O-*t*-butyl-L-threonine *t*-butyl ester, acetic acid salt, mp 54–57° (*Anal.* Calcd for $C_{14}H_{29}NO_5$: C, 57.7; H, 9.95; N, 4.81. Found: C, 56.90; H, 9.81; N, 4.86) (582 mg, 2 mmoles), was added. The container was rinsed twice with 0.5-ml portions of THF. The mixture was stirred in ice for 10 min and at room temperature for 4 hr and was kept in a refrigerator overnight.

The solvent was removed *in vacuo*, and ethyl acetate (about 40 ml) and a little water were added. The ethyl acetate layer was washed with 1 *N* citric acid (50 ml in three portions), 10% potassium bicarbonate solution (50 ml in three portions), and a little saturated sodium chloride solution. The aqueous phases were extracted twice with ethyl acetate. The combined ethyl acetate extracts were dried over sodium sulfate and the solvent removed *in vacuo;* 950 mg of a solid remained. It was recrystallized from little ether by addition of petroleum ether, yield 450 mg, mp 138–40°. To this material ether (10 ml) was added; 135 mg of crystals remained undissolved, mp 139–53°, $[\alpha]^{25}D$ −15.6° (*c* 2, methanol).

Anal. Calcd for $C_{19}H_{36}N_2O_5$: C, 61.26; H, 9.74; N, 7.52. Found: C, 61.26; H, 9.92; N, 7.42.

Most of the ether was allowed to evaporate and petroleum ether was added; 130 mg, mp 142–145°, $[\alpha]^{25}D$ +4.8° (*c* 2, methanol).

Anal. Calcd for $C_{19}H_{36}N_2O_5$: C, 61.26; H, 9.74; N, 7.52. Found: C, 61.22; H, 10.21; N, 7.33.

From the mother liquor, 65 more mg was obtained, mp 151–158°, $[\alpha]^{25}D$ −6.3° (*c* 2, methanol).

Anal. Calcd for $C_{19}H_{36}N_2O_5$: C, 61.26; H, 9.74; N, 7.52. Found: C, 61.38; H, 9.82; N, 7.54.

B. Mixed Anhydride with Isobutyl Chloroformate. The mixed anhydride was prepared exactly the same way as described under A, using 0.275 ml of isobutyl chloroformate (2.1 mmoles). The reaction mixture was stirred overnight at room temperature. After the same work-up as under A, 640 mg of an oil was obtained. It was dissolved in cyclohexane and petroleum ether was added. In a refrigerator 285 mg of crystals melting at 146–152° separated, $[\alpha]^{25}D$ −35.8° (*c* 2, methanol).

Anal. Calcd for $C_{19}H_{36}N_2O_5$: C, 61.26; H, 9.74; N, 7.52. Found: C, 61.56; H, 10.06; N, 7.55.

A small second fraction of beautiful crystals, mp 148–151°, was obtained, whereas a third fraction of 120 mg did not give a correct analysis.

C. Anderson's method with Tetraethyl Pyrophosphite. Formyl-L-leucine (318 mg, 2 mmoles) was dissolved in diethyl phosphite with warming. O-*t*-Butyl-L-threonine *t*-butyl ester, acetic acid salt (582 mg, 2 mmoles), was dissolved in this solution and triethylamine (0.28 ml, 2 mmoles) was added followed by tetraethyl pyrophosphite (0.54 ml, 2.2 mmoles). The mixture was heated on a steam bath for 30 min and stored in a refrigerator overnight. The solution was concentrated *in vacuo* at a bath temperature of up to 65°. The work-up was the same as described under A. The residue was dissolved in a little ether and a large volume of petroleum ether and seed crystals were added. Crystallization started immediately and was completed in a refrigerator, yield 190 mg, mp 154–156°, $[\alpha]^{25}D$ −45.5°. The relatively low yield may be due to the use of the acetic acid salt of the threonine derivative which may give rise to the formation of acetyl-O-*t*-butyl-L-threonine *t*-butyl ester.

