may well be attacking the lactone carbonyl whose activity is enhanced by the γ-chlorine, with explusion of the chloride ion (SN_2, or in classical terminology, a 1,4-reaction as numbered in V), followed by release of a proton from nitrogen. The less active aryl amines on the other hand, may not be sufficiently basic to initiate this mode of attack, but may be attracted rather to the readily ionizing quaternary γ-carbon in an SN_1 mechanism. Rate studies are in progress to test these ideas.

It is noteworthy that the one γ-aminolactone obtained which carries an N–H group, the anilino compound XIV (IIIa), was shown to be quite acidic in that it formed a sodium salt with sodium hydroxide and was regenerated upon acidification.[5] In 50% ethanol the compound shows an ultraviolet absorptivity of ε 21,000 at its maximum at 235 mμ and falling through ε 5,000 at 262.5 mμ which is the position of the maximum for the acyclic anion XVI (shown below) and for the acyclic anil ester XVIII. Acidification of the 5×10^{-5} *M* solution to 0.1*N* in hydrochloric acid did not alter the absorption curve nor significantly increase the absorptivity at 262.5 mμ as it would have done if there had been an appreciable (and suppressible) equilibrium concentration of the acyclic anil form XV or XVI. The compound is thus shown in highly dilute solution to be chiefly in the γ-anilinolactone form XIV. Infrared analyses in 10% chloroform solution and in potassium bromide pellet consistently show the characteristic absorptivity for the lactone carbonyl and absence of the conjugated carbonyl and anilide group absorptions. There was no observable spectral indication of basic reaction in the sense of conversion into a cation of the anil type XVII in mod-

(24) It is possible, though seemingly unlikely here, that there occurs an actual completed rearrangement step from the cyclic V to a more active acyclic form of the chloride VI which then reacts in the two ways suggested (above).

erately acidic solution as doubtless must happen to some small extent under very strongly acid conditions (*e.g.* during oxindole formation[3]).



The development of an intense ultraviolet absorption maximum at 262.5 mμ when the 5×10^{-5} *M* 50% ethanol solution is made 0.2*N* in sodium hydroxide (ε 23,850 which is only slightly above the value at 0.1*N*) shows that ionization is essentially complete under these conditions and that the ion is in the anil or Schiff base form XVI. The disappearance of this absorption band upon neutralization or acidification to 0.1*N* in hydrochloric acid, and reversion to an absorption pattern exactly the same as that initially, show complete regeneration of the γ-anilinolactone XIV. The relatively high order of the acid strength of the γ-anilinolactone is evident from the further fact that at 5×10^{-5} *M*, 1.7 equivalents of sodium hydroxide cause formation of approximately 70% of the anion, a percentage estimated from the increase in absorptivity at 262.5 mμ toward the maximum ε value for the anion determined in the presence of a large concentration of base where dissociation must be essentially complete. In a futher and quantitative test the γ-anilinolactone was shown to have a relative pK_a' of 8.4 which is close to that of the largely cyclic β-bromobenzoyl-α,β-dimethylacrylic acid (Xc). This acidity, like that of Xc, is accounted for in terms of the ability readily to lose the proton from the nitrogen and thus to give directly the relatively stable carboxylate type anion.

