[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Reaction of Propiolactone with Aniline Derivatives

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Propiolactone reacts directly with aminobenzoic acids or esters, sulfanilic acid or amide, *p*-methylaminobenzoic acid, ethyl *p*-(2-carbethoxyethylamino)-benzoate, *p*-chloroaniline, *p*-bromoaniline, *m*- and *p*-nitroaniline exclusively to form β-amino acids: $ArNHR + \begin{matrix}CH_2—CH_2\\ |\quad\quad |\\ O——CO\end{matrix} \rightarrow ArNRCH_2CH_2COOH$. 3-*p*-Toluidinopropionic acid was the major product also with *p*-toluidine but a little hydracrylo-*p*-toluidide appeared here as well. These reactions are not catalyzed by sodium ethoxide or sulfuric acid. Hydracrylanilide and aniline do not react to yield 3-anilinopropionic acid or anilide under conditions which cause formation of 3-anilinopropionic acid from propiolactone. A mechanism for these findings is presented.

Recently, Gresham and co-workers[1] reported the behavior of propiolactone (I) toward a variety of amines. The products were β-hydroxy amides (II) and β-amino acids (III).

$\begin{matrix}CH_2—CH_2\\ |\quad\quad |\\ O——C=O\end{matrix}$ I

$HOCH_2CH_2CONR_2$ II

$R_2NCH_2CH_2COOH$ III

$p\text{-}H_2N—C_6H_4—COOC_2H_5$ IV

This bidirectional result resembles the bidirectional process found with alcohols,[2] since β-hydroxy esters were reported with basic catalysts and β-alkoxy acids with acidic catalysts.

No simple generalization serves to explain why II is formed from some amines and III from others. Thus ammonia, dimethylamine, ethylamine and dodecylamine all yielded III predominantly with acetonitrile as solvent, whereas methylamine, diethylamine and propylamine produced II. Aniline and ortho substituted anilines produced some of both products but the yield of acid always surpassed that of amide. Indeed, yields were above 90% with aniline (water, solvent), *o*-chloroaniline (acetonitrile) and *o*-nitroaniline (acetonitrile). They did not study meta or para substituted anilines.

At the time when this article on amines appeared we had completed a study of propiolactone with amino acids related to aniline. Amino acids were not included in Gresham's paper except as reaction products. β-Anilinopropionic acid, $C_6H_5NHCH_2CH_2COOH$, was formed from aniline, for example, but there was no suggestion that it might react further with the lactone. Our work shows that reactions of this type can occur.

The compounds which we studied included aminobenzoic acids or esters, sulfanilic acid and amide, *p*-methylaminobenzoic acid, and *p*-(2-carbethoxyethylamino)-benzoic ester. The last compound in this list is the product formed by addition of (I) to ethyl *p*-aminobenzoate (IV). For purposes of comparison, *p*-toluidine, *p*-chloro- and *p*-bromoaniline, *m*- and *p*-nitroaniline were studied also.

Toluidine alone of these compounds gave rise to both the acid and amide. All others yielded only the acid: $YC_6H_4NH_2 + (I) \rightarrow YC_6H_4NHCH_2CH_2COOH$ (Y represents COOH, COOEt, SO_3H, SO_2NH_2, Cl, Br, NO_2) when acetonitrile, acetone and water were the solvents used. It was established that primary amines such as ethyl *m*-aminobenzoate, ethyl *p*-aminobenzoate or *p*-chloroaniline could be made to react not only with one but also with two parts of propiolactone to form the tertiary amine, $YC_6H_4N(CH_2CH_2CO_2H)_2$.

Bartlett and Rylander[3] offer evidence to show that methyl hydracrylate is the initial product of the alkaline methanolysis of propiolactone, subsequent changes leading to methyl acrylate, methyl 3-methoxypropionate and finally 3-methoxypropionic salt. The hydracrylic ester was not only isolable

$$(I) + CH_3OH \xrightarrow{-H_2O} HOCH_2CH_2COOCH_3 \xrightarrow{CH_3OH} CH_2{=}CHCOOCH_3 \xrightarrow[H_2O]{CH_3ONa} CH_3OCH_2CH_2COONa$$

(17% yield in 18 minutes) but also it could be substituted for propiolactone to produce the final sodium 3-methoxypropionate.