Benzyloxycarbonyl-L-asparaginyl-L-phenylalanine Methyl Ester *via* Mixed Anhydride with 1-Adamantyl Chloroformate. Benzyloxycarbonyl-L-asparagine (5.32 g, 0.02 mole) was suspended in dry tetrahydrofuran (40 ml), triethylamine (2.78 ml, 0.02 moles) was added, and the mixture was stirred in an ice bath. From a solution of 1-adamantyl chloroformate (4.5 g, 0.021 moles) in benzene, the solvent was removed *in vacuo*, and the residue was dissolved in dioxane (20 ml) and added to the solution of the asparagine derivative. The mixture was stirred in ice for 20 min when a mixture of methyl phenylalaninate hydrochloride (4.31 g, 0.02 mole) in dioxane and triethylamine (2.78 ml, 0.02 mole) was added. Stirring was continued for 0.5 hr in ice and 1.5 hr at room temperature when the solvents were removed *in vacuo*. The residue was dissolved in water and ethyl acetate. The ethyl acetate layer was washed with 1 *N* citric acid, 10% potassium bicarbonate, and saturated sodium chloride solution. A flocky precipitate appeared in the ethyl acetate at the end of these operations. It was removed by filtration, washed with ethyl acetate, and dried, yield 1.18 g, mp 192–193°. The ethyl acetate was evaporated *in vacuo* and the residue was recrystallized from methanol. A second fraction, mp 191–194°, was obtained, total yield 24%. A sample was recrystallized once more from methanol. The melting point was then 195–197°, $[\alpha]^{25}D$ +16.5° (*c* 2, glacial acetic acid).

Anal. Calcd for $C_{22}H_{25}N_3O_6$: C, 61.81; H, 5.90; N, 9.83. Found: C, 61.75; H, 6.14; N, 9.66.

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The Diazapentalene System. IV. The Parent Pyrazolo[1,2-*a*]pyrazole and Derivatives[1]

T. W. G. Solomons and Charles F. Voigt[5]

Contribution from the Department of Chemistry, University of South Florida, Tampa, Florida. *Received January 22, 1966*

Abstract: Proton magnetic resonance evidence is presented for the preparation of pyrazolo[1,2-*a*]pyrazole and its 2-bromo, 1-phenyl, and 2-*p*-chlorophenyl derivatives. These molecules are all very easily oxidized and this property is correlated with the Hückel molecular orbital prediction of an orbital lying at or near the nonbonding level. Hydropicrates of all of these molecules have been prepared and were found to be stable.

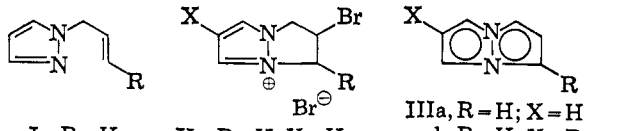
In earlier publications[2,3] we postulated that the pentalene system[6] with nitrogen atoms at the bridgehead positions, *i.e.*, structure IIIa,[8] would be aromatic. This prediction was based on Hückel molecular orbital (HMO) calculations,[9] as well as on steric and electronic similarities between I and the pentalene dianion.[7] The

(1) For parts I, II, and III, see ref 2–4, respectively.
(2) T. W. G. Solomons and F. W. Fowler, *Chem. Ind.* (London), 1462 (1963).
(3) T. W. G. Solomons, F. W. Fowler, and J. Calderazzo, *J. Am. Chem. Soc.*, 87, 528 (1965).
(4) T. W. G. Solomons and C. F. Voigt, *ibid.*, 87, 5256 (1965).
(5) American Chemical Society Petroleum Research Fund Scholar, 1964–1965. National Science Foundation Undergraduate Research Participant, 1965.
(6) For a review see the chapters by E. D. Bergmann and D. Craig in "Non-Benzenoid Aromatic Compounds," D. Ginsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, and ref 7.
(7) (a) T. J. Katz and M. Rosenberger, *J. Am. Chem. Soc.*, 84, 865 (1962); (b) T. J. Katz, M. Rosenberger, and R. K. O'Hara, *ibid.*, 86, 249 (1964); (c) a dibenztetraazapentalene has also been described: R. A. Carboni and J. E. Castle, *ibid.*, 84, 2453 (1962).
(8) Pyrazolo[1,2-*a*]pyrazole.
(9) E. Hückel, *Z. Physik*, 70, 204 (1933).

HMO calculations predicted an aromatic system for IIIa with two electrons in a nonbonding orbital, and thus one which should be very susceptible to oxidation. This prediction was partially borne out by our earlier findings[3] that pyrazolo[1,2-*a*]pyrazole derivatives having an electron-withdrawing benzoyl group at the 1 position were stable in air, but, when the benzoyl group was removed, an unstable molecule resulted.[10]

Recently, we[4] and others[11] have published communications describing the synthesis of the parent molecule and other derivatives not stabilized by electron-withdrawing groups. These results demonstrated that the HMO prediction of an aromatic system was correct. They also indicated that the highest occupied molecular orbital is very near the nonbonding level in that these molecules were very easily oxidized. We now record the details of our synthetic work and our preliminary findings as to the properties of this new aromatic system.