It has been pointed out earlier[5a] that the γ-anilinolactone XIV undergoes hydrolytic and alcoholytic elimination of aniline and stereoinversion to the *trans* acid (or ester) IX under strongly acidic conditions, and that it behaves quite differently from the γ-methylanilino analog IIIb which is rearranged under these conditions to the β-bromophenacyloxindole.[3] This hydrolysis or alcoholysis of XIV does not involve either the *cis* acid Xa, the *cis* cyclic or acyclic ester VII or VIII, or the *cis* or *trans* anilides IVc or Ic, all of which are known and either are stable or react differently under the same conditions.[5] With the information now available it is possible to explain these results. Simple hydrolytic or alcoholytic elimination of methylaniline from IIIb is undoubtedly impeded seriously by the steric hindrance to which the *N*-methyl group contributes very materially, and the slow and somewhat difficult rearrangement to the oxindole[3] is thus allowed to compete successfully. Without the *N*-methyl group, the anilino group of the parent γ-anilinolactone XIV is hydrolytically or alcoholytically eliminated much more easily, probably by the following steps illustrating hydrolysis (alcoholysis would be similar but would involve acid-ester equilibration at the several points): concerted protonation at the lactone bridge or carbonyl oxygen and ring opening to the protonated anil-onium ion, XIV → XVII; stereoisomerization to the *trans* anil XIX; and subsequent *but not prior* hydrolysis of the anil group to the ketone, IX. The point at which the steric effect of the N-methyl in the γ-methylanilinolactone IIIb must operate to block this reaction course, presumably is the step involving formation of the *N*-methyl analog of XVII where the necessary approach to planarity of the *N*-methylanilonium system would face considerable, perhaps prohibitive, steric interference. The steric interference involved in the anilino compound itself at XV or XVII, even though not prohibitive, obviously would greatly increase the lability of the *cis* configuration and would reasonably account for the facile stereoinversion under the strongly acidic conditions which are without effect on the labile, but evidently less labile, *cis* acid or its ester (Xa or VIII).

The γ-anilinolactone XIV, consistent with and supporting the formulations XIV and XVI and the possibility of equilibrations involving the acyclic anil forms XV and XVII, reacted albeit somewhat slowly with diazomethane to give the expected acyclic methyl ester which must have the fixed anil structure XVIII (it is isomeric with the γ-methoxy-*N*-phenyllactam obtained by acid-catalyzed methylation of the hydroxylactam IVc, and it is isomeric with the γ-methylanilinolactone IIIb). Its structure was shown by basic hydrolysis to the original γ-anilinolactone XIV, by the acid-catalyzed configurational inversion with hydrolytic elimination of aniline to give the *trans* ester IXb, by the intense

ultraviolet absorption maximum of 262.5 mμ, ε 23,500, and by the infrared absorptions at 5.81 and 6.06 μ which represent ester and anil groups respectively. The diazomethylation reaction may involve a concerted (1,4) mechanism (XIV), prior removal of the proton of XIV, or possibly actual tautomerization through XV. This problem is being explored further.

EXPERIMENTAL[25]

cis-β-(*p*-Bromobenzoyl)-β-methylacrylyl piperidide and morpholinide, IIc and IId, were made by addition to an 80-ml. sodium-dried dioxane solution of 0.1 mol. of the acid chloride V[5] at 50°, 0.2 mol. of piperidine or morpholine, under stirring; it was then allowed to stand at this temperature for 1 hr. The mixture containing the precipitated amine hydrochloride was cooled and treated with excess water, and the precipitated amide was filtered, washed, dried, and recrystallized. The *pyrrolidide* and *dibenzylamide* were similarly prepared but by working entirely at room temperature. The *dimethylamide*[5] was also obtained working at 10° using 100 ml. of dry benzene saturated with dimethylamine, adding V, allowing the mixture to warm to room temperature, filtering, evaporating, and treating the residue with petroleum hexane. Repetition of the preparation of the γ-anilinolactone IIIa[5] was less successful (yield 70%), and hydrolysis by an acetic–concentrated hydrochloric acid mixture to purified IXa was only 27%.

Sodium β-(*p-bromobenzoyl*)-β-*methylacrylate* was prepared by mixing 2.9 g. of Xa with 80 ml. of 20% sodium hydroxide, filtering the resulting paste, and washing with hot benzene. Xa was recovered upon treatment with 5% hydrochloric acid.

Anal. (Vanadium pentoxide added to aid combustion, otherwise analyses were consistently low). Calcd. for $C_{11}H_8BrNaO_3$: C, 45.39; H, 2.77. Found: C, 45.52; H, 3.03.

