[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, XAVIER UNIVERSITY]

# Itaconic Acid Derivatives of Sulfanilamide

BY PETER L. PAYTASH, MALCOLM J. THOMPSON[1] AND MAURICE E. FYKES[1]

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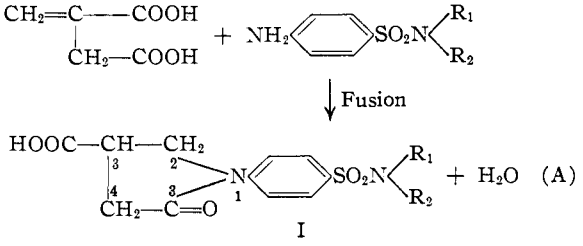
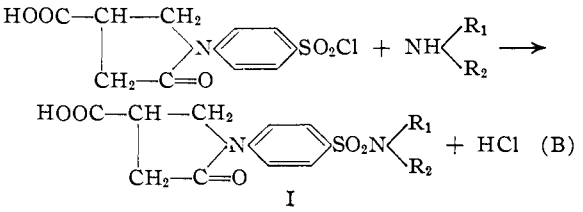
Fusion of itaconic acid and sulfanilamides formed $N^4$-itaconyl acid sulfanilamides rather than 1-(*p*-sulfamyl)-phenyl-5-oxo-3-pyrrolidinecarboxylic acid derivatives. Derivatives of 1-(*p*-sulfamyl)-phenyl-5-oxo-3-pyrrolidinecarboxylic acid were readily formed by condensing 1-(*p*-chlorosulfonyl)-phenyl-5-oxo-3-pyrrolidinecarboxylic acid with amines. $N^4$-Itaconyl acid sulfanilamides are not intermediates in the formation of 1-(*p*-sulfamyl)-phenyl-5-oxo-3-pyrrolidinecarboxylic acid derivatives.

Reactions involving the condensation of primary amines with itaconic acid to give 1-(alkyl or aryl)-5-oxo-3-pyrrolidinecarboxylic acid derivatives were previously reported.[2] This investigation is a continuation of that work as applied to sulfanilamides.

Little success was attained by fusion of sulfanilamide with itaconic acid to give similar compounds. Fifty sulfanilamides were investigated by reaction (A) with only eleven giving the desired 1-(*p*-sulfamylphenyl)-5-oxo-3-pyrrolidine carboxylic acid derivatives (I). The yields were very poor except in the case of sulfanilamide[2] (74%) and sul-



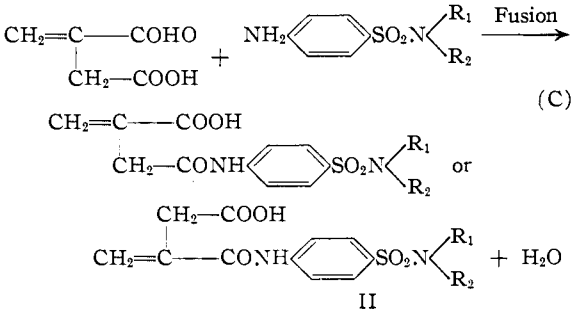
faguanidine[2] (61%). However, the sulfanilamide derivatives could be synthesized readily by condensing 1-[*p*-(chlorosulfonyl)-phenyl]-5-oxo-3-pyrrolidine carboxylic acid with primary and secondary amines[3] by reaction (B)



Their properties are given in Table I.

In the other cases, $N^4$-itaconyl acid sulfanilamides (II) were formed by reaction (C). The forty derivatives thus obtained are listed in Table II. Only a short fusion time is required for the formation of these itaconyl derivatives, and in some cases longer fusion produces compounds of Type I as well as those of Type II in addition to a by-product of undetermined structure which also resulted from the fusion of substances of type II with itaconic acid.

Derivatives of type I could not be prepared from



II

the itaconyl derivatives II, nor could the reverse reaction be accomplished. Condensing of (II) with its corresponding sulfanilamide under varying conditions such as temperature, time and concentration did not form product (I).

In attempting to separate mixtures of derivatives (I) and (II) it was found that both types dissolved in sodium bicarbonate (*p*H 8.4) and were reprecipitated by acids; that recrystallization from different solvents was of no value; and that separation from solutions buffered from *p*H 0 to *p*H 6 also failed. However, they can be separated by acid or base hydrolysis: derivatives of type (II) produce itaconic acid and the corresponding sulfanilamide (insoluble in sodium bicarbonate) while derivatives of type (I) remain unchanged (soluble in sodium bicarbonate).

