λ_{max} (EtOH) 225 mμ log (ε 4.37), 291 (4.66), and 357 (3.89); λ_{max} (EtOH–NaOH) 312 (4.45) and 375 (4.00); nmr δ 8.36 (d, 1, J = 2 cps, H-4), 8.95 (d, 1, J = 2 cps, H-2), and 10.09 ppm (s, 1, aldehyde H); mass spectrum m/e 220 (M^+).

Anal. Calcd for $C_{14}H_8ON_2$: C, 76.36; H, 3.66; O, 7.27; N, 12.72. Found: C, 76.58; H, 3.81; O, 7.55; N, 12.16.

1-Cyano-3-hydroxymethylcarbazole (11b).—Reduction of aldehyde **11a** followed the procedure for the conversion of **10a** into **10b** (*vide infra*). Crystallization of the product from 1:1 chloroform–methanol gave **11b**: mp 150°; λ_{max} (EtOH) 222 mμ (log ε 4.59), 253 (4.31), 278 (4.33), and 366 (3.77); λ_{max} (EtOH–NaOH) 250 (4.38), 278 (4.36), 294 (shoulder, 4.22), 366 (3.54), and 417 (3.14); mass spectrum m/e 222 (M^+).

Anal. Calcd for $C_{14}H_{10}ON_2$: C, 75.65; H, 4.54. Found: C, 74.42; H, 4.90.

1-Cyano-3-(β-hydroxymethylvinyl)carbazole (10b).—Sodium borohydride, 50 mg, was added in small portions to a solution of 50 mg of aldehyde **10a** in 15 ml of methanol. After 2 hr the mixture was diluted with water and extracted with chloroform. Evaporation of the extract and crystallization of the residue, 50 mg, from methanol yielded alcohol **10b**, mp 204°, mass spectrum m/e 248 (M^+).

Anal. Calcd for $C_{16}H_{12}ON_2$: C, 77.40; H, 4.87; O, 6.44; N, 11.28. Found: C, 77.28; H, 4.82; O, 6.64; N, 11.39.

Alcohol **10b** was acylated by dissolution in a mixture of acetic anhydride and pyridine at room temperature. The usual work-up and crystallization of the crude product from 1:1 acetone–hexane gave acetate **10c**, mp 185°.

Anal. Calcd for $C_{18}H_{14}O_2N_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.26; H, 4.70; N, 9.56.

1-Cyano-3-(β-carbomethoxyvinyl)carbazole (10e).—A solution of 200 mg of aldehyde **11a**, 160 mg of malonic acid, and a few drops of piperidine in 8 ml of pyridine was kept at 80° for 1 hr and then at 100° for 2 hr, refluxed for 0.5 hr, and poured into a 10% hydrochloric acid solution. Crystallization of the resultant precipitate, 197 mg, from 3:2 methanol–acetone yielded acid **10d**, mp >260°, nmr δ 6.70 (d, 1, J = 16 cps, olefinic H) and 7.83 ppm (d, 1, J = 16 cps, olefinic H). A solution of 50 mg of the acid and 3 drops of concentrated sulfuric acid in 10 ml of methanol was refluxed for 18 hr and poured into saturated brine solution. Crystallization of the precipitate, 38 mg, from methanol yielded ester **10e**, mp 250°, mass spectrum m/e 276 (M^+).

Anal. Calcd for $C_{17}H_{12}O_2N_2$: C, 73.90; H, 4.38; N, 10.14. Found: C, 73.87; H, 4.20; N, 10.10.

A solution of 30 mg of acid **10d** and a few drops of oxalyl chloride in 10 ml of tetrahydrofuran was stirred at room temperature for 90 min. The solvent and excess reagent were evaporated under reduced pressure. The residue was redissolved in 10 ml of anhydrous tetrahydrofuran and mixed with a solution of 20 mg of lithium tri-*t*-butoxyaluminum hydride in 10 ml of tetrahydrofuran. The mixture was stirred at room temperature for 1 hr, diluted with saturated brine solution, and extracted with chloroform. Evaporation of the extract and crystallization of the residue from methanol yielded a crystalline alcohol, identical in all respects with **10b** (*vide supra*). Its treatment with acetic anhydride yielded an acetate, identical in all respects with **10c** (*vide supra*).