II	NR_2	M.P.	Yield, %	Cryst. from
a[5]	$N(CH_3)_2$	115–116.5	50	C_6H_6-C_6H_{14}
c	Piperidyl	141–142	96	65% CH_3OH
d	Morpholinyl	150.5–151.5	82	65% CH_3OH
e	Pyrrolidyl	120–121	75	C_6H_6; C_2H_5OH
f	$N(CH_2C_6H_5)_2$	103–104	78	C_6H_6; C_2H_5OH

		C		H	
Anal.		Calcd.	Found	Calcd.	Found
a	$C_{13}H_{14}BrNO_2$	52.72	53.03	4.76	4.99
c	$C_{16}H_{18}BrNO_2$	57.23	57.08	5.39	5.28
d	$C_{15}H_{16}BrNO_3$	53.27	53.31	4.77	4.63
e	$C_{15}H_{16}BrNO_2$	55.91	55.92	5.00	5.15
f	$C_{25}H_{22}BrNO_2$	66.96	67.25	4.94	5.05

β-(*p-Bromobenzoyl*)-β-*methylacrylic methyl ester anil* (XVIII). Excess of diazomethane in 100 ml. of ether was added to a solution of 8.9 g. (0.0258 mol.) of the γ-anilinolactone (XIV) in 100 ml. of ether. The solution was allowed to stand for 36 hr. at 5° and 24 hr. at room temperature (the reaction is slow). Evaporation gave 9.3 g. (nearly quantitative) of crude product of m.p. 93–97°. Extraction with 0.1*N* sodium hydroxide solution and two recrystallizations from benzene and two from hexane gave an analytical sample, m.p. 101–102.5°.

(25) (a) Microanalyses were by Mrs. Margaret Logan. (b) Ultraviolet determinations were at *ca.* $5 \times 10^{-5}M$ in 95% ethanol unless otherwise specified, using a Beckman DU quartz spectrophotometer. (c) Infrared determinations were made with a Perkin-Elmer spectrophotometer, model 21 or Infracord.

Anal. (Vanadium pentoxide added to aid combustion). Calcd. for $C_{13}H_{16}BrNO_2$: C, 60.34; H, 4.50. Found: C, 60.45, 60.63; H, 4.29, 4.50. Three analyses in which the use

TABLE I

ULTRAVIOLET AND INFRARED ABSORPTION MAXIMA[m]

Ic, mμ[a] 238, 267, ε 18,100, 17,700.

Ie, mμ[a] 264, ε 15,900; μ[f] 6.03s, 6.12s (shoulder), 6.29s, 6.67s.

IIa, mμ[a] 260, ε 21,000; μ[f] 6.00s, 6.17s, 6.29s, 6.74s, 6.94s.

IIb, mμ[a] 261, ε 26,000; μ[e] 6.00–6.04bs, 6.16s, 6.27s, 6.69s, 6.92s.

IIc, mμ[a] 262, ε 21,200; μ[f] 5.96s, 6.04s, 6.18s, 6.29s, 6.84s, 6.95m.

IId, mμ[a] 262, ε 21,700; IIe, 260, ε 22,000;[a] IIf, 260, ε 21,000[a].

IIIa (XIV), mμ[a] 236, ε 19,800. In 50% ethanol: mμ, 235, ε 21,000; when made 0.1*N* in NaOH, see XVI below; then, when neutralized, mμ, 235, ε 27,220; acidified to 0.1*N* HCl, mμ, 235, ε 27,260. mμ,[c] 235, ε 19,320, sloping through 262.5 mμ, ε 2,500; after addition of two equivalents of sodium methoxide solution, 235 mμ, ε 17,000, sloping through shoulder at 262.5 mμ, ε 9,450. μ[e] 5.68s, 6.05w, 6.24m; μ[f] 2.97s, 5.76s, 6.06m, 6.23s, 6.58s, 6.67s, 6.73s, 6.95s.

IIIb, mμ[a] 240, ε 14,600; μ[e] 5.71s, 6.05s, 6.25–6.30bm; μ[f] 5.68s, 6.04m, 6.24m, 6.67s (shoulder 6.72m), 6.95bm.

IVa, mμ[a] 229–250, ε 10,700–3,600; [g,h] μ[f] 2.95–2.99–3.05s (trifurcation), 5.20w, 5.90bs, 6.02m (shoulder), 6.25m, 6.32m, 6.68s, 6.95s.

IVb, mμ[a] 230, ε 12,700;[h,i] μ[f] 3.04s, 3.33–3.37m, 3.47m, 4.23w, 4.55w, 5.20w, 5.89bs, 6.03s, 6.23m, 6.29m, 6.67s, 6.76s, 6.95s, 7.15s, 7.26s.

