Table I. Yields and Physical Data

compd	yield, %	mp, °C (purification)	formula	calcd C	calcd H	calcd N	found C	found H	found N
1b	87[a]	103.5-104.5 (ethanol/water)	$C_{12}H_{11}F_3N_2O_6$	42.86	3.30	8.33	42.97	3.40	8.30
1e	35[b]	134-135 (ethanol/water)	$C_{12}H_{11}F_4NO_4$	46.61	3.85	4.53	46.64	3.54	4.48
1f	70	276-279[c] (water)	$C_9H_{10}FNO_3$	54.27	5.06	7.03	54.02	5.22	6.92
2a	91	105-105.5 (ethanol/water)	$C_{12}H_{10}F_4N_2O_6$	40.69	2.85	7.91	40.62	3.01	7.87
2d	34[d]	142-144 (ethanol/water)	$C_{12}H_{10}F_5NO_4$	44.05	3.08	4.28	44.05	3.10	4.32
2e	81	267-269 (water)	$C_9H_9F_2NO_3$	49.77	4.08	6.45	49.91	4.29	6.22
2f	30[d]	165.5-166.5 (ethanol/water)	$C_{12}H_{11}F_4NO_5$	44.23	3.41	4.31	44.11	3.47	4.18

[a] Yield based on tyrosine methyl ester hydrochloride. [b] Yield based on 1b. [c] Lit.[5] mp 278-279 °C. [d] Yield based on 2a.

Table II. Proton Nuclear Magnetic Resonance Spectral Data (ppm)[a]

	CH_3	CH_2	CH	aromatic protons[b] H_2	H_5	H_6
1b	3.81	3.20 (dd, 6)	4.84 (dt, 6)	7.81 (d, 2)	7.08 (d, 8.5)	7.31 (q, 2, 8.5)
1e	3.80	3.14 (dd, 5)	4.84 (dt, 6)	ABC portion of ABCX multiplet 6.64-7.04		
1f[c]		3.24 (dd, 7)	4.36 (t, 7)	ABC portion of ABCX multiplet 6.90-7.20		
2a	3.82	3.16 (dd, 7)	4.83 (dt, 7)	7.16 (q, 2, 10.5)		7.65 (m)
2d	3.82	3.12 (dd, 6)	4.83 (dt, 6)	A_2 portion of A_2X_2 multiplet centered at 6.68 (H_2, H_6)		
2e[c]		3.24 (dd, 6)	4.38 (t, 6)	A_2 portion of A_2X_2 multiplet centered at 6.96 (H_2, H_6)		
2f	3.81	8.07 (d, 6)	4.78 (t, 6)	AB portion of ABX multiplet 6.28-6.48 (H_2, H_6)		

[a] 100-MHz spectra measured in $CDCl_3$ except where indicated. Multiplicity and coupling constants (hertz) are given in parentheses. [b] 1b-f, H_2 is ortho to R_1. 2a-e, H_2 is ortho to F. [c] Measured in 0.1 M DCl.

plates, Analtech) and mass spectrometry (Finnigan, model 1015 D). Yields and physical data are shown in Table I. Proton NMR data are given in Table II. The fluorination procedure was identical with that described previously.[7]

***N*-(Trifluoroacetyl)-3-nitro-L-tyrosine Methyl Ester (1b).** To 100 g of trifluoroacetic anhydride cooled in an ice bath was added in portions 25 g (0.11 mol) of L-tyrosine methyl ester hydrochloride. After the exothermic reaction had subsided, the solution was stirred at room temperature for 2 h, and the excess trifluoroacetic anhydride was removed by rotary evaporation. Methanol was added and removed by rotary evaporation. The residue (**1a**) was dissolved in 100 mL of glacial acetic acid, the solution was cooled to 10 °C in an ice bath, and 5.5 mL of fuming nitric acid was added dropwise over 10 min. The solution was stirred for 1 h at 10 °C, warmed to room temperature and stirred for 1 h, and poured into 500 mL of an ice–water slurry. The precipitate was collected by filtration and recrystallized from water/ethanol to give pure **1b**.

