Polycondensed Nitrogen Heterocycles. VI. Pyrrolo[3,4-*b*]-1,4-thiazine. A New Heterocyclic Ring System.

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This paper describes the synthesis of a new ring system, pyrrolo[3,4-*b*]-1,4-thiazine, obtained *via* II → III → IV.

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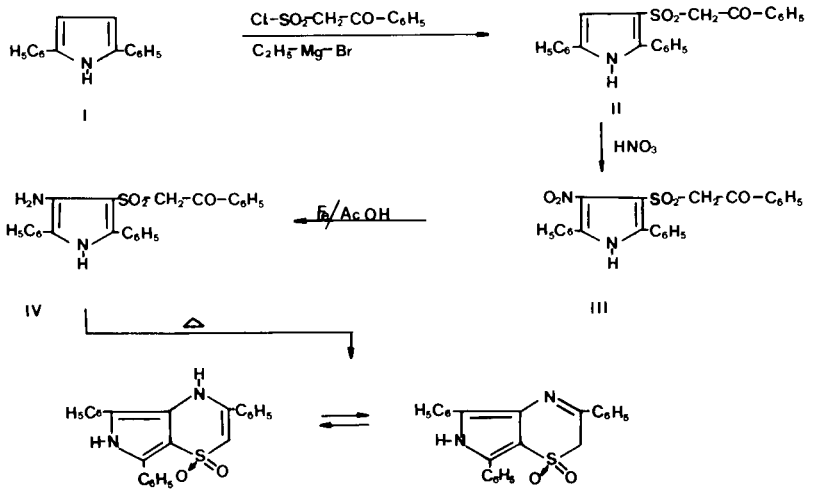
In a continuing investigation of the synthesis of polycondensed nitrogen heterocycles (I) we recently had occasion to use phenacylsulfonyl chloride. This versitile intermediate in organic syntheses, is useful in the preparation of nitrogen and sulfur-containing heterocycles. This paper describes a new heterocycle, pyrrolo[3,4-*b*]-1,4-thiazine (V). obtained *via* II → III → IV. (See Scheme). The first step in this sequence, the formation of the organometallic derivative of diphenylpyrrole (I) and its subsequent reaction with phenacylsulfonyl chloride, was in practice, the most difficult to effect in good yield. The more convenient route was the Grignard reaction of 2,5-diphenylpyrrole (I) with ethyl bromide and subsequent reaction of phenacylsulfonyl chloride at low temperature. The action of a mixture of acetic anydride and nitric acid on II afforded compound III, which was reduced with several reducing agents all producing brown oils not readily purified. When reduction was carried out with iron and acetic acid it was possible to obtain an isolable product (IV) which could be separated by column chromatography. The ir spectrum of IV displayed three weak absorption bands at 3580, 3510 and 3230 cm^{-1} (NH_2 and NH) and was in agreement with an amino derivative (IV) but the analytical data indicated a high value for carbon. Indeed, attempts to crystallize the chromatographed product led to partial cyclization of IV into V. In fact, simple refluxing of IV in acetic acid or in ethylene glycol afforded a product as yellow needles, which by gc-mass spectroscopy, nmr, ir and analytical data is considered to be pyrrolo[3,4-*b*]-1,4-thiazine. The gc-mass spectrum exhibited a single peak with M^+ = 398. The nmr spectrum was in agreement with the two tautomeric structures Va and Vb in equilibrium in DMSO solution since it showed two singlets at 4.85 δ and 5.82 δ attributable to the thiazine CH_2 and CH protons (Vb and Va). Furthermore, two broad signals at 9.70 δ and



12.15 δ for the thiazine and pyrrole NH hydrogen atoms, respectively and a multiplet (7.20-8.30 δ) for the aromatic protons were observed.

EXPERIMENTAL

All melting points are uncorrected; the spectral data were obtained as follows: ir: (nujol mull), Perkin-Elmer Infracord 137 spectrophotometer; nmr: Jeol C-60 spectrometer (TMS as the internal reference). A 270 Perkin-Elmer gc-mass spectrometer was employed for determination of the low resolution 70 eV gc-mass spectra.

2,5-Diphenyl-3-phenacylsulfonylpyrrole (II).

