[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

REACTIONS OF NITROPARAFFINS.* III. DERIVATIVES OF 3-METHYL-3-NITRO-1,2-BUTANEDICARBOXYLIC ACID[1]

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Received August 4, 1953

In an earlier paper of this series (1) it was reported that dimethyl 3-methyl-3-nitro-1,2-butanedicarboxylate (I) could be hydrolyzed stepwise through an intermediate monomethyl ester (II) to the dicarboxylic acid (III) which could then be selectively esterified to yield the isomeric monoester (IV).

The reactions of III and some of its derivatives now have been investigated more fully and the transformations shown in Figure 1 have been effected.

3-Methyl-3-nitro-1,2-butanedicarboxylic acid (III) was obtained directly in 91% yield when the dimethyl ester (I) was heated for 30 hours with 10% hydrochloric acid.

When a solution of the dicarboxylic acid (III) in 96% sulfuric acid was poured into cooled methanol and the resulting solution was poured onto ice, monomethyl ester IV was obtained in 52% yield. Monoester II yielded dimethyl ester I in 72% yield under similar conditions. This constitutes an extremely rapid method for esterifying an aliphatic acid.[2]

Conversion of III to the anhydride (V) was effected readily by means of acetic anhydride, acetyl chloride, or thionyl chloride, in yields of more than 90%. Methanolysis of V yielded the same monoester (IV) as did direct esterification of III.

Since dimethyl ester I is converted by diethylamine to the dimethyl ester of teraconic acid (X) in high yield (1), it was of interest to determine the behavior of V toward various amines. Aminolysis of the anhydride with primary amines proceeded smoothly in benzene (see Table I). Only one amide was isolable in each instance, the yield of pure material being as high as 96% in the case of the *o*-toluidide (VI). Reaction with the aliphatic amines was less successful in benzene although an aqueous solution of *n*-propylamine readily cleaved the anhydride to yield the corresponding amide in 61% yield.

Structure VI for the *o*-toluidide is virtually certain since this amide was obtained in nearly quantitative yield from the sterically-hindered *o*-toluidine. On the basis of this assumption, the structure of ester II has been confirmed through the following sequence of reactions. *o*-Toluidide VI was converted to its silver salt which subsequently reacted with methyl iodide to yield ester VII. When ester II was allowed to react with thionyl chloride and the resulting acid halide was treated with *o*-toluidine, VII was again obtained. These experiments con-

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* Presented at the W. E. Bachmann Memorial Session, Organic Chemistry Division, American Chemical Society, Chicago Meeting, September 8, 1953.

[1] Abstracted from the M.S. thesis of Philip S. Magee.

[2] Newman, *J. Am. Chem. Soc.*, **63**, 2431 (1941), has shown that benzoic acid does not esterify when its solution in 100% sulfuric acid is poured into methanol.

firm structures II and IV and demonstrate that methanolysis and aminolysis of anhydride V yield derivatives having a free secondary carboxyl group.

Infrared absorption spectra (Figure 2) of monoesters II and IV show the broad absorption band between 3 and 4 microns characteristic of hydroxyl association. Comparison of the spectra of I and IV (Figures 2 and 3) yields no clear evidence of strong intramolecular hydrogen bonding involving the nitro group in IV.

Elimination of the elements of nitrous acid from III occurred slowly when the dibasic acid was refluxed in acetic acid solution containing 25% by volume of acetic anhydride. After 40 hours of reflux a 52% yield of teraconic acid (X) was isolated. The dimethyl ester (I) was stable under these conditions. A rapid evolution of nitrogen dioxide occurred when III was heated at 80–90° in 96%