***N*-(Trifluoroacetyl)-3-fluoro-L-tyrosine Methyl Ester (1e).** Hydrogenation (3 atm) of 9 g (0.025 mmol) of **1b** in 200 mL of ethanol over 200 mg of platinum oxide was complete in 2 h. Removal of the catalyst by filtration and evaporation of solvent afforded **1c**. This was dissolved in 500 mL of cold 50% fluoroboric acid. Diazotization was accomplished by addition of 1.9 g (0.28 mol) of $NaNO_2$ dissolved in 5 mL of water. After 2 h, the solution of diazonium fluoroborate **1d** was irradiated (Pyrex filter) for 3 h. The fluoroboric acid was neutralized to pH 7 with concentrated aqueous sodium hydroxide while the solution was cooled in dry ice/acetone. The solution was then extracted with ether until TLC showed no more product in the extract. After the solution was dried (Na_2SO_4) and the solvent removed by rotary evaporation, the residue obtained was chromatographed on silica gel (0.5% methanol/chloroform) to give **1e**, purified further by recrystallization from aqueous ethanol.

3-Fluoro-L-tyrosine (1f). A 1.0-g (3.23 mmol) sample of **1e** dissolved in 20 mL of 6 N HCl was heated on a steam bath overnight. Rotary evaporation gave a white crystalline residue, which was dissolved in a minimum quantity of water. Neutralization with a concentrated solution of sodium acetate precipitated the free amino acid **1f**: 450 mg recrystallized from water; $[\alpha]^{25}_D$ −8.7° (*c* 0.2, 0.5 N HCl) (lit.[5] $[\alpha]^{26}_D$ −5.7°).

***N*-(Trifluoroacetyl)-3,5-difluorotyrosine Methyl Ester (2d).** Nitration of **1e** (2.0 g, 6.5 mmol) in 20 mL of acetic acid with 0.35 mL of fuming nitric acid and workup as before gave **2a**. Hydrogenation of **2a** (1.7 g 4.8 mmol) gave the amine **2b**, which was diazotized in 200 mL of cold fluoroboric acid. Irradiation (1 h) and isolation as before afforded a mixture of **2d** and **2f**. Chromatography (silica gel, 0.5% methanol/chloroform) gave 541 mg of **2d**.

3,5-Difluoro-L-tyrosine (2f). A 250-mg (0.76 mmol) sample of **2d** was hydrolyzed by heating (steam bath) overnight in 10 mL of 6 N HCl. Isolation and recovery of the free amino acid was performed as for **1f** to give 133 mg of **2e**: $[\alpha]^{25}_D$ −4.7° (*c* 0.2, 0.5 N HCl).

3,4-Dihydroxy-5-fluoro-L-phenylalanine (5-Fluoro-L-DOPA) (2g). Continued elution of the column used for the isolation of **2d** with 1% methanol–chloroform afforded **2f**. Aqueous acid hydrolysis of **2f** (HBr or HCl) produced the corresponding hygroscopic noncrystalline salts of **2g**, which proved resistant to recrystallization attempts. Attempts to isolate the free amino acid likewise were unrewarding. Tentative identification of **2a** was based on identical TLC behavior with authentic 5-fluoro-D,L-DOPA and on chemical-ionization mass spectral data.

Registry No. **1a**, 1604-54-2; **1b**, 5106-00-3; **1c**, 73210-50-1; **1d**, 73210-52-3; **1e**, 73210-53-4; **1f**, 139-26-4; **2a**, 73210-54-5; **2b**, 73210-55-6; **2d**, 73210-56-7; **2e**, 73246-30-7; **2f**, 73210-57-8; L-tyrosine methyl ester hydrochloride, 3417-91-2.

pK_a Values of Arsabenzenecarboxylic Acids. Empirical Estimate of the Charge Distribution of Arsabenzene

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Since the study of aromatic compounds has provided excellent tests of the validity of various MO methods, calculations on the new aromatic arsabenzene[2] should be particularly interesting. Results from CNDO/2[3] and ab