## Experimental

**Preparation of Sulfanilamides.**—The sulfanilamides used in this investigation were synthesized according to methods found in the literature and verified for their authenticity by melting points.

**Reaction (A). Procedure.**—Five grams of itaconic acid (technical grade)[4] (m.p. 165–171°) was heated to a temperature of about 180° (125-ml. erlenmeyer flask). To this was added, in one portion, two grams of the appropriate sulfanilamide. The mixture was heated to reflux stage (evidence of water in flask) for two to five minutes and cooled to room temperature. Forty ml. of 6 *N* sodium hydroxide[5] was added and the mixture was refluxed for approximately two hours. It was then cooled to room temperature, acidified with dilute hydrochloric acid, made alkaline to litmus with solid sodium bicarbonate and the insoluble precipitate (original sulfanilamide) filtered off. The clear filtrate was purified with activated charcoal, finally precipitating any derivative (I) that may have formed when the solution was made acid to litmus with dilute hydrochloric acid. Further purification was attained by recrystallization from dilute alcohol, dilute acetic or dilute hydrochloric acid. The diazotization test was negative for all compounds prepared.

**Reaction (B). Preparation of 1-[(*p*-Chlorosulfonyl)-phenyl]-5-oxo-3-pyrrolidinecarboxylic Acid (IV).**—Forty grams (0.2 mole)[6] of purified[6] 1-phenyl-5-oxo-3-pyrrolidine-

(1) Excerpts from dissertations presented to the Graduate School of Xavier University in partial fulfillment of the requirements for the Degree of Master of Science.

(2) P. L. Paytash, E. Sparrow and J. C. Gathe, THIS JOURNAL, **72**, 1415 (1950).

(3) We wish to express our gratitude to several industrial chemical companies for supplying the amines.

(4) Supplied by Pfizer Company.

(5) Acid hydrolysis (3 *N* hydrochloric acid) may be used instead.

(6) The crude compound decomposes in chlorosulfonic acid.

TABLE I[a]