1-Allylpyrazole[12] (Ia) was dissolved in 48% hydrobromic acid and treated with bromine. The dibromo compound that formed underwent cyclization in boiling acetone to give IIa in 85% over-all yield. When a similar bromination was carried out using chloroform as the solvent the major product isolated after cyclization was the dibromobromide IIb. 1-Cinnamylpyrazole (Ic) reacted with bromine in chloroform to yield the salt IIc directly.



Ia, R = H; c, R = C_6H_5

IIa, R = H; X = H; b, R = H; X = Br; c, R = C_6H_5; X = H

IIIa, R = H; X = H; b, R = H; X = Br; c, R = C_6H_5; X = H

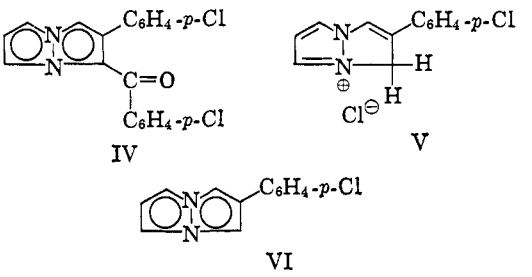
The pmr spectra of the salts IIa, b, and c, showed that the structures were correctly assigned. The protons of the pyrazolium ring absorbed at low field strength (*i.e.*, in IIa a doublet at τ 1.33 and a triplet at 2.98 with area ratio of 2:1). The aliphatic protons, as would be expected, appeared at higher fields.

Conversion of the salts II to the corresponding pyrazolo[1,2-*a*]pyrazoles by dehydrobromination was possible with several base–solvent combinations. For purposes of pmr studies, lithium hydride in deuteriodimethyl sulfoxide proved to be best. When the salt IIa was treated with lithium hydride and deuteriodimethyl sulfoxide in a nitrogen atmosphere, the pmr spectrum showed the characteristic A_2X pattern expected for the 4,8-diazapentalene (IIIa). The spectrum consisted of a doublet at τ 2.95 and a triplet at 3.52 with J = 2.5 cps. The ratio of intensities was 2:1.[13] The aliphatic protons of IIa disappeared and the only other peaks present were assigned to LiOH[14] and the solvent. It was helpful to note the shift in positions of the A_2X protons of the pyrazolium ring in IIa as it was transformed to IIIa. The 1 and 3 protons of the pyrazolium ring were shifted upfield by 96 cps, while the 2 proton is shifted upfield by only 32 cps. This is consistent with the change from a ring bearing a positive charge (IIa) to a neutral ring (IIIa) in which resonance structures place a negative charge on the 1 and 3 positions.

2-Bromopyrazolo[1,2-*a*]pyrazole (IIIb) and 1-phenylpyrazolo[1,2-*a*]pyrazole (IIIc) were produced by similar dehydrobrominations in deuteriodimethyl sulfoxide. The spectrum of IIIb was essentially first order with a singlet at τ 2.71, a doublet (J = 2.5 cps) at 2.81, and a triplet (J = 2.5 cps) at 3.47. The ratio of intensities was 2:2:1. The pmr spectrum of the phenyl derivative IIIc was more complicated and consisted of multiplet in the region τ 2.33–3.36.

Crystalline hydropicrate derivatives were prepared from dimethylformamide solutions of the pyrazolo[1,2-*a*]pyrazoles. These picrates were stable and gave correct analytical data.

A 2-(*p*-chlorophenyl)pyrazolo[1,2-*a*]pyrazole has been prepared by a somewhat different route. 1-(*p*-Chlorobenzoyl-2-(*p*-chlorophenyl)pyrazolo[1,2-*a*]pyrazole[3] (IV) was debenzoylated by the action of boiling hydrochloric acid. The hydrochloride V which was produced yielded a free base which on pmr analysis had only aromatic protons.



IV

V

VI

All of the pyrazolo[1,2-*a*]pyrazole derivatives (IIIa–c and VI) were oxidized instantly by exposure to only traces of air.

The oxidation appears to proceed through two stages. The pale yellow solution first produced first became green and then deep red-orange. Similar color changes occurred when solutions of IIIa were treated with hydrogen peroxide and chloranil. The structures of these oxidation products are now under investigation.[15] Not surprisingly, acidic solutions of IIIa are quite stable to air and are nearly colorless.