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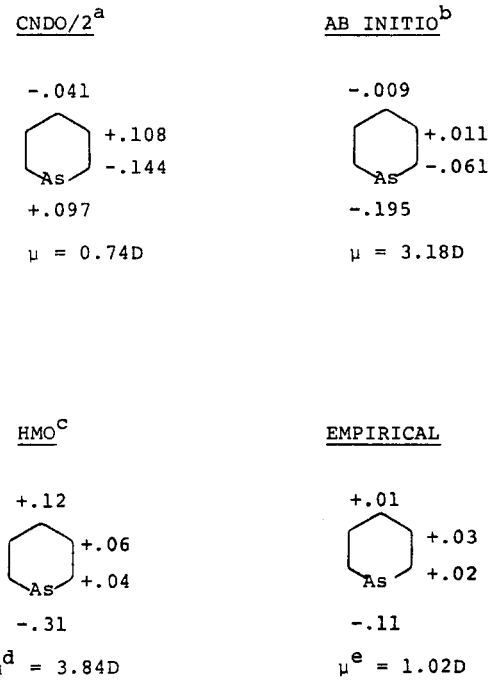

Figure 1. Dipole moments and charge distributions on the ring atoms of arsabenzene by various methods: a, ref 3; b, ref 4; c, ref 5; d, calculated from the charge densities in ref 5 and the geometry from ref 15; e, ref 6.

initio (STO-3G basis set)[4] calculations have been published, and calculated dipole moments and charge densities are available. More recently an HMO treatment, parameterized from the UV photoelectron spectrum, has appeared.[5] Although all three methods correctly predict that the negative end of the dipole is toward the arsenic,[6] the calculated charge densities on individual atoms diverge greatly (see Figure 1). Thus an independent empirical estimate of charge densities seems highly desirable. While ^1H and ^{13}C chemical shift values from the NMR spectra are most frequently used to correlate charge densities in aromatic compounds,[7] the NMR spectra of arsabenzene are dominated by very large diamagnetic effects due to the arsenic atom[8] and do not lead to charge density information. Our approach has been to obtain the Hammett substituent constants (σ) for each of the three positions on the arsabenzene ring and to use the values to estimate the charge desities.

Although the Hammett σ–ρ relationship was originally defined to correlate electronic effects on benzene rings, it should be valid to extend the relationship to heteroaromatic systems, with the heteroatom treated as a substituent.[9] Thus the pK_a values of 2-, 3-, and 4-arsabenzenecarboxylic acids define the corresponding σ constants. The pK_a value of 4-arsabenzenecarboxylic acid has been reported.[10] The necessary 2- and 3-arsabenzenecarboxylic acids have been obtained by the hydrolysis of their methyl esters, which were prepared by a modification of our previous procedure.[11] The pK_a values of the three arsabenzenecarboxylic acids as well as that of benzoic acid are listed in Table I.

Table I. pK_a's of Benzoic Acid and Arsabenzenecarboxylic Acids at 20.0 °C with the Derived σ Values

acid	pK_a	σ
benzoic	4.20 ± 0.03	0
2-arsabenzenecarboxylic	3.93 ± 0.03	0.3
3-arsabenzenecarboxylic	3.79 ± 0.03	0.4
4-arsabenzenecarboxylic	(4.10)[a]	0.1

[a] Reference 10.

The order of increasing acidity is benzoic < 4- < 2- < 3-arsabenzenecarboxylic acid, while the corresponding σ values are 0, 0.1, 0.3, and 0.4. It should be recognized that the carboxylic acid and carboxylate anion groups of the 2-acid may be subjected to relatively large proximity effects from the adjacent arsenic atom which could influence its pK_a value.[12] Nonetheless, it is tempting to assign the relative electron densities of these positions as benzene > 4- > 2- > 3-arsabenzene. The small but positive σ values clearly indicate that all of the carbon atoms are slightly electron deficient with respect to benzene, which requires the arsenic to be slightly electron rich. We have arrived at a similar conclusion independently from an analysis of the ESCA and Auger spectra of arsabenzene.[13] However, the small differences in values of the σ constants suggest that there is not much difference in electron density between different carbon atoms.

The dipole moment of arsabenzene can be thought of as the vector sum of the charge densities on individual atoms. If it is assumed that σ values are directly proportional to charge density at the corresponding carbon atoms,[14] the known structure[15] and dipole moment[6,16] of arsabenzene can be used to calculate the empirical charge densities tabulated in Figure 1. These empirical charge densities must be regarded as very approximate because of our assumptions and the fact that we have neglected any contribution from the hydrogen atoms.