Registry No.—**2**, 22433-55-2; **7**, 22433-56-3; **8**, 22433-57-4; **8** methiodide, 22433-61-0; **9**, 17517-71-4; **10a**, 22487-48-5; **10b**, 22430-80-4; **10c**, 22430-81-5; **10d**, 22430-82-6; **10e**, 22430-83-7; **11a**, 22433-59-6; **11b**, 22433-60-9.

Aziridines. XXII. The Reactions of Some 1-Substituted Aziridines with Carbethoxymethylenetriphenylphosphorane and Carbethoxyethylidinetriphenylphosphorane

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1-Aroylaziridines and related systems have been shown to react with carbethoxymethylenetriphenylphosphorane and carbethoxyethylidinetriphenylphosphorane. The products of reaction arise from intermediates formed by the carbanionic center of the ylide attacking the aziridinyl carbon.

Reactions of nucleophiles or reagents possessing nucleophilic sites with either 1-aroylaziridines or aziridines bearing other unsaturated 1 substituents have been well studied in recent years.[1-7] The products resulting from these reactions may be rationalized, usually, as arising from intermediates formed by an attack of the nucleophile at the 2 position of the aziridine ring. A new and potentially useful reaction that follows this general pattern, namely, the reaction of 1-aroylaziridines and related systems with carbethoxymethylenetriphenylphosphorane (**1**) and carbethoxyethylidinetriphenylphosphorane (**8**), has now been observed.

Results

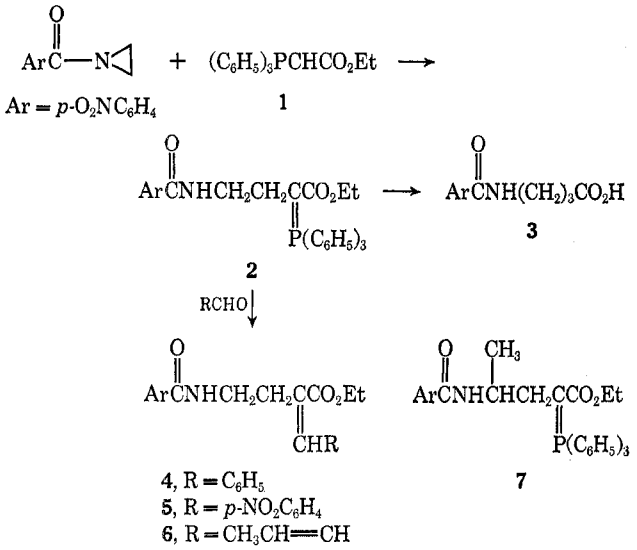
Carbethoxymethylenetriphenylphosphorane (**1**) and 1-*p*-nitrobenzoylaziridine in refluxing toluene formed the new and isolable ylide **2** (Scheme I). The structure of **2** was demonstrated by spectral data and conversion into 4-(*p*-nitrobenzamido)butanoic acid (**3**). The ir spectrum of **2** showed NH absorption and no carbonyl absorption below 6.15 μ, evidence that the ester carbonyl group was participating in charge delocalization. Heating of **2** with benzaldehyde and *p*-nitrobenzaldehyde gave the corresponding ethyl 2-benzylidine-4-(*p*-nitrobenzamido)butanoates **4** and **5**, respectively, and similar heating of **2** with 2-butenal gave compound **6**.

Compound **1** also reacts with 1-*p*-nitrobenzoyl-2-methylaziridine to produce ethyl 4-(*p*-nitrobenzamido)-2-triphenylphosphoranylpentanoate (**7**). Compound **7** was hydrolyzed to 4-(*p*-nitrobenzamido)pentanoic acid. The structure of this acid was authenticated by an alternate preparation involving the reaction of 4-aminopentanoic acid with *p*-nitrobenzoyl chloride and by mass spectroscopy.

