## Synthesis of 5H-Thieno[2,3-c]pyrrole

## Chin-Kang Sha\* and Chiu-Peng Tsou

Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30043, Republic of China

5H-Thieno[2,3-c]pyrrole (4) was synthesized by a novel phosphineimine-alkylidenemalonate cyclization reaction.

Thienopyrrole ring systems, including the six isomeric ring structures, (1)—(6), are interesting heterocyclic compounds. They are of theoretical interest because their unique structures consist of five-membered rings with well known properties.<sup>1</sup> The synthesis of thienopyrroles has attracted much attention from organic chemists mainly because they are of pharmacological importance.<sup>2</sup> However, the existing methods for the synthesis of thienopyrroles are laborious and have a number of limitations. Among the parent compounds of these isomeric thienopyrroles only  $(1)^3$  and  $(2)^4$  have been synthesized. The rest of the parent compounds (3)—(6) have not been synthesized owing to the lack of mild synthetic methods for the preparation of these highly labile ring systems.

Herein, we report<sup>5</sup> the synthesis of 5*H*-thieno[2,3-c]pyrrole (4),<sup>6</sup> the parent compound of its ring system, by a novel phosphineimine-alkylidenemalonate cyclization reaction. Knoevenagel condensation of 3-methylthiophene-2carboxaldehyde (7) (Aldrich) with diethyl malonate gave compound (8) (98%). Bromination of compound (8) with N-bromosuccinimide-dibenzoyl peroxide afforded bromide (9) (80%). Treatment of (9) with sodium azide in aqueous ethanol at room temperature produced azido compound (10) (92%). Treatment of azido compound (10) with triphenylphosphine in tetrahydrofuran followed by hydrolysis gave a mixture of compound (14), diethyl malonate, and triphenylphosphine oxide. Upon silica gel chromatography compound (14) tautomerized into (4), which was isolated in 78% yield as colourless crystals, m.p. 68.5-69.5 °C, which turned into dark purple liquid after melting in the air. In acidic solution, (4) easily polymerized into dark polymeric material. The spectroscopic data for (4) are as follows:  ${}^{1}H n.m.r.$ : ([ ${}^{2}H_{6}$ ]acetone, 400 MHz): 8 6.908, 6.921, 6.964, and 6.978 (AB q, 2H), 6.951 (br. s, 1H), 7.055 (br. s, 1H), 10.400–11.000 (br. s, NH, 1H); <sup>13</sup>C n.m.r.: ([<sup>2</sup>H<sub>6</sub>]acetone, 100.6 MHz): δ 106.97 (d), 107.15 (d), 116.76 (d), 124.14 (s), 125.93 (d), 133.17 (s); i.r. (KBr): 3400, 3100, 3080, 1575 cm<sup>-1</sup>; u.v. (ÈtOH): λ<sub>max</sub>, 285 (ε  $7.35 \times 10^3$ ), 230 nm ( $\varepsilon 13.37 \times 10^3$ ); mass spectrum (m/z): 123  $(M^+, 100\%).$ 

This novel intramolecular reaction between phosphineimine and alkylidenemalonate could be rationalized by the mechanism proposed in Scheme 1. Staudinger reaction<sup>7</sup> of (10) with triphenylphosphine gave phosphineimine (11). Upon the addition of water, phosphineimine (11) reacted with water to give compound (12). Compounds (11) and (12) could be detected by <sup>1</sup>H n.m.r. spectroscopy. After stirring with



water for 2.5 h, compound (12) cyclized to give diethyl malonate, triphenylphosphine oxide, and product (14) presumably via intermediate (13). Product (14) tautomerized during silica gel chromatography to give the more stable tautomer, (4). As far as we know this cyclization reaction of phosphineimine and alkylidenemalonate has not been reported before. The formation of very stable triphenylphosphine oxide probably was the driving force for the elimination of diethyl malonate from the intermediate (13). In order to prove the structure of tautomer (4), compound (4) was treated with *N*-phenylmaleimide in a Diels-Alder reaction to give the *exo*adduct (15) (39%) and *endo*-adduct (16) (4%), Scheme 2.

On the other hand, a molecular orbital calculation of 5*H*-thieno[2,3-*c*]pyrrole (4) has been reported. The calculated lower singlet transition energies ( $\Delta E/eV$ : 5.17 and 4.48) of (4) are in good agreement with the experimental u.v. data ( $\Delta E/eV$ : 5.39 and 4.35;  $\lambda_{max}$ : 230 and 285 nm). However, the





experimental intensities of the u.v. bands of (4) (5.39 eV,  $\varepsilon$  13400; 4.35 eV,  $\varepsilon$  7400) are not correctly predicted by theoretical transition moments (M<sup>2</sup> 0.40 for 5.17 eV; M<sup>2</sup> 0.97 for 4.48 eV).<sup>1</sup>

In conclusion, we have prepared the parent compound (4) of the 5*H*-thieno[2,3-*c*]pyrrole ring system by the novel phosphineimine-alkylidenemalonate cyclization reaction. The applications of this novel cyclization reaction to the syntheses of other pyrrolo-heterocyclic ring systems are under investigation.

We acknowledge a grant from the National Science Council of the Republic of China.

Received, 30th September 1985; Com. 1413

## References

- 1 L. Klasinc and N. Trinajstic, Tetrahedron, 1971, 4045.
- 2 For a review of thienopyrrole synthesis: F. Garcia and C. Galvez, *Synthesis*, 1985, 143.
- 3 H. R. Snyder, L. A. Carpino, J. F. Zack, and J. F. Mills, J. Am. Chem. Soc., 1957, 79, 2566.
- 4 M. Farnier, S. Soth, and P. Fournari, C. R. Acad. Sci., Ser. C, 277, 1973, 1149.
- 5 For a related study see: C. K. Sha, K. S. Chuang, and J. J. Young, J. Chem. Soc., Chem. Commun., 1984, 1552.
- 6 D. J. Zwanenburg, J. Feijen, and H. Wynberg, *Recl. Trav. Chim. Pays-Bas*, 1967, **86**, 589; J. Feijen and H. Wynberg, *ibid.*, 1970, **89**, 639.
- 7 Yu. G. Gololobov, I. N. Zhmurova, and L. F. Kasukhin, *Tetrahedron*, 1981, 437.