One may inquire if an analogous mechanism might hold for the amino acids. If so, hydracrylic amides, β-amino amides and β-amino acids would be the sequence of steps.

Four observations from our work bear on this topic. (1) No β-amino amide was isolated in the presence of acetonitrile as solvent using the reactants as such, or in the presence of sulfuric acid (which merely precipitated the salt of the amine and thus lowered the yield), or in the presence of sodium ethoxide. The chief effect of the latter was to retard the reaction velocity; *e.g.*, instead of ethyl *p*-aminobenzoate being nearly quantitatively consumed by the lactone on standing overnight more than four-fifths of it was recovered. No doubt, the sodium ethoxide sponsored the competing reaction of ring opening and polymerization of the lactone.

(2) Essentially the same results were obtained in the presence of sodium ethoxide when benzene was substituted for acetonitrile, but here a small yield of the β-hydroxy amide (*p*-carbethoxyhydracrylanilide) was obtained.

(3) In the reaction of two moles of (I) with one of *p*-chloroaniline, the product was N-β-(*p*-chloro-

(1) T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert and F. T. Fiedorek, THIS JOURNAL, **73**, 3168 (1951). These authors used the name of β-propiolactone, but since α-lactones are not known and since the γ-lactone here is impossible we are omitting "β" in this name. Propiolactone, of course, is an abridgment of the more correct names: propionolactone or propionic lactone.

(2) T. L. Gresham, *et al.*, *ibid.*, **70**, 1004 (1948).

(3) P. D. Bartlett and P. N. Rylander, *ibid.*, **73**, 4273 (1951).

phenylimino)-dipropionic acid, not 3-*p*-chloroanilinopropiono-(*p*-chloroanilide).

(4) One mole each of hydracrylanilide and aniline in acetonitrile was refluxed for 25 hours. Much of the original anilide was recovered, and there was no formation of 3-anilinopropionanilide or 3-anilinopropionic acid.

From these observations it seems evident that the mechanism of the reaction of propiolactone with amines and amino acids differs from the reaction with alcohols.

Although there is no previous record of reaction of propiolactone and amino acids, there is one recorded application of it to proteins. It has been used by Jones and Lundgren[4] to modify the properties of wool to impart a felting property.

The *m*- and *p*-isomers of N-(carboxyphenyl)-β-alanine are new compounds, but the *o*-isomer was made earlier[5] in a 3-step process from isatin and acrylonitrile, followed by hydrolysis and oxidation.

The reaction of sulfanilamide with (I) in acetone or hot water was straightforward, giving rise to a good yield of *p*-(2-carboxyethylamino)-benzenesulfonamide. Hot water also was a suitable reaction medium for (I) and sulfanilic acid, but to separate the product from unreacted sulfanilic acid it was necessary to convert it to a monomethyl ester. That the structure of this ester was V, not VI, was established by comparing its potentiometric titra-

$CH_3OOCCH_2CH_2\overset{+}{N}H_2—C_6H_4—SO_3^-$ V

$HOOCCH_2CH_2NH—C_6H_4—SO_3CH_3$ VI

tion curve with those of benzoic and sulfanilic acids (Fig. 1).

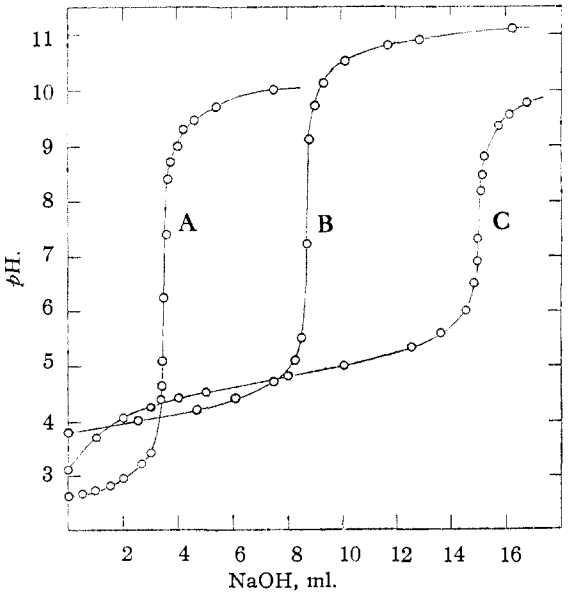
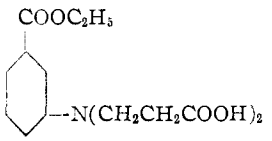
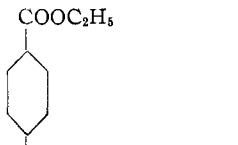