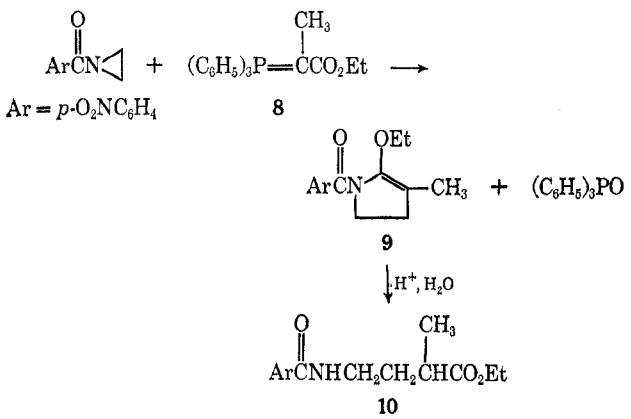
Reaction of carbethoxyethylidinetriphenylphosphorane (**8**) in refluxing toluene formed triphenylphosphine oxide and 1-(*p*-nitrobenzoyl)-2-ethoxy-3- methyl- 2-pyrroline (**9**) (Scheme II) as well as a small quantity (8%) of 2-*p*-nitrophenyl-2-oxazoline. The structure of

(1) H. W. Heine, *Angew. Chem. Intern. Ed. Engl.*, **1**, 528 (1962).
(2) J. E. Dolfini and J. D. Simpson, *J. Amer. Chem. Soc.*, **87**, 4381 (1965).
(3) P. Thyrum and A. R. Day, *J. Med. Chem.*, **8**, 107 (1965).
(4) G. E. Ham, U. S. Patent 3,247,220; *Chem. Abstr.*, **64**, 19622*h* (1966).
(5) H. W. Heine and T. Newton, *Tetrahedron Lett.*, 1859 (1967).
(6) H. W. Heine and M. S. Kaplan, *J. Org. Chem.*, **32**, 3069 (1967).
(7) S. Fujita, T. Hiyama, and H. Nozaki, *Tetrahedron Lett.*, 1677 (1969).

SCHEME I



SCHEME II

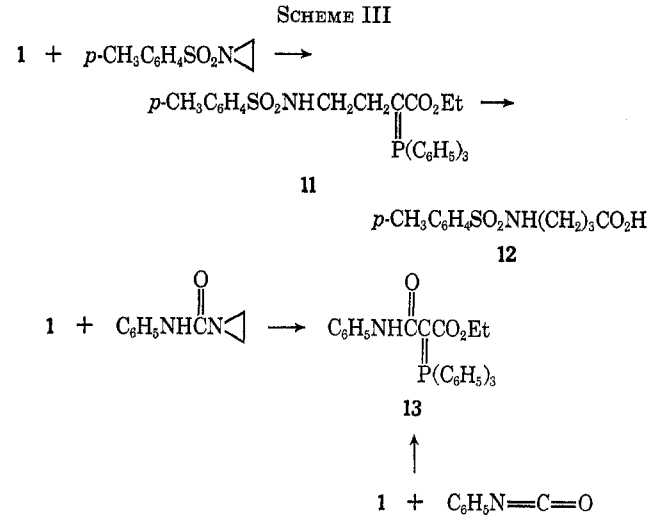


the novel enamide **9** was deduced from elemental analyses, nmr spectroscopy, and the mild acid hydrolysis of **9** at room temperature to ethyl 2-methyl 4-(*p*-nitrobenzamidobutanoate (**10**), the structure of which was verified by nmr and mass spectroscopy. The nmr spectrum of **9** taken in deuteriochloroform shows (a) the four hydrogens of the *p*-nitrophenyl group as two doublets at *ca.* 8.24 and 7.61 ppm, (b) the characteristic splitting pattern of the ethyl group with the methylene and methyl moieties absorbing at 3.40 and 0.68 ppm, respectively; (c) the 3-methyl group as a singlet at 1.68 ppm; and (d) the protons at C-4 and C-5 of the ring as triplets centered at *ca.* 2.42 (2 H) and 4.00 ppm (2 H).