| Amine | 1-(*p*-Sulfamylphenyl)-5-oxo-3-pyrrolidinecarboxylic acid derivative, $R_1$ | Yield,[f] % | M.p., °C. | N, % Calcd.[c] | N, % Found[c] | Neut. equiv. Found | Mol. wt.[d] Calcd. | Mol. wt.[d] Found |
|---|---|---|---|---|---|---|---|---|
| Methylamine | Methyl | 49 | 204–206 | 9.38 | 9.44 | 305 | 298 | 297 |
| Dimethylamine | Methyl,[b] $R_2$ Methyl[b] | 70 | 220–223<br>237–239 | 8.96 | 8.97 | 307 | 312 | .. |
| Ethylamine | Ethyl | 46 | 198–199 | 8.96 | 8.99 | 314 | 312 | 317 |
| Diethylamine | Ethyl, $R_2$ Ethyl | 51 | 152–153 | 8.23 | 8.27 | 336 | 340 | 340 |
| Isopropylamine | Isopropyl | 81 | 190–191 | 8.55 | 8.55 | 330 | 326 | |
| 3-Methoxypropylamine | 3-Methoxypropyl | 37 | 104–106 | 7.82 | 7.84 | 390 | 356 | .. |
| 3-Isopropoxypropylamine | 3-Isopropoxypropyl | 60 | 105–107 | 7.21 | 7.27 | 382 | 385 | 381 |
| *n*-Butylamine | *n*-Butyl | 51 | 168–169 | 8.23 | 8.23 | 343 | 340 | 340 |
| Di-*n*-butylamine | *n*-Butyl,[b] $R_2$ *n*-Butyl[b] | 48 | 74–76 | 7.06 | 7.04 | 396 | 396 | .. |
| Cyclohexylamine | Cyclohexyl[b] | 83 | 174–175 | 7.64 | 7.60 | 369 | 366 | 367 |
| 2,4,4-Trimethyl-2-aminopentane | 2,4,4-Trimethyl-2-pentyl | 75 | 185–186 | 7.06 | 7.03 | 394 | 396 | 394 |
| 3,5,5-Trimethylhexylamine | 3,5,5-Trimethylhexyl | 35 | 156–157[e] | 6.82 | 6.88 | 409 | 410 | 403 |
| Aminoacetic acid | Carboxymethyl | 35 | 190–192 | 8.18 | 8.24 | 172 | 342 | .. |
| Aniline | Phenyl[b] | 67 | 192–193 | 7.77 | 7.78 | 359 | 360 | .. |
| Ethylaniline | Phenyl, $R_2$ Ethyl | 72 | 188–189 | 7.21 | 7.18 | 388 | 388 | .. |
| *o*-Chloroaniline | 2-Chlorophenyl | 57 | 166–168 | 7.09 | 7.09 | .. | 395 | 390 |
| *m*-Chloroaniline | 3-Chlorophenyl | 85 | 209–210 | 7.09 | 7.08 | -- | 395 | 400 |
| 2,4-Dichloroaniline | 2,4-Dichlorophenyl | 75 | 210–211 | 6.52 | 6.52 | .. | 429 | 428 |
| 2,5-Dichloroaniline | 2,5-Dichlorophenyl | 65 | 104–106 | 6.52 | 6.52 | .. | 429 | 433 |
| *o*-Nitroaniline | 2-Nitrophenyl | 30 | 189–191 | 10.37 | 10.18 | 402 | 405 | 400 |
| *m*-Nitroaniline | 3-Nitrophenyl | 85 | 233–235 | 10.37 | 10.20 | 400 | 405 | 406 |
| *p*-Nitroaniline | 4-Nitrophenyl | 60 | 220–226 dec. | 10.37 | 10.18 | 400 | 405 | 413 |
| *o*-Toluidine | 2-Tolyl | 65 | 160–161 | 7.48 | 7.49 | 378 | 374 | .. |
| *m*-Toluidine | 3-Tolyl | 68 | 178–179 | 7.48 | 7.57 | 378 | 374 | 379 |
| *p*-Toluidine | 4-Tolyl | 41 | 150–151 | 7.48 | 7.49 | 375 | 374 | 374 |
| *m*-Nitro-*p*-toluidine | 3-Nitro-4-tolyl | 30 | 156–157 | 10.25 | 10.17 | 413 | 419 | .. |
| Benzylamine | Benzyl[b] | 47 | 194–195 | 7.48 | 7.44 | 379 | 374 | 366 |
| β-Phenethylamine | β-Phenethyl[b] | 92 | 187–188 | 7.21 | 7.24 | 395 | 388 | 387 |
| *o*-Anisidine | 2-Methoxyphenyl[b] | 77 | 182–183 | 7.17 | 7.25 | 391 | 390 | 390 |
| *p*-Chloroanisidine | 2-Methoxy-5-chlorophenyl | 86 | 188–189 | 6.59 | 6.54 | 439 | 425 | 420 |
| 2,5-Dimethoxyaniline | 2,5-Dimethoxyphenyl[b] | 90 | 157–158 | 6.61 | 6.63 | 428 | 420 | 416 |
| 2,5-Diethoxyaniline | 2,5-Diethoxyaniline | 49 | 159–160 | 6.24 | 6.26 | 456 | 448 | 445 |
| β-3,4-Dimethoxyphenethylamine | β-3,4-Dimethoxyphenethyl[b] | 68 | 114–115 | 6.24 | 6.19 | 449 | 448 | .. |
| *o*-Aminodiphenyl | 2-Diphenyl | 50 | 199–200 | 6.41 | 6.39 | 437 | 437 | 445 |
| *p*-Aminodiphenyl | 4-Diphenyl | 75 | 214–215 | 6.41 | 6.41 | 437 | 437 | 433 |
| *p*-Phenylenediamine | 1-*p*-(*p*-Sulfamylphenyl)-phenyl-5-oxo-3-pyrrolidylcarboxylic acid | 80 | 280 dec. | 8.70 | 8.61 | 326 | 643 | .. |
| Benzidine | 1-*p*-(*p*-Sulfamyldiphenyl)-phenyl-5-oxo-3-pyrrolidylcarboxylic acid | 80 | 315–320 dec. | 7.80 | 7.83 | 355 | 719 | .. |
| *p*-Aminoazobenzene | Azobenzene | 75 | 252–254 | 12.06 | 12.20 | 460 | 464 | 451 |
| *l*-Naphthylamine | 1-Naphthyl[b] | .. | 192–193 | 6.82 | 6.82 | 426 | 410 | 408 |
| *o*-Aminobenzoic acid | 2-Carboxyphenyl | 18 | 218–220 dec. | 6.92 | 6.87 | .. | .. | .. |
| *m*-Aminobenzoic acid | 3-Carboxyphenyl | 24 | 228–230 | 6.92 | 6.92 | .. | .. | .. |
| *p*-Aminobenzoic acid | 4-Carboxyphenyl | 30 | 245 dec. | 6.92 | 6.90 | .. | .. | .. |