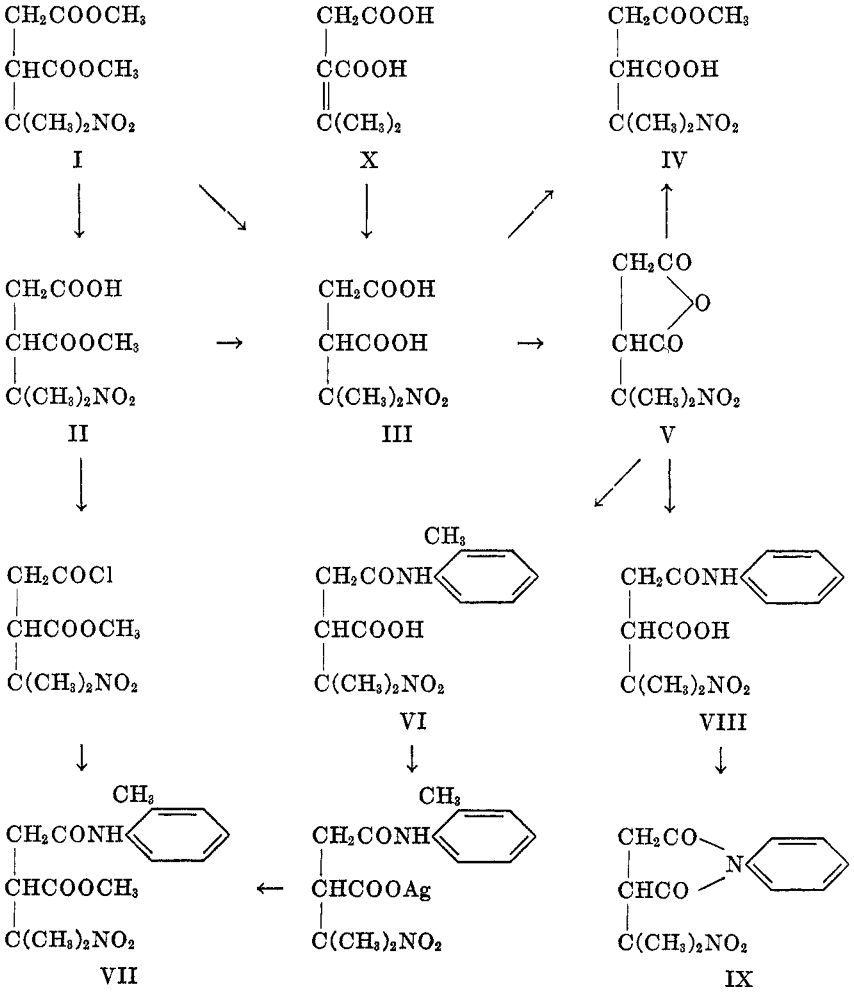

Fig. 1

TABLE I

AMIDES FROM 3-METHYL-3-NITRO-1,2-BUTANEDICARBOXYLIC ANHYDRIDE

AMINE	YIELD, %	M.P., °C.	ANALYSES, %					
			Calc'd			Found		
			C	H	N	C	H	N
o-Toluidine	96	148–149 dec.	57.13	6.16	—	57.41	6.36	—
Aniline	87	123–124 dec.	55.70	5.75	—	55.64	5.71	—
Phenylhydrazine	82.5	149–150 dec.	52.87	5.80	—	52.76	5.88	—
n-Propylamine[a]	61	148–149 dec.	—	—	11.37	—	—	11.25
n-Dodecylamine	34	131–131.5 dec.	61.26	9.74	—	61.12	9.53	—

[a] Aqueous method.

sulfuric acid and terebic acid (lactone of X) was isolated from the diluted solution. Elimination of nitrous acid from III occurs even in hot 10% hydrochloric acid, though very slowly. For example, after 150 hours of reflux it was possible to isolate only 13% of terebic acid.

Dicarboxylic acid III also decomposed when heated alone at 145°, yielding 58% of teraconic acid within two hours. Anhydride V could not have been an