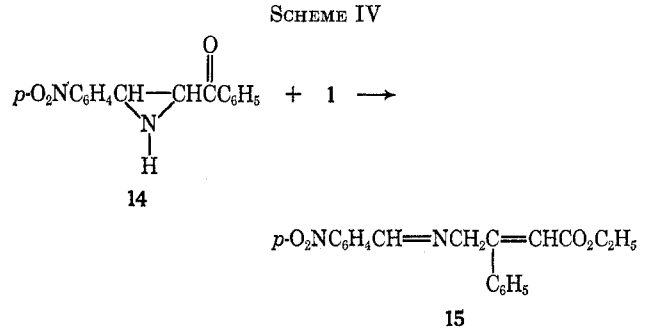
Reaction of 1-*p*-tolylsulfonylaziridine with **1** formed the ylide **11** (Scheme III). The structure of **11** was confirmed by elemental analyses and conversion into the known 4-(*p*-tolylsulfonamido)butanoic acid (**12**). As with compound **2**, the ester carbonyl absorption of **11** was at *ca.* 6.15 μ. Compound **1** with 1-aziridinecarboxanilide in refluxing toluene did not open the aziridine ring but instead displaced it to form the ethyl ester of 2-(triphenylphosphoranylidene)malonanilic acid (**13**), a known compound[8] prepared by reaction of **1** with phenyl isocyanate (Scheme III).

Carbethoxymethylenetriphenylphosphorane (**1**) and *trans*-2-*p*-nitrophenyl-3-benzoylaziridine (**14**) in refluxing chloroform formed the Schiff base **15** (Scheme IV). The structure of **15** was deduced by elemental analyses, nmr spectroscopy, and the formation of the *p*-nitrobenzaldehyde 2,4-dinitrophenylhydrazone when **15** was treated with 2,4-dinitrophenylhydrazine. The nmr spectrum of **15** in $CDCl_3$ with TMS as an internal standard showed the methylene group as a sharp singlet at 4.13 ppm and the ethyl group with its characteristic splitting pattern as a quartet centered at about 4.08 ppm and a triplet centered at 1.18 ppm. The two vinylic hydrogens absorbed in the same region as the two aromatic moieties (6.8–7.9 ppm). A control run of **14** in refluxing chloroform resulted in the recovery of the starting reagent.

SCHEME III



SCHEME IV



Discussion

It seems that, in the reactions of 1-*p*-nitrobenzoylaziridine and 1-*p*-tolysulfonylaziridine with **1**, the carbanionic center of the ylide attacks the aziridinyl carbon and opens the ring to form **2** and **11**, respectively. Compound **1** reacts in a similar fashion at the methylene carbon rather than the methine carbon of 1-*p*-nitrobenzoyl-2-methylaziridine to produce ethyl 4-(*p*-nitrobenzamido)- 2- triphenylphosphoranylpentanoate (**7**). This result is akin to the selective isomerizations by iodide ion of 1-*p*-nitrobenzoyl-2-methylaziridine to 2-*p*-nitrophenyl-4-methyl-2-oxazoline[9] and 1-*p*-nitrophenylazo-2-methylaziridine (**16**) to 1-*p*-nitrophenylazo-4-methyl-Δ^2-1,2,3-triazoline (**17**).[10,11]

(8) S. Tripett and D. M. Walker, *J. Chem. Soc.*, 3874 (1959).

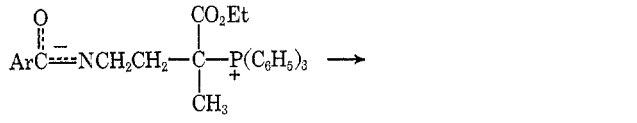
(9) H. W. Heine, W. G. Kenyon, and E. M. Johnson, *J. Amer. Chem. Soc.*, **83**, 2570 (1961).

(10) H. W. Heine and D. A. Tomalia, *ibid.*, **84**, 993 (1962).

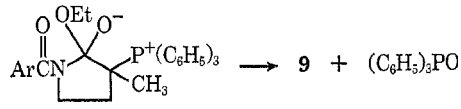
(11) R. Huisgen and G. Szeimies, personal communication. These investigators proved unequivocally that the product of isomerization of **16** was **17** by oxidation of **17** to the corresponding triazole, which was synthesized by an alternate route.

The reaction of **8** with 1-*p*-nitrobenzoylaziridine probably proceeds *via* a ring opening of the aziridine by the ylide to give **18**. Intermediate **18** could undergo an internal nucleophilic addition by the benzamido nitrogen to the ester group to yield a typical Wittig intermediate **19**, which could form triphenylphosphine oxide and **9** (Scheme V). The small quantity of 2-*p*-nitrophenyl-2-oxazoline (8%) formed in this reaction may arise by the well known pyrolysis of 1-acylaziridines to 2-oxazolines.