Fig. 1.—Titration curves for acids: A, *p*-(2-carbomethoxyethylamino)-benzenesulfonic acid, 98.5 mg. (0.1090 *N* base); B, sulfanilic acid, 199.9 mg. (0.1315 *N*); C, benzoic acid, 200.4 mg. (0.1090 *N*).

It was a simple matter to convert ethyl *m*-aminobenzoate into β-(*m*-carbethoxyphenylimino)-dipropionic acid (VII) by adding two moles of (I)

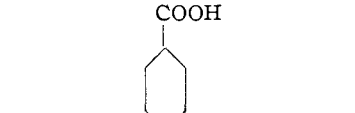


VII

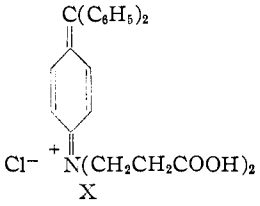


VIII

to one mole of the amino ester, but no such synthesis of the para analog (VIII) was possible out of several approaches tried. Sulfanilamide likewise resisted direct reaction with two moles of (I). Synthesis of VIII was achieved, however, by starting with ethyl *p*-(2-carbethoxyethylamino)-benzoate. The gummy reaction product (an acid diester) was saponified to give a diacid monoester which could have had structure VIII or IX. Evidence for VIII was es-

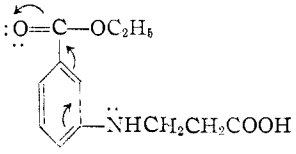


IX

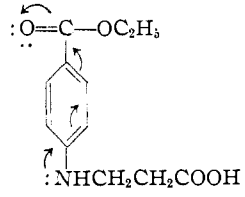


X

tablished by reaction of this colorless compound with phenylmagnesium bromide. An acid solution of the product possessed a deep red color, indicative of a tri-



XI



XII

phenylmethane dye (X). This evidence is inconclusive, however, because the observed effect could be explained by a relatively small amount of highly colored product in otherwise colorless material. A definite proof was sought in the attempted condensation of ethyl acrylate and N-*p*-carboxyphenyl-β-alanine. An adduct should have been of structure IX but no reaction occurred on a steam-bath under these conditions: (a) the ester and the free acid in acetic acid during 24 hours, (b) the ester and the disodium salt of the acid in water (two layers) during 2 to 5 hours, (c) the ester and the solid bis-(benzyltrimethylammonium) salt of the acid. The hot ester did not dissolve the salt but made it gummy.

It seems evident from Gresham's work[1] on simple amines that base strength is not the determining factor in the reaction with propiolactone, for *o*-nitroaniline (k_B 10^{-14}) reacted readily in acetonitrile and diphenylamine (k_B 10^{-15}) reacted at 140–160°

(4) H. W. Jones and H. P. Lundgren, *Textile Research J.*, **11**, 620 (1951).

(5) F. J. DiCarlo and H. G. Lindwall, THIS JOURNAL, **67**, 199 (1945).