[a] $R_1$ 4-chlorophenyl, $R_1$ 4-methoxyphenyl, $R_1$ β-naphthyl, $R_1$ 2-pyridyl, $R_1$ pyrimidyl and $R_1$ 2-thiazolyl derivatives could not be confirmed due to the lack of sufficient analytical data or unsuccessful synthesis. [b] Also prepared by reaction (A) with poor yields. [c] Gunning, Arnold and Dyer modified Kjeldahl method. H. C. Sherman, *Methods of Organic Analysis*, 291 (1931). Nitro and azo compounds were first reduced with salicylic acid and sodium thiosulfate. [d] Rast camphor method. [e] Melting point of mixture with the corresponding N⁴-itaconyl acid sulfanilamide gave a strong depression. [f] Two or more recrystallizations.

carboxylic acid was added slowly with stirring to 150 g. (1.0 mole) of chlorosulfonic acid at a temperature of 60–65°. The temperature was kept between 65–70° with stirring until the evolution of hydrogen chloride had ceased (15–20 minutes). The sirupy liquid, cooled to room temperature, was poured slowly with stirring into large excess of crushed ice to precipitate (IV). (IV) was filtered by suction and washed well with cold water. The crude yield was 45–50 g. (76–85%). Melting point of purified compound was 164–166° (from benzene).

*Anal.* Calcd. for $C_{11}H_{10}ClNO_5S$: N, 4.60. Found: N, 4.58.

**Preparation of 1-(*p*-Sulfamyl)-phenyl-5-oxo-3-pyrrolidinecarboxylic Acid Derivatives (I).**—The crude compound (IV) was condensed with primary and secondary amines (mole ratio of 1–1.5) by bringing about the reaction in an alkaline medium (sodium bicarbonate) or acetone. Some of the reactions proceeded better in one solvent than the other depending upon the solubility of the amines. At room temperature, completion of the reactions in alkaline medium took from a few hours to standing overnight while in acetone it took one-quarter to three hours. In most cases, condensation of (IV) with amines produced a gummy product which gave upon successive recrystallization from water, dilute alcohol, or dilute hydrochloric acid a purified crystalline substance.

**Reaction (C). Procedure.**—Ten grams of itaconic acid (technical grade) was heated to a temperature of about 180° (125-ml. erlenmeyer flask). To this was added in one por-

TABLE II[a]