SCHEME V



18



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All of the above reactions of aziridines with ylides involve nucleophilic displacement at the aziridinyl carbon. In contrast, it appears that the carbonyl carbon of 1-aziridinecarboxanilide is the site of attack by **1**. Reactions taking place at the carbonyl group of 1-acylaziridines are not unknown. Examples are the easy methanolysis of 1-*p*-nitrobenzoylaziridine catalyzed by iodide ion[12] and the reaction of 1-acylaziridines with lithium aluminum hydride to yield aldehydes.[13]

It is also conceivable that the ylide **1** reacts with 1-aziridinecarboxanilide to give phenyl isocyanate, which, as previously shown by Tripett,[8] could react with the ylide to form **13**.

The formation of **15** from **1** and **14** involves cleavage of the carbon–carbon bond of the aziridine ring and a Wittig reaction with the carbonyl group of the aziridine. Isomerizations of 2,3-disubstituted aziridines into Schiff bases have been reported. Thus at 225° 2,3-diphenylaziridine isomerizes into benzalbenzylamine,[14] and at 205° 2,2-diphenyl-3-methylaziridine is converted into ethyliminobenzophenone.[15] *trans*-2-phenyl-3-benzoylaziridine and **14** have been shown to add to dimethyl acetylenedicarboxylate and diethyl acetylenedicarboxylate, respectively, by carbon–carbon scission of the aziridine ring.[16,17] Our experimental results indicate that **1** plays a role in the isomerization, but do not permit a conclusion as to whether the Wittig reaction precedes or follows the isomerization.

Experimental Section

Ethyl 4-(*p*-Nitrobenzamido)-2-triphenylphosphoranylbutanoate (2).—A mixture of 348 mg of carbethoxymethylenetriphenylphosphorane and 192 mg of 1-*p*-nitrobenzoylaziridine[12] in 25 ml of dry toluene was refluxed for 2 hr. The solvent was evaporated and the 529 mg of crude **2** that remained was recrystallized three times from equal portions of benzene and petroleum ether (bp 90–115°) to give crystals, mp 191–192°.

Anal. Calcd for $C_{31}H_{29}N_2O_5P$: C, 68.88; H, 5.41; N, 5.18. Found: C, 68.92; H, 5.26; N, 5.04.

4-(*p*-nitrobenzamido)butanoic Acid (3) was obtained by dissolving 540 mg of **2** in 25 ml of hot 10% aqueous methanol. A solution containing 56 mg of KOH in 25 ml of aqueous methanol (1:1) was added and the entire mixture was refluxed for 1 hr. The reaction mixture was cooled and then poured into 500 ml of water. The solvent was evaporated to 50 ml and the precipitated triphenylphosphine oxide was filtered. The filtrate was adjusted to a pH of 1–3 with 10% H_2SO_4. Evaporation of the filtrate gave 201 mg of **3**. Recrystallization from acetone–CCl_4 and then 95% ethanol formed **3**, mp 165–167°. Compound **3** was also prepared by the reaction of 4-aminobutanoic acid with *p*-nitrobenzoyl chloride.

Anal. Calcd for $C_{11}H_{12}N_2O_5$: C, 52.38; H, 4.80; N, 11.11. Found: C, 52.55; H, 5.03; N, 11.01.

Ethyl 4-*p*-nitrobenzamido-2-benzylidenebutanoate (4) was prepared by refluxing a mixture of 540 mg of **2** and 15 ml of benzaldehyde for 24 hr. Evaporation of the excess benzaldehyde and dissolution of the residual oil in 15 ml of C_6H_6 followed by the addition of 20 ml of petroleum ether gave 211 mg of **4**. Four recrystallizations from 95% ethanol gave **4**, mp 137–138°.

Anal. Calcd for $C_{20}H_{20}N_2O_5$: C, 65.21; H, 5.47; N, 7.60. Found: C, 65.17; H, 5.64; N, 7.46.