Our charge densities are in modest qualitative agreement with those obtained by Clark's ab initio calculations and Herndon's HMO model. However, both treatments predict too large a charge separation as indicated by their unrealistic dipole moments. On the other hand, while Schweig's CNDO/2 calculation predicts a reasonable value for the dipole moment, both the low electron density on arsenic and the relatively large difference in electron density between C_2 and C_3 are not supported by our work. We hope that our estimate of the charge distribution of arsabenzene will be useful to others applying MO methods to arsabenzene and other group 5 heterobenzenes.

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(14) Considerably better correlations are found by using multiparameter substituent constants. See: Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 1. Although our approach is recognized to be naive, at present the single-parameter σ constants are the only experimental measure of electron availability on the arsabenzene ring. However, we are encouraged that the pK_a values of azuloic acids show reasonable correlations with charge densities calculated by HMO and VESCF methods. See: McDonald, R. N.; Reitz, R. R. *J. Org. Chem.* **1972**, *37*, 2703.
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Experimental Section

Methyl 3-Arsabenzenecarboxylate and Methyl 2-Arsabenzenecarboxylate. A solution of 1.7 g (12 mmol) of arsabenzene and 2.3 g (27 mmol, 2.2 equiv) of methyl propiolate in 20 mL of mesitylene was heated at 120 °C for 15 h, after which all low-boiling materials were removed by vacuum distillation. Analysis of the residue by GLC ($^1/_4$ in. × 8 ft column, packed with 20% Carbowax 20-M on Chromosorb W at 185 °C) showed methyl 1-arsabicyclo[2.2.2]octa-2,5,7-triene-3- and -2-carboxylate present in the ratio of 63:37. The mixture of carboxylates was used without further purification.

A solution of the two carboxylates obtained above and 2.8 g (12 mmol) of 3,6-bis(2-pyridyl)tetrazine in 20 mL of methylene chloride was stirred for 16 h. GLC ($^1/_4$ in. × 5 ft column packed with 5% SE-30 on Chromosorb W at 150 °C) showed no unreacted starting materials. The suspension was then filtered, and the residue was washed with cold benzene. The solvent was then removed from the filtrate and the residual oil distilled under vacuum to give a light yellow oil: bp 67 °C (0.1 torr); yield 1.67 g (70% based on arsabenzene).

GLC analysis ($^1/_4$ in. × 5 ft column packed with 15% XF-1150 on Chromosorb W at 175 °C) of the oil showed the presence of methyl 3- and 2-arsabenzenecarboxylate in the ratio of 62:38. The two carboxylates can be separated by preparative GLC and were found to be identical with those obtained by the pyrolysis of the corresponding methyl arsabicyclo[2.2.2]octatrienecarboxylates.[11]

3-Arsabenzenecarboxylic Acid. To a solution of 102 mg (1.9 mmol) of sodium methoxide in 10 mL of 1:1 (v/v) water–methanol was added 119 mg (0.6 mmol) of methyl 3-arsabenzenecarboxylate in 200 μL of methanol. The mixture was heated at 70 °C for 15 h. It was then extracted once with methylene chloride, which was found to contain no starting material. The base was then neutralized with a solution of 409 mg (2.15 mmol) of *p*-toluenesulfonic acid monohydrate in 5 mL of water, and the product was extracted into methylene chloride (4 × 7 mL). Removal of solvent by distillation gave a white solid. The crude yield was 111 mg (100%). A 98-mg sample was recrystallized from 6 mL of water to give 70 mg (71%) of white needles: mp 86 °C; ^{1}H NMR ($CDCl_3$) δ 8.07 (1 H, t, J = 9 Hz), 8.43 (1 H, d, J = 9 Hz), 10.03 (1 H, d, J = 9 Hz), 10.63 (1 H, s), 11.67 (1 H, br s); mass spectrum, m/e 184 (M^+, $C_6H_5AsO_2$, base peak). Anal. Calcd for $C_6H_5AsO_2$: C, 39.16; H, 2.74. Found: C, 39.21; H, 2.84.