| Sulfanilamide | $N^4$-Itaconyl acid[d] sulfanilamide, $R_1$ | Yield,[c] % | M.p., °C. | N, % Calcd. | Found |
|---|---|---|---|---|---|
| Sulfanilamide | H, $R_2$, H | 5 | 198–199 | 9.86 | 9.83 |
| Sulfanilylmethylamine | Methyl[b] | 31 | 188–189 | 9.38 | 9.40 |
| Sulfanilylethylamine | Ethyl | 23 | 185–186 | 8.96 | 8.93 |
| Sulfanilyldiethylamine | Ethyl, $R_2$ Ethyl | 40 | 156–157 | 8.23 | 8.20 |
| Sulfanilylisopropylamine | Isopropyl | 53 | 210–211 | 8.55 | 8.45 |
| Sulfanilyl-3-methoxypropylamine | 3-Methoxypropyl | 7 | 168–169 | 7.82 | 7.80 |
| Sulfanilyl-3-isopropoxypropylamine | 3-Isopropoxypropyl | 36 | 174–175 | 7.21 | 7.25 |
| Sulfanilyl-*n*-butylamine | *n*-Butyl | 60 | 183–184 | 8.23 | 8.22 |
| Sulfanilyl-di-*n*-butylamine | *n*-Butyl, $R_2$ *n*-Butyl | 40 | 120–122 | 7.06 | 7.10 |
| Sulfanilylcyclohexylamine | Cyclohexyl | 40 | 184–185 | 7.64 | 7.62 |
| Sulfanilyl-2,4,4-trimethyl-2-aminopentane | 2,4,4-Trimethyl-2-pentyl | 29 | 163–164 | 7.06 | 7.04 |
| Sulfanilyl-3,5,5-trimethylhexylamine | 3,5,5-Trimethylhexyl | 10 | 156–157 | 6.82 | 6.86 |
| Sulfanilylaniline | Phenyl | 15 | 179–180[f] 183–184 | 7.77 | 7.80 |
| Sulfanilylethylaniline | Phenyl, $R_2$ Ethyl | 29 | 148–149 | 7.21 | 7.20 |
| Sulfanilyl-*o*-chloroaniline | 2-Chlorophenyl | 37 | 197–198 | 7.09 | 7.12 |
| Sulfanilyl-*m*-chloroaniline | 3-Chlorophenyl | 36 | 184–185 | 7.09 | 7.05 |
| Sulfanilyl-*p*-chloroaniline | 4-Chlorophenyl | 36 | 208–209 | 7.09 | 7.19 |
| Sulfanilyl-2,4-dichloroaniline | 2,4-Dichlorophenyl | 37 | 189–190 | 6.52 | 6.40 |
| Sulfanilyl-2,5-dichloroaniline | 2,5-Dichlorophenyl | 41 | 177–178 | 6.52 | 6.35 |
| Sulfanilyl-*o*-nitroaniline | 2-Nitrophenyl | 2 | 175–176[e] | 10.37 | 10.18 |
| Sulfanilyl-*m*-nitroaniline | 3-Nitrophenyl | 1 | 179–180 | 10.37 | 10.25 |
| Sulfanilyl-*p*-nitroaniline | 4-Nitrophenyl | 3 | 210–211 | 10.37 | 10.15 |
| Sulfanilyl-*o*-toluidine | 2-Tolyl | 31 | 184–185 | 7.48 | 7.50 |
| Sulfanilyl-*m*-toluidine | 3-Tolyl | 30 | 189–190 | 7.48 | 7.45 |
| Sulfanilyl-*p*-toluidine | 4-Tolyl | 53 | 213–214 | 7.48 | 7.47 |
| Sulfanilyl-*m*-nitro-*p*-toluidine | 3-Nitro-4-tolyl | 4 | 162–163 | 10.25 | 10.00 |
| Sulfanilylbenzylamine | Benzyl | 20 | 186–188 dec. | 7.48 | 7.50 |
| Sulfanilyl-β-phenethylamine | β-Phenethyl | 57 | 180–181 | 7.21 | 7.23 |
| Sulfanilyl-*o*-anisidine | 2-Methoxyphenyl | 4 | 163–165 dec. | 7.17 | 7.17 |
| Sulfanilyl-*p*-anisidine | 4-Methoxyphenyl | 35 | 193–194 | 7.17 | 7.20 |
| Sulfanilylchloroanisidine | 2-Methoxy-5-chlorophenyl | 37 | 172–173 | 6.59 | 6.50 |
| Sulfanilyl-2,5-dimethoxyaniline | 2,5-Dimethoxyphenyl | 8 | 82– 83 | 6.61 | 6.60 |
| Sulfanilyl-2,5-diethoxyaniline | 2,5-Diethoxyphenyl | 10 | 167–168 | 6.24 | 6.20 |
| Sulfanilyl-β-3,4-dimethoxyphenethylamine | β-3,4-Dimethoxyphenethyl[g] | 7 | 157–158 | 6.24 | 6.18 |
| Sulfanilyl-*o*-aminodiphenyl | 2-Diphenyl | 15 | 191–192 | 6.41 | 6.45 |
| Sulfanilyl-*p*-aminodiphenyl | 4-Diphenyl | 20 | 217–218 | 6.41 | 6.50 |
| Bis-(sulfanilyl)-*p*-phenylenediamine | Bis-($N^4$-itaconyl acid sulfanilyl)-*p*-phenylenediamine | 15 | 207–208 | 8.70 | 8.65 |
| Sulfanily-1-naphthylamine | 1-Naphthyl[g,h] | 35 | 175–176[f] 180–182 dec. | 6.82 | 6.75 |
| Sulfanilyl-2-naphthylamine | 2-Naphthyl[g,h] | 30 | 181–183 | 6.82 | 6.80 |
| Sulfanilyl-*o*-aminobenzoic acid | 2-Carboxyphenyl | 25 | 133–135 | 6.92 | 6.90 |
| Sulfanilyl-*m*-aminobenzoic acid | 3-Carboxyphenyl | 40 | 195–196 | 6.92 | 7.00 |
| Sulfanilyl-*p*-aminobenzoic acid | 4-Carboxyphenyl | 54 | 225–226 dec.[i] | 6.92 | 6.85 |