Ethyl 4-(*p*-Nitrobenzamido)-2-(*p*-nitrobenzylidene)butanoate (5).—A mixture of 540 mg of **5**, 151 mg of *p*-nitrobenzaldehyde, and 25 ml of $CHCl_3$ was refluxed for 2 hr. The solvent was evaporated and the residual oil was dissolved in 15 ml of C_6H_6. The addition of 15 ml of petroleum ether precipitated 342 mg of **5**. Three recrystallizations from $CHCl_3$ gave **5**, mp 175–177°.

Anal. Calcd for $C_{20}H_{19}N_3O_7$: C, 58.11; H, 4.63; N, 10.16. Found: C, 58.43; H, 4.87; N, 10.35.

Ethyl 4-(*p*-Nitrobenzamido)-2-(2-butenylidene)butanoate (6).—A mixture of 540 mg of **2** and 20 ml of crotonaldehyde was refluxed for 12 hr. The excess aldehyde was evaporated, the residual oil was dissolved in 15 ml of C_6H_6, and 156 mg of crude **6** was precipitated by the addition of 20 ml of petroleum ether. Five recrystallizations from 95% ethanol gave **6**, mp 145–147°.

Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.36; H, 5.99; N, 8.25.

Ethyl 4-(*p*-Nitrobenzamido)-2-triphenylphosphoranylpentanoate (7) was prepared by refluxing in 30 ml of toluene for 5 hr a mixture of 348 mg of **1** and 206 mg of 1-*p*-nitrobenzoyl-2-methylaziridine.[9] The solvent was evaporated and the residual oil was dissolved in 50 ml of ethyl ether. Slow evaporation gave 381 mg of crude **7**, which was recrystallized four times from ethyl ether to give **7**, mp 183–184°.

Anal. Calcd for $C_{32}H_{31}N_2O_5P$: C, 69.31; H, 5.63; N, 5.05. Found: C, 69.16; H, 5.65; N, 4.98.

1-(*p*-Nitrobenzoyl)-2-ethoxy-3-methyl-2-pyrroline (9).—A mixture of 1.45 g of **8** and 0.768 g of 1-*p*-nitrobenzoylaziridine in 70 ml of dry toluene was refluxed for 6 hr. The solvent was evaporated and 3–4 ml of dry Et_2O was added to the residual oil. The $(C_6H_5)_3PO$ that precipitated was filtered and the solvent was evaporated. The residue was dissolved in a minimum amount of dry C_6H_6 and the solution was chromatographed on a column of neutral alumina with C_6H_6. The first 50-ml fraction was evaporated to give 70 mg of crude 2-*p*-nitrophenyl-2-oxazoline. The next fraction of 150–200 ml eluent, when evaporated, gave 360 mg of **9**. Compound **9** was then dissolved in a minimum of DMF, and water was added until **9** precipitated; the compound was redissolved in DMF and precipitated again with H_2O. Pure **9** melted at 142.5–145.5°.

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.85; H, 5.85; N, 10.14. Found: C, 61.04; H, 5.91; N, 10.16.

Ethyl 2-Methyl-4-(*p*-nitrobenzamido)butanoate (10).—To 1 ml of acetone was added 39 mg of **9**, 0.4 ml of glacial acetic acid, and 0.4 ml of H_2O. In 10 min the initially bright yellow solution turned colorless. At this point 3.6 ml of H_2O was added and the solution was allowed to stand for 1–3 days. Crystals of **10** gradually appeared and were filtered. The yield of crude **10** was 30 mg. Four recrystallizations from petroleum ether (bp 100–115°) gave **10**: mp 65.5–66.5°; nmr ($CDCl_3$) δ 1.26 (t, 3, J = 6 Hz, CH_2CH_3), 1.22 (d, 2, J = 7 Hz, $CHCH_3$), 1.91 (m, 1, $CHCH_3$), 2.55 (quintet, 2, J = 7 Hz, CH_2CH), 3.52 (q, 2, J = 6 Hz, NCH_2), 4.23 (q, 2, J = 7 Hz, OCH_2), 7.05 (m, 1, NH), and

(12) H. W. Heine, M. E. Fetter, and E. M. Nicholson, *J. Amer. Chem. Soc.*, **81**, 2202 (1959).

(13) H. C. Brown and A. Tsukamoto, *ibid.*, **83**, 2016, 4549 (1961).