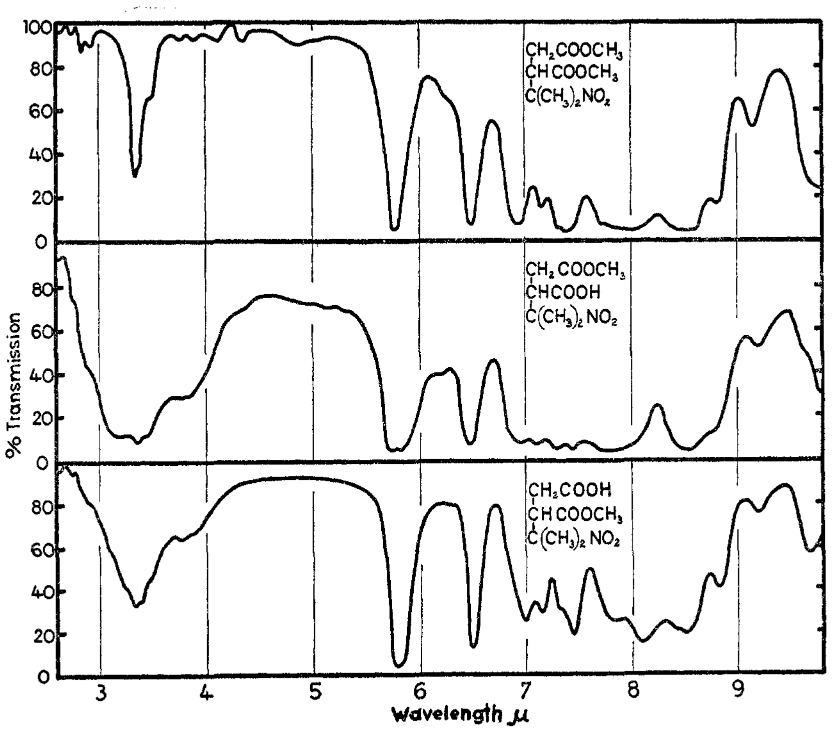

FIG. 2. INFRARED ABSORPTION SPECTRA IN SATURATED CHLOROFORM SOLUTIONS (Beckman spectrophotometer, model IR2T; NaCl prism; cell thickness, 0.1 mm.).

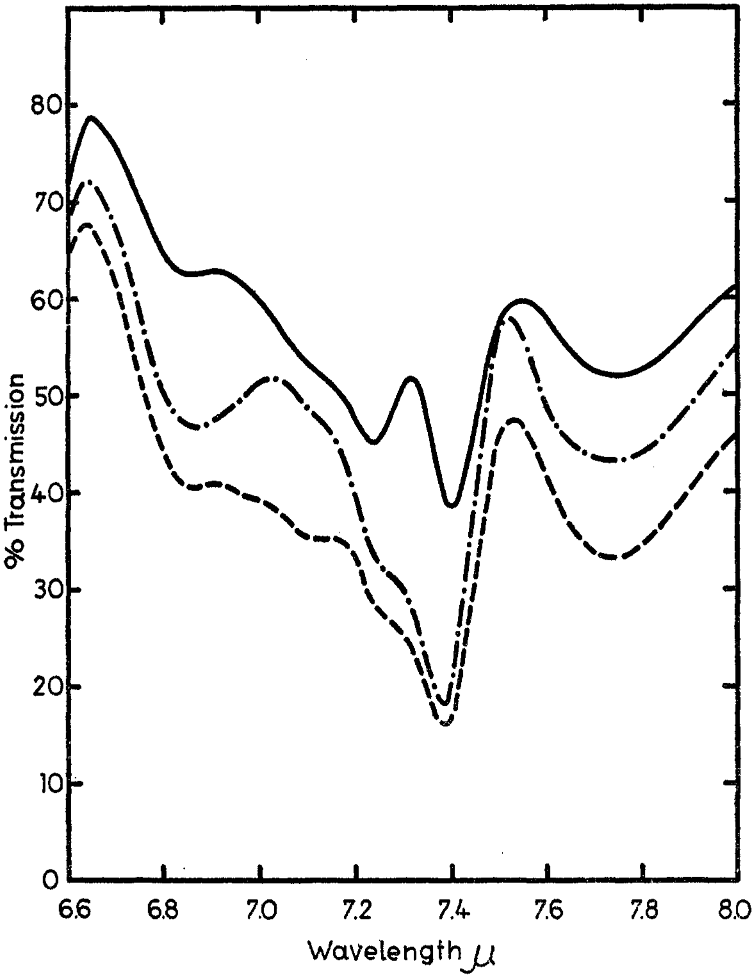

FIG. 3. INFRARED ABSORPTION SPECTRA IN SATURATED CHLOROFORM SOLUTIONS DILUTED 1:4; cell thickness, 0.1 mm.; curve – – – –, monomethyl ester II; curve —•—•—, dimethyl ester I; curve ————, monomethyl ester IV.

intermediate in this decomposition, for the anhydride is stable under these conditions. Neither dimethyl ester I nor monomethyl ester II[3] suffered significant nitrous acid elimination at 145° but monomethyl ester IV lost nitrous acid to the extent of at least 26% within 2½ hours at this temperature.

Substituted succinic acid monoamides have been reported to form cyclic imides upon being heated (2). However, the phenylhydrazide, anilide (VIII), and *n*-propylamide described in Table I rapidly decomposed at their melting

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[3] Some ester interchange evidently occurred when ester II was heated to 145°, for the ester was then difficult to purify by crystallization. However, nitrous acid elimination could not have exceeded 3% since hydrolysis of the heated ester yielded only 3% less 3-methyl-3-nitro-1,2-butanedicarboxylic acid (III) than did hydrolysis of pure, unheated ester.

points to form dark oils from which, by acid hydrolysis, teraconic acid was obtained in yields of 14%, 31% and 65%, respectively. It is evident that elimination of the elements of nitrous acid is a major process in the pyrolytic decomposition of these amides. It was possible, however, to prepare the N-phenylimide (IX) in 61% yield by allowing the anilide (VIII) to react with acetyl chloride in warm benzene. The N-phenylimide could not have been an intermediate in the pyrolytic decomposition of the anilide, for the imide is stable at 145°.