Because of the extreme ease with which the pyrazolo[1,2-*a*]pyrazole derivatives are oxidized, visible ultraviolet spectra have been difficult to obtain accurately. Spectra for molecules IIIa and IIIc were reported earlier[4] to have absorption bands in the visible region. It now appears that the band was due to oxidation products due to dissolved oxygen in the solvent. In runs where the solvent was deoxygenated the bands in the visible region were very weak but when the solutions were exposed to air the visible absorption gradually became more intense. In deoxygenated ethanol, ultraviolet absorption peaks were found at 284 mμ for IIIa, at 300 mμ for IIIb, at 244 mμ for IIIc, and at 280 mμ for VI.

(10) It is presumed that an electron-withdrawing group at the 1 position will lower the energy of the highest occupied orbital to a bonding level.

(11) S. Trofimenko, *J. Am. Chem. Soc.*, 87, 4393 (1965).

(12) I. L. Finar and K. Utting, *J. Chem. Soc.*, 5272 (1960).

(13) The diazapentalene absorbs at lower field strength than the pentalene dianion and the relative positions of the doublet and triplet are reversed.[9a,b]

(14) The salt IIa was hydrated.

(15) It may be that the process is from pyrazolo[1,2-*a*]pyrazole → cation radical → dication, or that the colors are due to reaction of the cation radical or dication with the base that is present.

Experimental Section[16]

1-Cinnamylpyrazole (Ic). Pyrazole (8.67 g, 0.128 mole) was added in one lot to a solution of potassium hydroxide (7.15 g, 0.128 mole) in 50 ml of ethanol. The resulting solution was then treated dropwise over a period of 0.5 hr with a solution of cinnamyl bromide (25.0 g, 0.128 mole) in 50 ml of ethanol. During the addition the temperature rose to 55° and potassium bromide began to precipitate. Stirring was continued at room temperature for 24 hr, after which the inorganic salt was separated and the filtrate was concentrated on a rotary evaporator. Distillation of the residual liquid through an 8-in. Vigreux column gave 12.5 g (53%) of a colorless liquid, bp 148–150° (0.75 mm).

The analytical sample was prepared by redistillation through an 18-in. spinning-band column, bp 101° (0.025 mm).

Anal. Calcd for $C_{12}H_{12}N_2$: C, 78.10; H, 6.56; N, 15.19. Found: C, 77.96; H, 6.68; N, 15.33.

2-Bromo-2,3-dihydro-1H-pyrazolo[1,2-*a*]pyrazolium Bromide (IIa). Allylpyrazole[12] (3.24 g, 0.030 mole) was added slowly to 10 ml of 48% hydrobromic acid. The solution was stirred and the temperature was maintained at −10° while bromine (4.80 g, 0.030 mole) was added dropwise. Stirring was continued for 1 hr after which the solution was diluted with 25 ml of water and made basic by the addition of potassium carbonate. This basic solution was extracted with chloroform (four 10-ml portions), and the combined extracts were dried over magnesium sulfate and evaporated on a rotary evaporator to leave a colorless oil. This oil was dissolved in 50 ml of dry acetone and heated under reflux with stirring for 66 hr. The mixture was cooled and the colorless solid which separated was collected. The yield after drying *in vacuo* was 6.24 g (78%), mp 157.5–159°. The pmr spectrum showed the following peaks: τ 1.33 (d), 2.98 (t), 4.38 (m), and 4.96 (m), ratio 2:1:1:4.

Anal. Calcd for $C_6H_8N_2Br_2$: C, 26.89; H, 3.01; N, 10.45. Found: C, 27.05; H, 3.16; N, 10.36.

The tetraphenylborate was prepared in methanol by the addition of excess sodium tetraphenylborate. The analytical sample was a colorless powder, mp 190–190.5°.

Anal. Calcd for $C_{30}H_{28}N_2BBr$: C, 71.03; H, 5.56; N, 5.52. Found: C, 71.05; H, 5.62; N, 5.40.

2,6-Dibromo-2,3-dihydro-1H-pyrazolo[1,2-*a*]pyrazolium Bromide (IIb). A solution of allylpyrazole (5.00 g, 0.0463 mole) in 35 ml of chloroform was cooled in a Dry Ice–acetone bath and stirred while a solution of bromine (7.41 g, 0.0463 mole) in chloroform was added[17] dropwise over a period of 1 hr. Stirring was continued for 1 additional hr, after which the chloroform was evaporated to leave an orange liquid. This liquid was dissolved in 40 ml of dry acetone and the resulting solution was heated under reflux for 4 days. The colorless solid which precipitated was collected and after drying *in vacuo* weighed 2.76 g (34%), melting point (slow decomposition) beginning at 230°. The pmr spectrum showed the following peaks: τ 1.37 (s), 4.45 (m), and 4.82 (m), ratio 2:1:4.