(14) (a) G. H. Coleman and G. P. Waugh, *Proc. Iowa Acad. Sci.*, **40**, 115 (1935); (b) G. H. Coleman and C. S. Nicholopoulos, *ibid.*, **49**, 286 (1942).

(15) B. K. Campbell and K. N. Campbell, *J. Org. Chem.*, **9**, 178 (1944).

(16) (a) A. Padwa and L. Hamilton, *Tetrahedron Lett.*, 4363 (1965); (b) A. Padwa and L. Hamilton, *J. Heterocycl. Chem.*, **4**, 118 (1968).

(17) H. W. Heine, A. B. Smith, III, and J. D. Bower, *J. Org. Chem.*, **33**, 1097 (1968).

7.88–8.35 (m, 4, aromatic); mass spectrum *m/e* 294 (molecular ion), 248, 193, 179, 150, and 102.

Anal. Calcd for $C_{14}H_{18}N_2O_5$: C, 57.11; H, 6.16; N, 9.52. Found: C, 57.44; H, 6.02; N, 9.80.

Ethyl 4-(*p*-Tolylsulfonyl)-3-triphenylphosphoranylbutanoate (11).—A mixture of 197 mg of *p*-tolylsulfonylaziridine,[9] 348 mg of **1**, and 25 ml of dry toluene was refluxed for 15 min. On cooling, a white solid, mp 240–260°, precipitated and was filtered. Evaporation of the filtrate gave 166 mg of crude **11**. Four recrystallizations from 95% ethanol gave **11**, mp 184–186°.

Anal. Calcd for $C_{31}H_{32}NO_4PS$: C, 68.23; H, 5.91; N, 2.56. Found: C, 68.27; H, 6.21; N, 2.61.

Conversion of 11 into 12.—To 272 mg of **11** in 20 ml of 10% aqueous methanol was added a solution of 28 mg of KOH in 15 ml of 50% aqueous methanol. The mixture was refluxed for 1 hr, cooled, and added to 175 ml of H_2O. The volume of solvent was reduced to 25 ml by evaporation and the triphenylphosphine oxide that had precipitated was filtered. The pH of the filtrate was adjusted to *ca.* 2 by 10% H_2SO_4 and then the filtrate was evaporated to give 115 mg of **12**. Recrystallization three times from aqueous ethanol gave **12**, mp 132–134°. An authentic sample of **12** prepared according to a published method[18] melted at 133–134°; the ir spectra of the two samples were identical.

Compound 11 was prepared by refluxing a mixture of 348 mg of **3**, 192 mg of 1-aziridinecarboxanilide,[19] and 25 ml of dry toluene for 4 hr. The solvent was evaporated and 306 mg of crude **11** was obtained and recrystallized from CCl_4–hexane, mp 182–184°. An authentic sample was prepared by a published method.[6] This sample of **11** melted at 188–189° and had an ir spectrum identical with that of **11** prepared from the 1-aziridinecarboxanilide.

Ethyl 3-Phenyl-4-(N-*p*-nitrobenzylidene)amino-2-butenoate (15).—A mixture of 268 mg of 2-*p*-nitrophenyl-3-benzoylaziridine, 351 mg of **1**, and 30 ml of $CHCl_3$ was refluxed for 24 hr. The solvent was evaporated and the glassy residue was slurried with a small amount of 95% ethanol. The yellow crystals of **15** were filtered and recrystallized from 95% ethanol to give 150 mg of **15**, mp 113–115°.

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.43; H, 5.36; N, 8.28. Found: C, 67.14; H, 5.46; N, 8.20.

Hydrolysis of 7 to 4-(*p*-nitrobenzamido)pentanoic acid was effected by adding 227 mg of **7** to 20 ml of CH_3OH-H_2O (1:1) and heating until **7** dissolved. A solution containing 28 mg of KOH in 20 ml of CH_3OH–H_2O (1:1) was added and the mixture was refluxed for 2 hr. Evaporation of the CH_3OH caused precipitation of Ph_3PO, which was filtered. The filtrate was acidified to pH 1–3 with 10% H_2SO_4. Evaporation of the filtrate gave 75 mg of 4-(*p*-nitrobenzamido)pentanoic acid. Recrystallization from aqueous ethanol gave material melting at 145–146°. Reaction of 4-aminopentanoic acid[20] with *p*-nitrobenzoyl chloride also formed 4-(*p*-nitrobenzamido)pentanoic acid in poor yield. The two samples gave identical ir spectra; mass spectrum molecular ion *m/e* 266, fragments *m/e* 249, 220, 193 [*p*-$O_2NC_6H_4CONHCHCH_3]^+$, 150, and 120.