IVc, mμ[a] 230–280, ε 16,800–3,000.[g,h,j]

V, mμ[a] 243–267, ε 8,700–1,600;[g] μ[e] 3.31m, 4.30m, 5.64s, 6.05m, 6.28w, 6.72m, 7.17m, 7.74w, 8.30s, 8.56w, 9.30m; μ[f] 5.51s, 5.61s, 6.02s, 6.25m, 6.69s, 6.95m.

VII, mμ[c] 232.5, ε 10,800; μ[f] 5.69bs, 6.05s, 6.28w, 6.36w, 6.73m, 6.98m.

VIII, mμ[c] 262.5, ε 18,400; μ[f] 5.81s, 5.95s, 6.06s, 6.28s, 6.74m, 6.94s.

IXa, μ[f] 3.30bm, 5.84–5.94–6.03s (trifurcation), 6.32s, 6.76w, 6.97m.

IXb, μ[f] 5.80s, 6.03s (shoulder 6.10m), 6.30s (shoulder 6.36m), 6.99m.

Xa, μ[f] 3.11bs, 5.76s (shoulder 5.83m), 6.06m, 6.28m, 6.73m, 6.97s, 7.18m, 7.27m, 7.65m, 7.96bs, 8.22s, 8.48m, 8.70s, 9.06m, 11.00bs.

Xb, μ[f] 3.40bm, 5.85–5.94s (bifurcation), 6.31s, 6.83m, 7.00m.

Xc, mμ[a] 230, ε 13,400. Anion:[k] mμ[a] 256, ε 15,500.

XIa, sodium salt, μ[f] 6.00–6.05bs, 6.21s, 6.33bs, 6.74m, 6.87s, 7.02–7.15bs.

XII, μ[f] 3.25–3.86m (broad, serrated), 5.79s–5.85s (bifurcation), 6.05m, 6.25s, 6.91bm, (no band at *ca.* 11 μ).

XVI, determined in 0.1*N* sodium hydroxide–50% ethanol, $5 \times 10^{-5}M$: mμ 262.5, ε 23,410; in 0.2*N* NaOH, ε 23,850.

XVIII, mμ[b] 262.5, ε 22,450 (minimum, 237.5 mμ, ε 12,880); mμ[c] 262.5, ε 23,500[l]. μ[f] 5.81s, 6.06s, 6.19s, 6.32s, 6.40s, 6.76s, 6.96s.

Solvent: [a] 95% C_2H_5OH; [b] abs. C_2H_5OH; [c] CH_3OH; [d] 2,2,4-trimethylpentane (isoöctane); [e] $CHCl_3$; [f] potassium bromide pellet. [g] No maximum; slope defined by the two figures given. [h] The absorption curve is negligibly affected by addition to the solution of a small amount of strong base. [i] Sloping through 244 mμ, ε 5,000. [j] Very broad shoulder centering at 276 mμ, ε 2,800. [k] Produced by adding a small amount of strong base to the solution. [l] On standing in sunlight for 2 days the ε value dropped to a half and after 11 days practically to zero. [m] For ultraviolet, important shoulders or absorption areas are footnoted. For infrared, important bands up to 7 μ are given, with s = strong, m = medium, w = weak, b = broad.

of vanadium pentoxide was omitted were consistently low in carbon by 0.77–0.81%, and indicated incomplete combustion.

Hydrolysis of 0.35 g. of XVIII in 20 ml. of glacial acetic acid and 3 drops of concentrated hydrochloric acid, with refluxing for 30 min., gave 0.18 g. (65%) of IXb, m.p. 72–73°, which was identified by recrystallization from hexane (m.p. 73–74°) and mixture m.p., and by identity of infrared spectrum with that of an authentic sample.

Hydrolysis of 0.53 g. of XVIII in 8 ml. of 95% ethanol containing 0.07 g. of dissolved sodium (24 hr. at room temperature) gave 0.38 g. (75%) of crude XIV which on two recrystallizations from benzene was identified by m.p. 168–168.5°, mixture melting point, and infrared absorption spectrum identical with that of an authentic sample.