To a stirred mixture of 2,5-diphenylpyrrole (40 mmoles), absolute ether (150 ml.) and magnesium (40 mmoles), an ethereal solution of ethyl bromide (40 mmoles) was added dropwise, cooling with ice bath as evolution of ethane began. The yellow mixture was then refluxed for 1 hour and after cooling at 0°, phenacylsulfonyl chloride (2) (40 mmoles) in absolute ether (300 ml.) was added dropwise with stirring. After standing at room temperature overnight, the solution was filtered and the filtrate washed with aqueous saturated sodium carbonate (3 x 150 ml.) followed by an equal volume of water. The organic solution was dried (sodium sulfate), the ether was removed (rotor evaporator) and the residue was recrystallized from benzene (yield 7%), m.p. 191°; ir cm^{-1}: 3300 (NH) 1670 (CO); nmr (DMSO-d_6) δ: 4.88 (2H, s, CH_2) 6.98 (1H, d, CH, J = 1.5 Hz) 7.20-8.00 (15H, m, 3 x C_6H_5) 12.16 (1H, d, NH, J = 1.5 Hz).

Anal. Calcd. for $C_{24}H_{19}NO_3S$: C, 71.81; H, 4.77; N, 3.49. Found: C, 71.70; H, 4.92; N, 3.60.

2,5-Diphenyl-3-phenacylsulfonyl-4-nitropyrrole (III).

A mixture of nitric acid (d = 1.52) (20 mmoles) and acetic anhydride (20 mmoles) was added dropwise with stirring to a suspension of II (20 mmoles) in nitromethane (40 ml.) at -15°. The resultant solution was allowed to warm to room temperature, neutralized with sodium bicarbonate and extracted with ether (6 x 100 ml.). The ether extracts were dried, yield 65% of III, m.p. 238° (benzene); ir cm^{-1}: 3240 (NH) 1660 (CO); nmr (perdeuterioacetone): δ: 5.36 (2H, s, CH_2) 7.20-8.28 (15H, m, 3 x C_6H_5) ~ 11.70 (broad, NH).

Anal. Calcd. for $C_{24}H_{18}N_2O_5S$: C, 64.57; H, 4.06; N, 6.28. Found: C, 64.69; H, 4.16; N, 6.16.

2,5-Diphenyl-3-phenacylsulfonyl-4-aminopyrrole (IV).

A solution of 1 g. of III in acetic acid (100 ml.) was heated at 60-70°, when iron powder (1.5 g.) was added over a period of 1 hour. After the addition was complete, the mixture was kept at 60-70° for 3 hours, then poured into crushed ice and extracted with ethyl acetate (2 x 150 ml.). The extracts were dried (sodium sulfate) and evaporated under reduced pressure to give a solid residue which was purified by column chromatography (20 x 3 cm) of silicagel (25 g.). Elution with benzene-ethyl acetate (99:1) gave 400 mg. of a product which melted at 170°; ir cm^{-1}: 3230, 3510 and 3580 (NH and NH_2) 1680 (CO).

Anal. Calcd. for $C_{24}H_{20}N_2O_3S$: C, 69.22; H, 4.84; N, 6.73. Found: C, 69.75; H, 4.96; N, 6.71.

2,5,7-Triphenylpyrrolo[3,4-*b*]-1,4-thiazine 4,4-Dioxide (V).

By refluxing IV, obtained directly by chromatography, in acetic acid for 30 minutes the bicyclic system V was obtained as a crystalline mass in quantitative yield, m.p. 230° (ethanol); ir: cm^{-1}: 3300 (broad) (NH); nmr (DMSO-d_6) δ: 4.85 (s, CH_2) 5.82 (s, CH) 7.20-8.30 (m, aromatic) ~ 9.70 (broad, NH) ~ 12.15 (broad, NH); M^+ = 398; 366, 334, 257, 248, 230, 199, 105 m/e.

Anal. Calcd. for $C_{24}H_{18}N_2O_2S$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.61; H, 4.86; N, 7.21.

REFERENCES AND NOTES

(1) For references to previous notes: E. Aiello, S. Plescia and G. Dattolo, *J. Heterocyclic Chem.*, submitted for publication.

(2) W. E. Truce and C. W. Vriesen, *J. Am. Chem. Soc.*, **75**, 2525 (1953).