EXPERIMENTAL[4]

3-Methyl-3-nitro-1,2-butanedicarboxylic acid (III). Dimethyl ester I (1) (30 g.) was refluxed for 30 hours with 300 ml. of 10% hydrochloric acid and the volume of the solution was then reduced to 40 ml. Cooling to 0° and seeding caused the separation of 24.0 g. (91%) of material, m.p. 135–140°dec. A single crystallization from water yielded the pure dicarboxylic acid, m.p. 144–145°dec.

Esterification of 3-methyl-3-nitro-1,2-butanedicarboxylic acid (III) *and 3-carbomethoxy-4-methyl-4-nitropentanoic acid* (II). Dicarboxylic acid (III) (10 g.) was powdered and dissolved in 40 ml. of 96% sulfuric acid. The solution was poured slowly, with stirring, into 150 ml. of methanol cooled in ice. The resulting solution was poured onto 200 g. of ice. Seeding with 1-carbomethoxy-3-methyl-3-nitro-2-butanecarboxylic acid (IV) caused the separation of solid material which melted at 69–73° after two recrystallizations from a mixture of ether and petroleum ether; yield, 5.5 g. (52%). The pure material melted at 73.5–75° and gave no m.p. depression upon admixture with authentic ester IV (1).

In a similar manner, a solution of 3 g. of ester II in 10 ml. of 96% sulfuric acid was poured into 15 ml. of methanol. The material which crystallized when this solution was poured onto 100 g. of ice weighed 2.3 g. (72% yield) and melted at 31–33°. A single crystallization from ether and petroleum ether raised the m.p. to 35–36° which was not depressed upon admixture with pure dimethyl ester (I).

3-Methyl-3-nitro-1,2-butanedicarboxylic anhydride (V). A mixture of 5.0 g. of dicarboxylic acid (III) and 4 ml. of acetic anhydride was heated on a steam-bath for 30 minutes. The anhydride crystallized readily upon cooling and was washed with petroleum ether; yield, 4.15 g. (91%), m.p. 110–112°. Crystallization from acetone and petroleum ether yielded small colorless plates, m.p. 112–112.5°.

Anal. Calc'd for $C_7H_9NO_5$: C, 44.92; H, 4.84.
Found: C, 45.06; H, 4.61.

The anhydride (V) was also prepared by refluxing a mixture of 2.05 g. of the acid (III) and 8 ml. of acetyl chloride until solution was complete (15 minutes). The cooled solution was diluted with 5 ml. of petroleum ether and, after standing at 0°, deposited 1.83 g. (98%) of colorless crystals, m.p. 104–108°.

In a similar manner, when 2.05 g. of acid III was refluxed for 30 minutes with 8 ml. of thionyl chloride, 1.86 g. (99%) of crude anhydride was obtained, m.p. 102–107°. Crystallization as before raised the m.p. to 110–112°.

Methanolysis of 3-methyl-3-nitro-1,2-butanedicarboxylic anhydride. A solution of 4 g. of anhydride (V) in 50 ml. of methanol was refluxed for 1 hour and the excess methanol was then removed under reduced pressure. The residual colorless oil crystallized from ether and petroleum ether to yield 2.95 g. (63%) of 1-carbomethoxy-3-methyl-3-nitro-2-butanecarboxylic acid (IV), m.p. 66–73°. Recrystallization yielded the pure material which did not depress the m.p. of ester IV obtained by esterification of acid III.

Aminolysis of 3-methyl-3-nitro-1,2-butanedicarboxylic anhydride. To a hot solution of 5 g. of anhydride V in 100 ml. of benzene was slowly added a solution of 1.86 g. of *o*-tolui-

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[4] All melting points are uncorrected. We are indebted to Mr. Joseph Pirie for microanalyses and to Mr. W. Netusil, University of California, Los Angeles, for infrared spectra.

dine in 20 ml. of benzene. A colorless solid separated rapidly. After 10 minutes of continued warming on a steam-bath the solution was allowed to cool. The benzene-washed product weighed 7.55 g. (96% yield) and melted at 143–145°dec. Crystallization from acetone and petroleum ether yielded an analytical sample of *o*-toluidide VI (see Table I).