TABLE I

N-SUBSTITUTED β-ALANINE DERIVATIVES $HOOCCH_2CH_2NH—R$

R	Mol. formula	Solvent	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
p-$C_6H_4CO_2Et$	$C_{12}H_{15}O_4N$	Acetonitrile	84	137–138	5.90	5.92	237	236.5
p-$C_6H_4CO_2H$	$C_{10}H_{11}O_4N$	Acetone	82.5	198.5 (d.)	6.69	6.63	104.5	105.0
o-$C_6H_4CO_2Et$[a]	$C_{12}H_{15}O_4N$	Acetonitrile	78	104–105	5.90	6.00	237	231
o-$C_6H_4CO_2H$[b]	$C_{10}H_{11}O_4N$	Acetone	82	172–172.5 (d.)	6.69	6.76	104.5	108.6
m-$C_6H_4CO_2Et$[c]	$C_{12}H_{15}O_4N$	Acetonitrile	72	96–98	5.90	6.03	237	234
m-$C_6H_4CO_2H$	$C_{10}H_{11}O_4N$	Acetonitrile	64	203–204	6.69	6.81	104.5	104.3
p-$C_6H_4SO_2NH_2 \cdot H_2O$[d]	$C_9H_{14}O_5N_2S$	Acetone	78	132–133	10.87	10.86	262.0	262.3
p-C_6H_4Cl	$C_9H_{10}NO_2Cl$	Acetone	92	122–122.5	7.02	7.23	199.5	199.4
p-C_6H_4Br	$C_9H_{10}NO_2Br$	Acetone	50.5[e]	102.5–103	5.73	5.68	...	...
p-$C_6H_4NO_2$	$C_9H_{10}N_2O_4$	Acetone	100[f]	156–157.5	13.30	13.57	...	...
m-$C_6H_4NO_2$	$C_9H_{10}N_2O_4$	Acetone	68[g]	119–120	13.30	13.53	210	214

[a] Strong blue fluorescence under ultraviolet lamp. [b] Reported m.p. 170° (ref. 5); alcoholic solution gave violet fluorescence. [c] Weak violet fluorescent under ultraviolet lamp. [d] Anhydrous product, m.p. 138–140°; neut. equiv. calcd. for $C_9H_{12}O_4N_2S$ 244, found 240. [e] Uncrystallizable oil was obtained as well as the crystalline product. [f] Yield based on the reacted amine. [g] Yield based on the reacted amine. A trace of disubstituted product was obtained (*cf.* Table II).

with no solvent. Nevertheless, the reactivity in acetonitrile of XI and the inertness of XII does align itself with basicity differences. That XI should be more basic than XII is evident because the unshared electrons of the para (but not the meta) nitrogen can participate in resonance involving the carbonyl group of the ester. Related also is the fact that reactivity is imparted to XII by esterification, a process which changes basicity by removing the acidity of the carboxy group.

Since sodium chloride and other salts react readily with propiolactone it is reasonable to believe that sulfanilic acid reacts in its dipolar form. If so, these reaction sequences would be anticipated

$$H_3\overset{+}{N}C_6H_4SO_3^- + \underset{\displaystyle O——CO}{\overset{\displaystyle CH_2——CH_2}{\overset{|\quad\quad|}{}}} \longrightarrow$$

$$[H_3{}^+NC_6H_4SO_2—O—CH_2CH_2COO^-] \longrightarrow$$

$$[H_2NC_6H_4SO_2—O—CH_2CH_2COOH]\ (XIII) \longrightarrow$$

$$HO_3S—C_6H_4—NH—CH_2CH_2COOH \quad (XIV)$$

That XIV is formed instead of XIII is reasonable since the latter is a sulfonic ester, hence an alkylating agent. XIV is the result of alkylation of the free amino group.

In these several reactions with propiolactone the driving force must be the strain of the 4-membered ring. Electron availability in the anion of the salt or at the nitrogen atom of the amine molecule must also be a contributing factor in the process.

Experimental

Only a few of the compounds made and listed in Tables I and II will be presented in detail. The others were synthesized by the same general method.

N-*p*-Carbethoxyphenyl-β-alanine.—To a solution of 17 g. (0.1 mole) of ethyl *p*-aminobenzoate in 65 ml. of acetonitrile was added 16 g. (0.22 mole) of propiolactone. Addition was dropwise with stirring at room temperature. The solution was kept overnight before collecting the long colorless needles on a filter; yield 7.74 g. (32.5%). The filtrate, which contained much more of this product, was processed below (filtrate A). The product was recrystallized once from aqueous methanol to give needles melting at 137–138°.