[a] ($R_1$ methyl and $R_2$ methyl), $R_1$ carboxymethyl, $R_1$ azobenzene, $R_1$ 2-thiazolyl, $R_1$ guanyl, $R_1$ 2-pyrimidyl and $R_1$ 2-pyridyl derivatives could not be confirmed due to the lack of sufficient analytical data or unsuccessful synthesis. [b] See (*b*) Table I. [c] Two or more recrystallizations. [d] All $N^4$-itaconyl acid sulfanilamide compounds listed gave itaconic acid and the original sulfanilamide upon hydrolysis. [e] If reprecipitated from basic solution by dilute acid, the melting point is 154–155°. Melting point of mixture gave no depression. [f] Gave two melting points. Melting point of mixture produced no depression. [g] 3 *N* sodium hydroxide was used in hydrolysis to isolate original sulfanilamide. [h] Became brown after standing a few days. [i] Melting point was 236–237° with rapid heating.

tion two grams of the appropriate sulfanilamide. When necessary heat was applied to maintain a molten state for 15 to 30 seconds.[7] Then this molten mass was immediately poured into cold water with stirring and the reaction mixture was allowed to stand for a while before the precipitate formed was redissolved by making the solution alkaline to litmus with solid sodium bicarbonate. The resulting solution was allowed to stand, any insoluble material[8] was filtered off, and the clear filtrate decolorized with activated charcoal. Finally derivative (II) was reprecipitated by making the solution acid to litmus with dilute hydrochloric acid. Further purification was attained by recrystallization from water or dilute alcohol. Diazotization test was negative for all compounds prepared.

**Hydrolysis of $N^4$-Itaconyl Acid Sulfanilamide** (II).—All of the derivatives prepared were subjected to acid hydrolysis (hydrochloric acid) for 30 minutes. From each hydrolysis itaconic acid and the original sulfanilamide were isolated.[9]

(7) Optimum fusion time for each reaction was not determined. Prolonged fusion may contaminate derivative (II) with (I) and with a by-product of undetermined structure. This substance is insoluble in a sodium bicarbonate solution but dissolves slowly in sodium hydroxide (3–6 *N*) forming a deep red solution which gradually turns yellow or orange. The solution after standing a few minutes gives a positive diazotization test. Both acidic and basic hydrolysis form itaconic acid and the corresponding sulfanilamide.

(8) Unreacted sulfanilamide or unknown product (III).

(9) Verified by mixed melting points.

**Diazotization Test.**—A solution of one gram of β-naphthol dissolved in 25 ml. of 3 *N* sodium hydroxide was prepared. A small amount of sample to be tested was dissolved in 1 *N* sodium hydroxide and a little solid sodium nitrite added. To this solution was added an excess of dilute hydrochloric acid and then poured into a few ml. of alkaline β-naphthol. Positive test was characterized by formation of azure-red color; negative, yellow or brown color. This test was used throughout our work to confirm the conjugation of free amino groups.