The anilide (VIII), phenylhydrazide, and *n*-dodecylamide listed in Table I were prepared in essentially the same manner, except that the *n*-dodecylamide separated best when the hot benzene solution was diluted with about half its volume of petroleum ether (b.r. 45–60°). The reaction with *n*-dodecylamine was exothermic and was accompanied by visible evolution of nitrogen oxides.

The *n*-propylamide was prepared by dissolving 5 g. of the anhydride (V) in 40 ml. of warm water containing 3.54 g. of *n*-propylamine. Acidification of the cooled solution with hydrochloric acid precipitated the colorless amide which was then crystallized from acetone and petroleum ether.

o-Toluidide of 3-carbomethoxy-4-methyl-4-nitropentanoic acid (VII). (*a*) *From o-toluidide* VI. *o*-Toluidide VI (3.60 g.) was suspended in 80 ml. of water and titrated to the phenolphthalein end-point with 10% sodium hydroxide solution. The silver salt was then precipitated by the addition of 2.5 g. of silver nitrate in 50 ml. of water. The moist salt, which had been washed with a small amount of water, was suspended in 200 ml. of benzene and the water was removed by co-distillation with benzene. To the resulting suspension of silver salt in benzene was added 5 ml. of methyl iodide and the mixture was refluxed for 6 hours. After filtration with the aid of activated carbon the colorless solution was allowed to evaporate spontaneously, leaving 1.15 g. (31%) of colorless needles, m.p. 122–125°. Crystallization from methanol yielded pure amide (VII), m.p. 124–126°.

Anal. Calc'd for $C_{15}H_{20}N_2O_5$: N, 9.09. Found: 9.20.

(*b*) *From 3-carbomethoxy-4-methyl-4-nitropentanoic acid* (II). Ester II (10 g.) was refluxed for 30 minutes with 60 ml. of thionyl chloride. To the resulting solution was added 300 ml. of benzene and the volume was then reduced to 100 ml. under reduced pressure. This process was repeated three times with 250-ml. portions of benzene in order to remove excess thionyl chloride. Finally, 9.8 g. of *o*-toluidine in 30 ml. of benzene was added to the cooled benzene solution of the acid chloride. After one hour at room temperature the solution was filtered from precipitated *o*-toluidine hydrochloride (6.35 g.; 97%) and the filtrate was washed with dilute hydrochloric acid and finally with water. The solution was dried by co-distillation of water with benzene, decolorized with activated carbon, and reduced in volume to 50 ml. Upon cooling, the solution deposited a colorless solid which was recrystallized from methanol to yield 4.94 g. (35%) of amide VII. This material, m.p. 124–126°, did not depress the m.p. of the amide prepared from VI.

Elimination of the elements of nitrous acid from dicarboxylic acid III. Visible evolution of nitrogen oxides occurred when a solution of 2 g. of III in 30 ml. of glacial acetic acid and 10 ml. of acetic anhydride was heated. After being refluxed for 40 hours the solution was diluted with 20 ml. of water and evaporated to dryness. The residual dark solid was dissolved in 20 ml. of water and the solution was decolorized with Nuchar. Evaporation to a small volume caused the separation of a solid which was recrystallized from acetone and petroleum ether; yield, 0.80 g., m.p. 153–156°dec. Recrystallization from water yielded colorless needles, m.p. 162–163°dec., which did not depress the m.p. of authentic teraconic acid (X) (1).

A rapid evolution of nitrogen oxides occurred when a solution of 2 g. of III in 10 ml. of 96% sulfuric acid was warmed to 80–90° for 10 minutes. The dark solution was cooled and poured onto 20 g. of ice. The resulting solution was warmed until there was no further evolution of nitrogen oxides (10 minutes) and was then cooled to 0°. Seeding caused the separation of 0.45 g. (29%) of colorless crystals, m.p. 170–171°dec., which did not depress the m.p. of authentic terebic acid (3).

Three grams of III was refluxed for 150 hours with 100 ml. of 10% hydrochloric acid and the solution was evaporated to dryness. Crystallization of the residual solid from water eventually yielded 0.30 g. (13%) of pure terebic acid.

Thermal decomposition experiments. (*a*) *3-Methyl-3-nitro-1,2-butanedicarboxylic acid* (III). When 1.0 g. of III was heated in an open tube for 2 hours at 145° nitrogen oxides were evolved and the initially-colorless melt gradually became dark red. A solution of the melt in the minimum quantity of hot water deposited 0.45 g. (58%) of colorless teraconic acid (X), m.p. 151–156°dec. Recrystallization from water raised the m.p. to 160–162°dec. and the material did not depress the m.p. of authentic teraconic acid.