N-*p*-Carboxyphenyl-β-alanine. Method 1.—Filtrate A was added to about 100 ml. of water and kept at −5° for 15 hours. The separated crystalline solid weighed 14.0 g. This solid was stirred with 10% sodium hydroxide solution, and 1 g. of insoluble ethyl *p*-aminobenzoate (m.p. 88–89°) was removed. The alkaline filtrate was immediately acidified at 0–5° to congo red to give 10.8 g. (52% yield) of a light tan precipitate melting at 195–198° (dec.). The sample was recrystallized twice from aqueous methanol to give colorless needles of the desired dicarboxylic acid, m.p. 198.5° (dec.).

Method 2.—A mixture of 0.1-molar portions of *p*-aminobenzoic acid and propiolactone in 180 ml. of acetone was refluxed for 4 hours, then was evaporated on the steam-bath. The resulting solid was treated with about 50 ml. of water to give 13.1 g. of the crystalline XII. Another 4.1 g. (82.5% yield, total) of less pure product was secured on evaporating the filtrate. It was recrystallized from the aqueous methanol, treating with decolorizing charcoal, to give 13.6 g. of white powder, m.p. 198.6–199° (dec.). This did not depress the m.p. of the material from method 1.

Effect of Added Bases. Sodium Ethoxide and Acetonitrile.—A mixture of 8.3 g. of ethyl *p*-aminobenzoate (IV), 4 g. of (I), 100 ml. of acetonitrile and 0.5 g. of sodium methoxide was refluxed for one hour, then was kept at 25° for 12 hours. The sodium ethoxide was almost insoluble in acetonitrile and larger amounts caused no essential difference from this experiment. The solvent was evaporated off, and from the residue 6.9 g. of IV remained undissolved by treatment with 50 ml. of 20% sodium carbonate solution. That this ester, m.p. 85–87°, contained none of *p*-carbethoxyhydracrylanilide was proved by its complete solubility in 10% hydrochloric acid solution.

Acidification of the alkaline filtrate to congo red yielded 1.8 g. of N-*p*-carbethoxyphenyl-β-alanine, m.p. 137–138° after two recrystallizations from aqueous methanol.

Sodium Ethoxide and Benzene.—The procedure was the same except for the use of 100 ml. of benzene in place of 100 ml. of acetonitrile. From the 8.5 g. of residue left after extraction of the acidic product (1.0 g.) with alkali and evaporation of the benzene solution, 1.7 g. of it was insoluble in 5% hydrochloric acid. The remainder was unused IV. The 1.7-g. portion was separated by crystallization from aqueous methanol into N-*p*-carbethoxyphenyl-β-alanine (m.p. 137–138°, 0.65 g., more insoluble) and *p*-carbethoxyhydracrylanilide (m.p. 117°, 0.5 g.). The latter was analyzed.

Anal. Calcd. for $C_{12}H_{15}NO_4$: N, 5.90. Found: N, 5.88.

Pyridine and Benzene.—A mixture of 8.3 g. of IV, 100 ml. of benzene, 4 g. of propiolactone and 2 ml. of dry pyridine was refluxed for 13 hours, then the solvent was removed under diminished pressure. Processing of the residue resulted in the separation of 5.3 g. of unused amine (m.p. 87–88°) and 2.5 g. of N-(*p*-carbethoxyphenyl)-β-alanine. The latter melted at 137–138° after recrystallization.

Effect of Added Acid.—When three drops of concd. sulfuric acid was added to a mixture of 8.3 g. of (IV), 100 ml. of acetonitrile and 4 g. of (I), there was an immediate precipitation of the sulfate of IV. Processing after 2.5 hours of refluxing and 14 hours at 25° resulted in the isolation of 0.75 g. of unused IV and 8.9 g. (75%) of N-*p*-carbethoxyphenyl-β-alanine, m.p. 137–138.5°.