Determination of acidities (pK_a').[2b] Because of difficult solubilities in water the determinations were made in 50% ethanol at 25° and they are therefore relative only. The true acids (*trans*), and the *cis* acids, which are partly or largely in the γ-hydroxylactone forms, and the γ-anilinolactone XIV, were sufficiently acidic so that the relative pK_a' values could be calculated from the apparent *p*H values at half neutralization as determined by means of a Beckman Model G *p*H meter. For calculation of the relative pK_a' values for the very weak acids, the γ-hydroxylactams, the apparent *p*H values were determined by the use of trinitrotoluene as an indicator for the range involved and a series of standard sodium hydroxide solutions, and by measuring absorptivities at 450 mμ, with time standardization to allow for slow deterioration of the standards. The relative pK_a' values were: Xa (*cis*), 6.39: IXa (*trans*), 4.37; Xc, 8.69; IVa, 11.8; IVb, 11.7; XIV, 8.40.

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[CONTRIBUTION FROM THE PIONEERING RESEARCH DIVISION, TEXTILE FIBERS DEPARTMENT, E. I. DU PONT DE NEMOURS & COMPANY, INC.]

Some Reactions of *p*-Toluenesulfonyl Isocyanate

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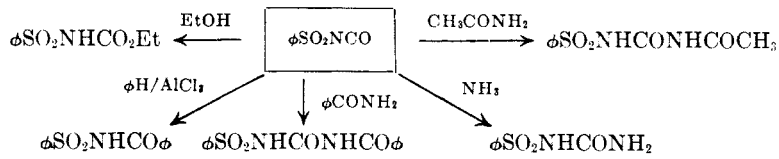
Several new reactions of *p*-toluenesulfonyl isocyanate (I) are reported. Reaction with *N,N*-dialkylamides gives *N,N*-dialkyl-*N'*-*p*-toluenesulfonylamidines (II), with elimination of carbon dioxide. Monoalkylamides give rise to *N*-alkyl-*N*-acyl-*N'*-*p*-toluenesulfonylureas (III) by simple addition, or to *N*-alkyl-*N'*-*p*-toluenesulfonylamidines (IV), with elimination of carbon dioxide. Isobutyraldehyde reacts to give VI. Dimethyl sulfoxide yields *N*-*p*-toluenesulfonyl dimethyl sulfilimine (VII).

Recent published work[1] has described reactions of *p*-toluenesulfonyl isocyanate (I), with monoalkyl- and dialkylamides. We wish to report work done independently in this laboratory on these and other unusual reactions of *p*-toluenesulfonyl isocyanate.

Sulfonyl isocyanates have only recently become readily and economically accessible from high temperature phosgenation of sulfonamides in inert solvents.[2] Billeter[3] had prepared methane- and benzenesulfonyl isocyanates by treating the appropriate sulfonyl chlorides with silver cyanate at 120–140°. With benzenesulfonyl isocyanate he observed typical addition reactions of isocyanates. He further noted that sulfonyl isocyanates undergo ready hydrolysis to sulfonamides, rather than to ureas, which are the usual hydolysis products of isocyanates. Prior to the work of Logemann this appears to be the only reported work on sulfonyl isocyanates.

The work in this paper deals with reactions on *p*-toluenesulfonyl isocyanate, for which a convenient preparation has been described in the patent literature.[2]

Reaction with N,N-dialkylamides. Smooth, rapid reaction occurred when *p*-toluenesulfonyl isocyanate was added to an excess of *N,N*-dialkylamide at room temperature. Reactions were exothermic, and it was not found necessary to add solvent or catalyst. Good yields of crystalline solids were obtained which were products of intermolecular elimination of carbon dioxide. Dialkylamides found to react in this manner were dimethylformamide, dimethylacetamide, *N*-formylpiperidine, *N*-acetylpiperidine, and *N*-methylpyrrolidone. It is believed that the reaction proceeds through a cyclic intermediate, leading to *N,N*-dialkyl-*N'*-*p*-toluenesulfonylamidines. Thus, for the reaction with dimethylformamide:



(1) W. Logemann, D. Artini, G. Tosolini, and F. Piccini, *Ber.* **90**, 2527 (1957); **91**, 951, 2566 (1958).

(2) British Patent **692,360**, June 3, 1953.

(3) O. C. Billeter, *Ber.*, **36**, 690–6 (1904); **37**, 2013–15 (1905).