(*b*) *1-Carbomethoxy-3-methyl-3-nitro-2-butanecarboxylic acid* (IV). The dark red melt obtained by heating 2.1 g. of IV to 145° for 2.5 hours was hydrolyzed with 10 ml. of hot 10% hydrochloric acid (4 hours) and then yielded 0.40 g. (26%) of teraconic acid, m.p 160–162°dec.

(*c*) *3-Carbomethoxy-4-methyl-4-nitropentanoic acid* (II). When 2.0 g. of II (m.p. 108–109°) was heated to 145° for 2 hours the melt remained colorless and no visible gas evolution occurred. However, even after the melt had been twice recrystallized from ether, recovery of relatively impure ester (m.p. 100–103°) was only 75%. Consequently a second sample of II (2.00 g.) was heated as before and then was hydrolyzed by refluxing for 30 hours with 20 ml. of 10% hydrochloric acid. The filtered solution was evaporated to a volume of 3 ml. and the material which crystallized upon cooling was washed with ice-water and dried; yield, 1.48 g. (79%), m.p. 130–137°. The mother liquor yielded additional material of approximately the same m.p., making the total yield 1.71 g. (92%) of crude acid. Painstaking fractional recrystallization from water finally yielded 1.53 g. (82%) of 3-methyl-3-nitro-1,2-butanedicarboxylic acid (III), m.p. 140–142° or better, and 26 mg. of terebic acid, m.p. 171–173°.

When a sample (1.40 g.) of pure, unheated ester II was hydrolyzed in the same manner, 1.12 g. (85%) of pure nitro acid (III) and 35 mg. of terebic acid were obtained.

(*d*) *Dimethyl ester I* did not decompose significantly when heated to 145° for 2 hours, for the m.p. of the solidified melt was only 3–4° lower than that of a pure sample. No evolution of gas was observed during the period of heating.

(*e*) When *anhydride V* was heated for 2 hours at 145° it became slightly yellow and its m.p. was reduced from 110–112° to 105–110°. No gas evolution occurred.

(*f*) *The monoamides* (*type VIII*) listed in Table I decomposed completely (as determined by gas evolution) within 5–20 minutes at their melting points. The dark melts, which would not solidify, were hydrolyzed by heating on a steam-bath with 10% hydrochloric acid. Yields of teraconic acid in representative experiments were 14% (from the phenylhydrazide), 31% (from anilide VIII), and 65% (from the *n*-propylamide).

(*g*) *o-Toluidide VII*, m.p. 124–126°, became slightly colored when it was heated to 145° for 2 hours but no gas was evolved. The melt solidified readily upon cooling and then melted at 120–125°, indicating but little decomposition.

3-Methyl-3-nitro-N-phenyl-1,2-butanedicarboximide (IX). A mixture of 16.8 g. of anilide VIII, 20 ml. of acetyl chloride, and 40 ml. of benzene was refluxed for 10 minutes. Additional acetyl chloride (15 ml.) was added and refluxing was continued until all solid had dissolved (30 minutes total). The red solution was concentrated to a volume of 40 ml., 20 ml. of benzene was added, and the solution was cooled to 5°. Crystallization of a colorless solid was induced by scratching; yield, 9.8 g. (62%), m.p. 131–133°. Recrystallization from acetone and petroleum ether yielded colorless needles but the m.p. was not raised.

Anal. Calc'd for $C_{13}H_{14}N_2O_4$: N, 10.68. Found: N, 10.47.

When 1 g. of the imide was heated at 145° for 1 hour the melt became red but no evolution of gas occurred. Crystallization from acetone and petroleum ether yielded 0.90 g. (90%) of unchanged imide, m.p. 131.5–132°.

SUMMARY

The monomethyl ester having a free secondary carboxyl group was obtained from the reaction of methanol with the anhydride of 3-methyl-3-nitro-1,2-butanedicarboxylic acid or with a sulfuric acid solution of the dibasic acid itself.

With amines the anhydride yielded monoamides having a free secondary carboxyl. The anilide was cyclized to the N-phenylimide with acetyl chloride.

Derivatives of 3-methyl-3-nitro-1,2-butanedicarboxylic acid having a free secondary carboxyl group readily eliminated nitrous acid upon heating. Those having no free secondary carboxyl were more stable.

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