***p*-(2-Carboxyethylamino)-benzenesulfonamide.**—To a solution of 17.2 g. (0.1 mole) of sulfanilamide in 100 ml. of

TABLE II

IRREGULAR N-SUBSTITUTED β-ALANINES

Reactant	Product	Solvent	Yield, %	M.p., °C.	Mol. formula	Nitrogen, % Calcd.	Nitrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
p-$EtO_2C(CH_2)_2NHC_6H_4CO_2Et$	*p*-$(HOOCCH_2CH_2)_2NC_6H_4COOEt$	Acetonitrile	84[a]	128–130	$C_{15}H_{19}O_6N$	4.53	4.85	154.5	153.4
m-NH_2-C_6H_4-COOEt	*m*-$(HOOCCH_2CH_2)_2NC_6H_4COOEt$	Acetonitrile	60	129–131	$C_{15}H_{19}O_6N$	4.53	4.61	154.5	158.1
p-NH_2-C_6H_4-SO_3H	*p*-$CH_3O_2CCH_2CH_2NHC_6H_4SO_3H$	Water	88[b]	197–199 (d.)	$C_{10}H_{13}O_5NS$	5.41	5.22	259	258
p-CH_3NH-C_6H_4-COOH	*p*-$HO_2CCH_2CH_2NC_6H_4COOH$ CH_3	Acetone	87	178–179 (d.)	$C_{11}H_{13}O_4N$	6.27	6.51	111.5	110.6
p-NH_2-C_6H_4-Cl	*p*-$(HOOCCH_2CH_2)_2N$-C_6H_4-Cl[c]	Acetone	90	133–133.5	$C_{12}H_{14}NO_4Cl$	5.16	5.25	135.8	136.6
p-NH_2-C_6H_4-Br	*p*-$(HOOCCH_2CH_2)_2NC_6H_4Br$[d]	Acetone	90	146–147	$C_{12}H_{14}NO_4Br$	4.43	4.61	158	159.6
m-NH_2-C_6H_4-NO_2	*m*-$(HOOCCH_2CH_2)_2NC_6H_4NO_2$	Acetone	Trace[e]	133.5–134.5	$C_{12}H_{14}N_2O_6$	9.93	10.15	...	...

[a] Yield based on the reacted starting material. [b] Yield based on the reacted sulfanilic acid. *Anal.* Calcd.: C, 46.3; H, 5.41. Found: C, 46.24; H, 5.28, neut. equiv. by potentiometric titration. [c] *Anal.* Calcd.: C, 53.04; H, 5.16. Found: C, 53.23; H, 5.15. [d] *Anal.* Calcd.: C, 45.6; H, 4.43. Found: C, 46.08; H, 4.49. [e] By-product from lactone and *m*-nitroaniline (1:1) *cf.* Table I.

acetone was added 7.2 g. of the lactone (0.1 mole) in one portion. The clear solution was refluxed for 2 hours and then kept at 25° overnight. The acetone was distilled off and the residue was treated with 50 ml. of water to give 18.9 g. (78% yield) of *p*-(2-carboxyethylamino)-benzenesulfonamide. The sample was recrystallized once from aqueous methanol to give colorless plates, m.p. 138–140°.

Repeated crystallization from water gave the monohydrate, m.p. 132–133°. This partly melted at 100° and evolved a bubble of water.

β-(*m*-Carbethoxyphenylimino)-dipropionic Acid (VI).—To the solution of 10 g. (0.06 mole) of ethyl *m*-aminobenzoate (b.p. 138–138.5° (4 mm.)) there was added 10 g. (0.14 mole) of the lactone dropwise in five minutes. Then the mixture was kept at 20–25° for two days. An aliquot was added to an excess of water. Since the resulting oil did not solidify the reaction mixture was refluxed for 4 hours and then poured into about 300 ml. of water. From the milky solution there was obtained 12 g. (60%) of solid on chilling to 0°. One recrystallization from methanol–water yielded a white powder of m.p. 119–124°. After several recrystallizations from water its m.p. was 129–131°.

Ethyl *p*-(2-Carbethoxyethylamino)-benzoate.—Into a refluxing suspension of 13.5 g. of N-*p*-carboxyphenyl-β-alanine in 100 ml. of absolute alcohol was bubbled dry hydrogen chloride for 45 minutes. The clear solution was condensed *in vacuo* and then an excess of ether was added to cause precipitation of the amino ester hydrochloride; yield 15.2 g. This salt was treated with saturated sodium carbonate solution. The insoluble white solid was collected and washed with water; yield 13.8 g. It was recrystallized from aqueous acetone to give 12 g. of white plates of m.p. 69.5–71°.