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NEW ORLEANS, LOUISIANA

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[CONTRIBUTION FROM NORTH TEXAS STATE COLLEGE]

# Reductions of 1-(4-Nitrophenacyl)-4-(1-hexyl)-pyridinium Bromide

BY PRICE TRUITT, BOB HALL[1] AND BENNIE ARNWINE[1]

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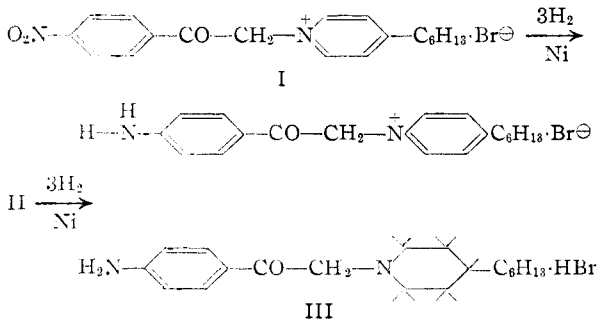
The synthesis and reduction of 1-(4-nitrophenacyl)-4-(1-hexyl)-pyridinium bromide are reported. The catalytic hydrogenation of this compound occurs stepwise. The rates of hydrogenation with Adams catalyst indicate the pyridinium function is reduced first followed by the nitro group. The reverse order of reduction was noted with Raney nickel. The carbonyl group was not reduced under the conditions reported. The structures of these compounds have been proved by alternate syntheses.

The catalytic reduction of 1-phenacylpyridinium bromide at low temperature and low pressure in the presence of platinum gives 1-phenacylpiperidine hydrobromide.[2] Riegel and Wittcoff[3] were able to reduce preferentially the carbonyl group of this ketone at low temperature and high pressure (80 atmospheres) with Adams catalyst. However, they found[4] that this preferential hydrogenation was often impossible to accomplish when the benzene ring of the pyridinium ketone was substituted with hydroxyl groups. Truitt and coworkers[5] have found that substituents on the pyridine nucleus influence the catalytic hydrogenation of 1-phenacylpyridinium halides at low temperature and low pressure. A methyl or an ethyl group on the pyridinium portion of the molecule gave the corresponding 1-phenacyl-4-alkylpiperidine salt. However, when the alkyl group was $C_5$, $C_6$, $C_8$ or $C_9$ and in the 4-position of the pyridine ring the only reduction product which could be isolated was a 4-alkyl-1-(2-hydroxy-2-phenylethyl)-piperidine hydrohalide. This type compound resulted from the reduction of both reducible functions of the parent compound. It was impossible to isolate a product from these reductions where only one of the unsaturated groups had been reduced. The benzene ring was not altered under these conditions.

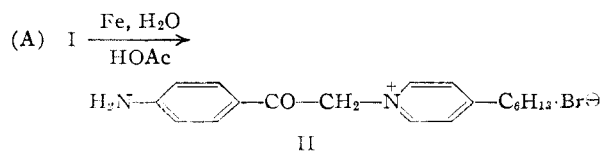
Our interest in compounds of this type for physiological studies necessitated our knowledge of the course of reduction of certain 1-(4-nitrophenacyl)-4-alkylpyridinium bromides. Since we were most interested in compounds in which the 4-alkyl group was rather large, we selected 1-(4-nitrophenacyl)-4-(1-hexyl)-pyridinium bromide for the present investigation.

The catalytic reduction of 1-(4-nitrophenyl)-4-(1-hexyl)-pyridinium bromide in the presence of Raney nickel at 50 p.s.i. and at room temperature proceeded stepwise as




Compounds II and III were isolatable from this hydrogenation, but compound II predominated. Raney nickel would not catalyze the reduction of the carbonyl group under these conditions and the entire hydrogenation was very slow. Reduction of I with Adams catalyst at room temperature and 50 p.s.i. of hydrogen behaved very differently. The first three moles of hydrogen was absorbed very rapidly (about 5–15 minutes for a 10-g. sample of I) while several hours were required for the absorption of an additional three moles of hydrogen. No additional hydrogen was taken up even with prolonged shaking. Compound III was the main product, but a small amount of II could be isolated. They were easily separated by alcohol recrystallization.

The structures of compounds II and III were determined with certainty by alternate modes of preparation and by study of their infrared spectra. Compounds I, II and III showed characteristic ketone absorption in the region of 6.2μ. The synthetic approaches to the reduction products are




(1) Parke, Davis and Company Research Fellows.
(2) F. Krohnke with K. Fasold, *Ber.*, **67**, 656 (1934).
(3) B. Riegel and H. Wittcoff, THIS JOURNAL, **68**, 1805 (1946).
(4) B. Riegel and H. Wittcoff, *ibid.*, **68**, 1913 (1946).
(5) Price Truitt, B. Bryant, W. E. Goode and B. Arnwine, *ibid.*, **74**, 2179 (1952).