The analytical sample was prepared from methanol–ethyl acetate as a colorless powder with similar melting behavior.

Anal. Calcd for $C_6H_7N_2Br_3$: C, 20.78; H, 2.03; N, 8.08. Found: C, 20.64; H, 2.16; N, 7.96.

1H-2-(*p*-Chlorophenyl)pyrazolo[1,2-*a*]pyrazolium Chloride (V). One gram of 1-(*p*-chlorobenzoyl-2-(*p*-chlorophenyl)pyrazolo[1,2-*a*]pyrazole (IV)[8] wad added to 25 ml of concentrated hydrochloric acid. The mixture which resulted was heated under reflux with stirring for 24 hr during which time a colorless solid[18] sublimed into the condensor. The reaction mixture was cooled, and a dark, insoluble material was separated by filtration. The filtrate was diluted with 25 ml of water and cooled to yield 0.601 g of pale yellow needles, mp 172–172.5°. The analytical sample was not recrystallized but was dried *in vacuo* at 55°.

The pmr spectrum showed the following peaks: τ 1.42, 1.62, 2.00, 2.57, 2.97 (*t*), and 4.46 (m), ratio 1:1:1:4:1:2.

Anal. Calcd for $C_{12}H_{10}Cl_2N_2 \cdot {}^5/_3\ H_2O$: C, 50.90; H, 4.74; N, 9.90; Cl, 25.04. Found: C, 50.85; H, 4.68; N, 9.83; Cl, 24.91.

A picrate was prepared from ethanol as a yellow powder, mp 188.5–191°.

Anal. Calcd for $C_{18}H_{12}ClN_5O_7$: C, 48.49; H, 2.72; N, 15.71. Found: C, 48.28; H, 2.68; N, 15.56.

Preparation of Solutions of Pyrazolo[1,2-*a*]pyrazoles IIIa–c and VI for Pmr Analysis. One hundred milligrams of each of the salts IIa–c and V was dissolved in 0.5 ml of deuteriodimethyl sulfoxide and transferred to a nitrogen-swept pmr tube containing excess lithium hydride. The tube was stoppered loosely, the reaction was allowed to proceed until hydrogen evolution had subsided (about 15 min), and the spectrum was determined.

Pyrazolo[1,2-*a*]pyrazole Hydropicrate. An excess of lithium hydride was added to 5 ml of dimethylformamide under a nitrogen atmosphere in a reaction flask equipped for filtration in an inert atmosphere. The salt IIa (0.500 g) was added and the solution was stirred for 15 min. Anhydrous ether (50 ml) was added to precipitate the inorganic salts. The solution was filtered into 50 ml of a saturated solution of picric acid in ethanol. On cooling, this solution deposited 0.322 g (48%) of a yellow solid, mp 140–141° dec.

Anal. Calcd for $C_{12}H_9N_5O_7$: C, 42.99; H, 2.71; N, 20.89. Found: C, 42.76; H, 2.70; N, 20.66.

2-Bromopyrazolo[1,2-*a*]pyrazole hydropicrate was prepared in 44% yield by the same method as an orange solid, mp 155.5–56° dec.

Anal. Calcd for $C_{12}H_7N_5O_7$: C, 34.80; H, 1.95; N, 16.91. Found: C, 35.18; H, 2.29; N, 16.66.

1-Phenylpyrazolo[1,2-*a*]pyrazole hydropicrate was obtained in the same way, yield 12%, mp 115–116°.

Anal. Calcd for $C_{18}H_{12}N_5O_7$: C, 52.56; H, 3.19; N, 17.03. Found: C, 52.85; H, 3.42; N, 17.05.

Acknowledgment. The authors are grateful to the donors of the Petroleum Research Fund administered by the American Chemical Society and to the National Science Foundation for support of this research.

(16) Analyses were by Galbraith Laboratories, Knoxville, Tenn. Melting points were taken with a Mel-Temp block and are not corrected. Proton magnetic resonance spectra were determined with a Varian A-60 spectrometer and visible–ultraviolet spectra were measured with a Perkin-Elmer Model 202 spectrophotomer.

(17) This experiment was carried out with the intention of preparing IIa which accounts for the use of only 1 equiv of bromine and the low yield.

(18) Identified by its mixture melting point as *p*-chlorobenzoic acid.