β-(*p*-Carbethoxyphenylimino)-dipropionic Acid (VIII).—To the solution of 10.5 g. of ethyl *p*-(2-carbethoxyethylamino)-benzoate in 80 ml. of acetonitrile was added 4 g. of the lactone (an excess). After 19 hours of refluxing, the solvent was removed and there was added 100 ml. of saturated sodium carbonate solution to cause separation of 3.2 g. (30%) of unreacted diester, m.p. 69–70° after one recrystallization from aqueous acetone. The alkaline filtrate was acidified to congo red with 20% hydrochloric acid. The resulting white gum did not crystallize. It was soluble in dilute hydrochloric acid.

The white gum was dissolved in about 30 ml. of 20% sodium hydroxide solution and heated on a steam-bath for two hours. On acidification to congo red with 20% hydrochloric acid another white gum resulted. It was extracted with ether and changed to a white, crystalline solid after removal of the ether; yield 7.2 g. or 84%, based on the diester which reacted. It was recrystallized from 150 ml. of 30% aqueous methanol to give colorless, long needles (3.9 g.) melting at 128–130°. From the filtrate another 2 g. of less pure product was obtained by concentrating it.

Reaction of Phenylmagnesium Bromide with (VIII).—The Grignard reagent was prepared from 0.7 g. of magnesium turnings, 5 g. of dry bromobenzene and 30 ml. of dry ether. To the reagent was added gradually during one hour a solution of 0.7 g. of (VIII) in 10 ml. of dry pyridine and 10 ml. of dry ether. Since immediate precipitation of the starting material was observed when a drop of the pyridine–ether solution hit the surface of the Grignard reagent, 200 ml. of dry benzene was added to the reagent and the addition of VIII was continued at reflux temperature. An intensely deep yellow color was observed and the reflux was continued for an additional hour and then the colored solution was kept overnight at room temperature. The next day it was again refluxed for an hour and then cooled and poured into 100 ml. of ice–water and 100 ml. of concd. hydrochloric acid.

A dark red coloration was observed in both organic and aqueous layers. The benzene layer was separated and extracted with two 50-ml. portions of 10% hydrochloric acid. The red color transferred to the acid layer. The combined acid layers were neutralized with solid sodium carbonate at first and a saturated solution of sodium carbonate at the end. Dark resinous material was obtained by the addition of sodium carbonate solution to the red acidic solution which caused the color to disappear completely. Addition of hydrochloric acid to the colorless basic solution restored the deep red color. The color change was, thus, reversible.

***p*-(2-Carbomethoxyethylamino)-benzenesulfonic Acid (V).**—Sulfanilic acid (8.7 g., 0.05 mole) was dissolved in 200 ml. of boiling water and propiolactone (7.2 g., 0.1 mole) was added dropwise during five minutes. The reaction

mixture was refluxed for two hours, then was evaporated to dryness *in vacuo* and the tan-colored solid residue was refluxed with 200 ml. of methanol for two hours. The insoluble sulfanilic acid was separated: weight 5.75 g., neut. equiv. 176 (calcd. 173). Thus, only 2.95 g. of sulfanilic acid entered into reaction. The methanolic solution was concentrated on a steam-bath and enough acetone was added to precipitate the product; yield 3.9 g. (88%, based on reacted sulfanilic acid). The precipitation was repeated thrice to give a white powder of m.p. 197–199° (dec.).

β-(*p*-Chlorophenylimino)-dipropionic Acid.—*p*-Chloroaniline (12.8 g., 0.1 mole), propiolactone (16 g., 0.22 mole) and acetone (50 ml.) were mixed and refluxed for four hours and then kept at room temperature for 24 hours. The solvent was removed and the resulting crystalline solid was treated with about 50 ml. of water at 5°. After several hours, the sticky, light gray solid was collected on a filter and air-dried to give 24.3 g. (yield 90%) of crude product. It was crystallized from aqueous methanol (50 ml. of methanol, 120 ml. of water, and some Norit) to give 19.4 g. of light gray crystalline solid. The sample was recrystallized twice more to yield fine, colorless crystals of m.p. 133–133.5°.