Registry No.—**1**, 1099-45-2; **2**, 22487-52-1; **3**, 22433-20-1; **4**, 22433-21-2; **5**, 22433-22-3; **6**, 22433-23-4; **7**, 22433-24-5; **8**, 5717-37-3; **9**, 22433-26-7; **10**, 22433-27-8; **11**, 22433-28-9; **12**, 1213-42-9; **15**, 22487-54-3.

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(18) D. Todd and S. Teich, *J. Amer. Chem. Soc.*, **75**, 1895 (1953).
(19) S. Gabriel and R. Stelzner, *Ber.*, **28**, 2929 (1895).
(20) J. Cologne and J. M. Pouchol, *Bull. Soc. Chim. Fr.*, 598 (1962).

Cyclization Reactions of Ninhydrin with Aromatic Amines and Ureas[1]

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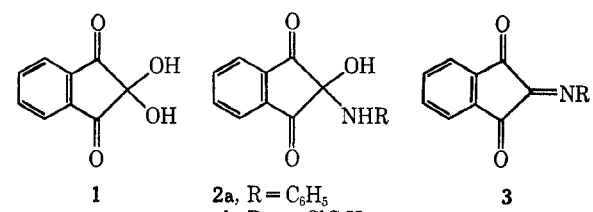
Ninhydrin (1,2,3-indantrione monohydrate, **1**) condenses with aromatic amines that contain an additional activating group in the *meta* position. The reaction proceeds with cyclization to give structures of type **5** (X = OH, OCH_3, or NH_2; R = H). These products are stable, show the appropriate number of aromatic protons in their nmr spectra, give strong parent peaks in their mass spectra, and yield well-characterized acetyl derivatives. These properties distinguish them from the products formed from **1** and less activated aromatic amines, in which reaction takes place only at the central carbonyl group of **1**. The reaction of **1** with urea and 1,3-dimethylurea also proceeds with cyclization, to give structures of type **6** (R = H or CH_3; R′ = H). 1,1-Dimethylurea does not react with ninhydrin.

In recent studies in this laboratory,[2,3] it was reported that ninhydrin reacted with the amino heterocycles guanine and cytosine to afford products which contained an additional heterocyclic ring. These results stood in contrast to earlier reports in the literature about the reactions of ninhydrin with simpler aromatic amines and ureas. Thus the reaction products of **1** with aniline,[4] *p*-chloroaniline,[4] *o*- and *m*-hydroxyaniline,[4] *p*-aminobenzoic acid,[5] 2-aminopyridine,[4] urea,[6,7] 1,1-dimethylurea,[6] and guanidine[7,8] were assigned structures of type **2**, while the corresponding dehydrated products (**3**) were obtained from *p*-hydroxyaniline and



1 **2a**, R = C_6H_5; **b**, R = *p*-ClC_6H_4; **c**, R = *m*-HOC_6H_4; **d**, R = $CONH_2$ **3**

p-phenylenediamine.[5] Only in the reaction of *o*-phenylenediamine with ninhydrin was a cyclized structure (**4**) ascribed to the product.[9]

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(2) R. Shapiro and J. Hachmann, *Biochemistry*, **5**, 2799 (1966).
(3) R. Shapiro and S. C. Agarwal, *J. Amer. Chem. Soc.*, **90**, 474 (1968).
(4) M. Friedman, *Can. J. Chem.*, **45**, 2271 (1967).
(5) R. Moubasher, *J. Chem. Soc.*, 1038 (1949).
(6) M. Polonovsky, P. Gonnard, and G. Glotz, *Bull. Soc. Chim. Fr.*, **6**, 1557 (1939).
(7) D. A. Mac Fayden, *J. Biol. Chem.*, **186**, 1 (1950).
(8) S. Ruhemann, *J. Chem. Soc.*, **97**, 2025 (1910).
(9) S. Ruhemann, *ibid.*, **97**, 1438 (1910).