2-Arsabenzenecarboxylic Acid. An analogous procedure was followed by using the following amounts of materials: 103 mg (1.9 mmol) of sodium methoxide, 127 mg (0.64 mmol) of methyl 2-arsabenzenecarboxylate, and 418 mg (2.20 mmol) of *p*-toluenesulfonic acid monohydrate. The crude yield was 110 mg (93%). A 93-mg sample was recrystallized from 6 mL of water to give 71 mg (76%) of yellow needles: mp 86 °C; ^{1}H NMR ($CDCl_3$) δ 7.70 (1 H, t, J = 8 Hz), 8.03 (1 H, t, J = 8 Hz), 8.70 (1 H, d, J = 8 Hz), 9.87 (1 H, d, J = 8 Hz), 11.85 (1 H, bs); mass spectrum, m/e 184 (M^+, $C_6H_5AsO_2$, base peak). Anal. Calcd for $C_6H_5AsO_2$: C, 39.16; H, 2.74. Found: C, 39.00; H, 2.80.

Determination of Dissociation Constants. The ionization constants of benzoic acid, 2-arsabenzenecarboxylic acid, and 3-arsabenzenecarboxylic acid at 20.0 ± 0.1 °C were determined by potentiometric titration under nitrogen, with a Radiometer titrator TTT2 and a Radiometer ABU 12 autoburet. The glass electrode was standardized before and after each determination. The method of Albert and Serjeant was used to determine the pK_a values.[17]

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Registry No. Arsabenzene, 289-31-6; methyl propiolate, 922-67-8; methyl 1-arsabicyclo[2.2.2]octa-2,5,7-triene-3-carboxylate, 63787-93-9; methyl 1-arsabicyclo[2.2.2]octa-2,5,7-triene-2-carboxylate, 63787-94-0; methyl 3-arsabenzenecarboxylate, 63787-90-6; methyl 2-arsabenzenecarboxylate, 63787-91-7; 3-arsabenzenecarboxylic acid, 73178-35-5; 2-arsabenzenecarboxylic acid, 73178-36-6; benzoic acid, 65-85-0.

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Syntheses with α-Heterosubstituted Phosphonate Carbanions. 10.[1a] Autoxidation of the Anion

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The autoxidation of alkylidenetriphenylphosphoranes (ylides) has been found to be a valuable method for the preparation of symmetrical olefins[2,3] including cyclic ones.[4,5] A similar method for the preparation of symmetrical olefins by autoxidation of the carbanion of benzyldiphenylphosphine oxide was reported by Horner and co-workers.[6] Ketones were obtained by the same author by autoxidation of (1-phenylalkyl)diphenylphosphine oxides.

In this report the autoxidation of the anions derived of diphenyl [aryl[(4-nitrophenyl)amino]methyl]phosphonates will be described which leads to the formation of the corresponding aroyl anilides. The phosphonates which are starting materials for this reaction are easily obtained in a one-pot reaction from diphenyl phosphite, an aniline, and an aromatic aldehyde[7,8] (Table I). They are transformed into the corresponding α-heterosubstituted phosphonate carbanions smoothly by using potassium *tert*-butoxide in dimethyl sulfoxide as base. For the autoxidation, the carbanions were placed under 50 psi of oxygen and shaken for 12 h. In every case the corresponding anilide (Table II) was isolated in a fair to good yield.

Discussion

The overall reaction sequence for the autoxidation of ylides was formulated by Bestmann[3] as in Scheme I. The ylide was cleaved by oxygen initially into one molecule of triphenylphosphine oxide and a molecule of aldehyde. The latter then reacts with an unoxidized ylide in a typical Wittig reaction to give the final products, the symmetrical olefin and a second molecule of triphenylphosphine oxide.

The mechanism of the autoxidation of the diphenyl [aryl[(4-nitrophenyl)amino]methyl]phosphonates of this study has not been investigated. Neither we nor the earlier investigators[3,5] have any evidence to decide upon the detailed mechanism of the oxygen carbanion interaction. Two modes of reaction seem to be the most reasonable: (a) the oxygen and the carbanionic species react in a concerted manner to form a 1,2-dioxaphosphetane as an intermediate which fragments into products, or (b) a peroxide intermediate forms first which collapses via the four-membered intermediate into products (Scheme II). In the light of recent findings it seems more probable to assume that the oxygen in the highly basic solution reacts

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