Hydracrylanilide and Aniline.—A mixture of 4.5 g. of hydracrylanilide,[1] m.p. 110–112°, 50 ml. of acetonitrile and 2.55 g. of aniline was refluxed for 25 hours. Then the solvent was removed and sodium carbonate solution was added to the residue. Ether extraction removed 2.3 g. of the original anilide, m.p. and m.m.p. 110–112°. No 3-anilinopropionanilide or 3-anilinopropionic acid was obtained on acidification of the sodium bicarbonate solution to congo red. The solution was clear and nothing in it was extracted by ether.

Reaction with *p*-Toluidine.—Equimolar portions of *p*-toluidine (21.4 g.) and propiolactone (14.4 g.) were dissolved in 100 ml. of ether. The clear solution boiled spontaneously in a few minutes and this boiling lasted an hour. The mixture was kept at 25° overnight, then solvent was removed. The acidic part of the white solid residue was taken up in sodium carbonate solution. There remained 12.5 g. of insoluble amide, and another 1.6 g. was obtained (39.5% total yield) from the aqueous solution by ether extraction. Recrystallization from 300 ml. of water (Norit) gave 12.1 g. of long, colorless needles of m.p. 64–66° (probably a hydrate). After desiccation, the weight dropped to 11.2 g. and the m.p. changed to 101–103°. Three more crystallizations and desiccation brought the m.p. to 104–105°. This was hydracrylo-*p*-toluidide.

Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.0; H, 7.26; N, 7.82. Found: C, 67.3; H, 7.40; N, 8.15.

Benzoyl Derivative.—3-Benzoxypropiono-*p*-toluidide, prepared by benzoylation of the above compound, melted at 135–137° after crystallization from methanol–water.

Anal. Calcd. for $C_{17}H_{17}NO_3$: N, 4.98. Found: N, 5.07.

N-*p*-Tolyl-β-alanine.—The sodium carbonate solution was made acid to litmus and the oil which appeared was taken up in ether, from which there was obtained 21.4 g. (59.5%) of brown sirup. No satisfactory way was found to crystallize this acid, but its salt was prepared by treating 10 g. of it in 60 ml. of absolute alcohol with sodium ethoxide from 1.2 g. of sodium. The sodium salt was quite soluble but 2.0 g. of white solid separated.

Anal. Calcd. for $C_{10}H_{12}NNaO_2$: Na, 11.44. Found: Na, 11.39.

These yields of 39.5% toluidide and 59.5% acid are in contrast to the yield of 14.5% of toluidide obtained when acetone was taken as solvent rather than ether.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, REED COLLEGE]

Attempts to Resolve Racemic Amines by Means of Optically Active, Acidic Synthetic Polymers[1a]

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Optically active phenol–formaldehyde type resins were prepared from both optical isomers of β-(*p*-hydroxyphenyl)-butyric acid (I) and from N-*p*-toluenesulfonyl-L-tyrosine (II). No substantial amount of racemization occurred during polymerization or subsequent treatments which the resins received. The optically active resins were placed in columns and solutions of racemic α-pipecoline, α-methylbenzylamine and other amines passed through slowly in the hope that one optical isomer might be preferentially bound to the resin. The first samples of amine which broke through were, however, devoid of optical activity. A theoretical discussion of the experiments is offered.

One would expect that if a racemic substance in solution were brought into contact with an optically active adsorbent, one constituent of the racemate would be more strongly adsorbed[2] than its antipode. This would constitute a method of resolution. The literature records a number of efforts,[3] some failures, others partially successful, to achieve such resolution using naturally occurring adsorbent materials such as wool, *d*-quartz and cellulose. The present work is a study, the first of its kind,[4] of the possibility of using synthetic optically active polymers as agents for the resolution of racemic substances.

In planning these experiments, a column type of operation was chosen so that any resolving effect would be magnified, as in the case of the usual ion exchange resins. It was clear that the synthetic optically active polymers should have the insolubility and chemical stability customary in ion exchange materials, and that the polymers should not be racemized by the reagents to which they would be exposed. For a monomer from which a polymer would be prepared, there were again three require-

(1) (a) Presented before the Division of Organic Chemistry at the 121st Meeting of the American Chemical Society, Milwaukee, Wis., April, 1952. (b) Chemistry Department, University of North Carolina, Chapel Hill, N. C.

(2) For present purposes, the term "adsorption" embraces strong binding forces such as salt formation as well as van der Waals and other weak binding forces.

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