4*H*-Thieno[3,4-*c*]pyrrole: Synthesis and Characterization of the Parent Ring System†

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4*H*-Thieno[3,4-*c*]pyrrole (**4**) was synthesised from the azide (**8**) by intramolecular 1,3-dipolar cycloaddition followed by acid-catalysed 1,3-dipolar cycloreversion of the dihydrotriazole intermediate (**9**); the crystal structure of one of the products formed on trapping (**4**) with *N*-phenylmaleimide has been determined.

$2\lambda^4\delta^2$-5*H*-Thieno[3,4-*c*]pyrroles, *e.g.* (**1**) and (**2**), containing a tetravalent sulphur atom have long been a subject of synthetic[1] and theoretical interest.[2] Although highly phenylated derivatives such as (**1**) and (**2**) have been prepared and well characterised,[3] the nature of the parent system (**3**), represented in resonance terms as the pyrrole form (A) containing a tetravalent sulphur atom or as the azomethine ylide form (B) having a divalent sulphur atom, remains a matter of some controversy. Herein we report the first synthesis of 4*H*-thieno[3,4-*c*]pyrrole (**4**), and direct evidence of the tautomeric equilibrium between (**4**) and $2\lambda^4\delta^2$-5*H*-thieno[3,4-*c*]pyrrole (**3**).

Knoevenagel condensation of the aldehyde (**5**)[4] with diethyl malonate gave the alkylidene malonate (**6**) (80%). Compound (**6**) was brominated with *N*-bromosuccinimide and dibenzoyl peroxide to give the bromide (**7**) (78%). Reaction of (**7**) with sodium azide in ethanol at room temperature afforded the azide (**8**) (98%). Intramolecular 1,3-dipolar cycloaddition of

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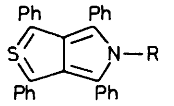
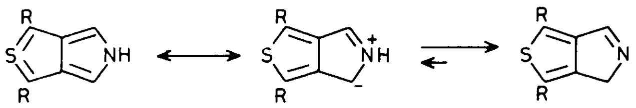
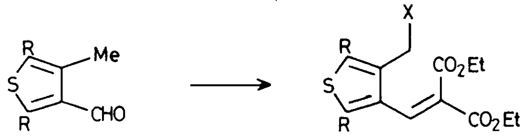


(1) R = Me
(2) R = Ph



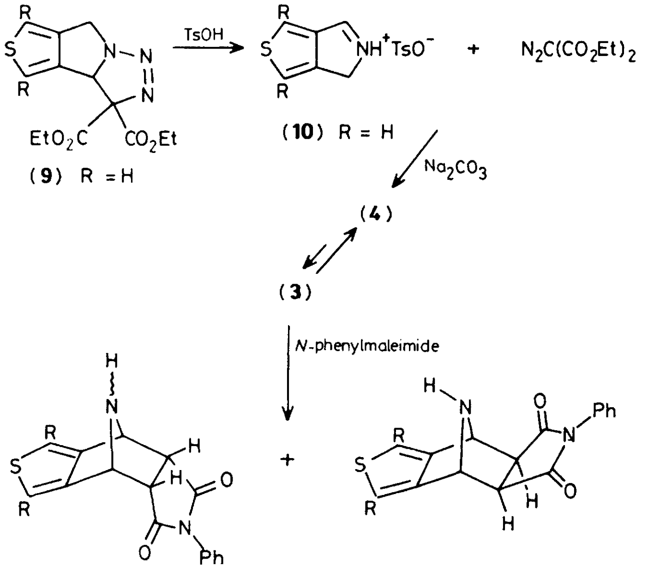
pyrrole form (A) azomethine ylide form (B)

(3) R = H (4) R = H



(5) R = H

(6) R = X = H
(7) R = H, X = Br
(8) R = H, X = N_3



(9) R = H (10) R = H (4) (3)

(12) R = H (13) R = H

In the labelled series, (3d)—(13d), R = D. Ts = p-$MeC_6H_4SO_2$.

(8) occurred on standing at room temperature for four days to give the dihydrotriazole (9) (80%, starting material was recovered). Treatment of (9) with toluene-p-sulphonic acid (1 equiv.) in dry ether gave the salt (10) (96%) *via* a 1,3-dipolar cycloreversion.[5] The salt (10) was then treated with saturated aqueous sodium carbonate; extraction with dichloromethane gave the parent compound (4) (93%) as a dark oil [^{1}H n.m.r. (400 MHz, $CDCl_3$) δ 4.54 (dd, *J* 2.7 and 1.4 Hz, 2H), 7.05 (br. s, 1H), 7.28 (d, *J* 2.2 Hz, 1H), and 8.24 (t, *J* 2.7 Hz, 1H); ^{13}C n.m.r. (100.6 MHz, $CDCl_3$) δ 58.59 (t), 113.53 (d), 114.44 (d), 149.29 (s), 151.71 (s), and 157.89 (d); *m/z* 123 (M^+, 100%); $\nu_{max.}$ ($CHCl_3$) 3010 and 1680 cm^{-1}; $\lambda_{max.}$ ($CHCl_3$) 254 (ε 7.4 × 10^3)]. Compound (4) decomposed into a dark polymeric material when kept at room temperature. Treatment of the salt (10) in dichloromethane with excess of triethylamine in the presence of *N*-phenylmaleimide gave the *endo*-adduct (12) (12%) and the *exo*-adduct (13) (38%).

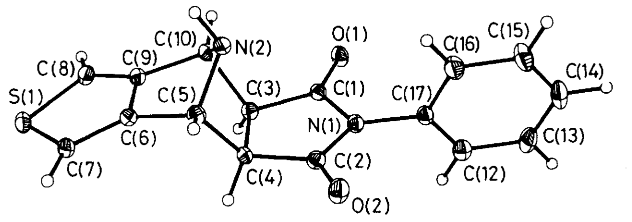


Figure 1. Molecular drawing of (13) generated by SHELXTL PLUS. Selected bond lengths (Å) and angles (°): C(3)–C(4) 1.541; C(3)–C(10) 1.556; C(4)–C(5) 1.549; N(2)–C(5) 1.492; C(2)–C(4)–C(3) 104.5; C(3)–C(4)–C(5) 103.0; C(1)–C(3)–C(10) 111.3; C(5)–N(2)–C(10) 96.2.

Alternatively, treatment of the azide (8) with triphenylphosphine followed by water[6] also afforded (4). In this case compound (4) was difficult to isolate, but once again could be trapped by reaction with *N*-phenylmaleimide to give (12) (25%) and (13) (17%). The facile cycloaddition with *N*-phenylmaleimide indicated a tautomeric equilibrium between (4) and (3), because (4) itself would not be expected to undergo cycloaddition with *N*-phenylmaleimide. The cycloaddition must have occurred *via* the tautomer (3). The site of cycloaddition, either the pyrrole or the thiophene ring, was then determined by use of the deuterium labelled (4d), which was prepared from (5d)‡ by the sequence used to synthesise (4). Reaction of (4d) with *N*-phenylmaleimide gave the cycloadducts (12d) and (13d), neither of which gave pyrrole aromatic ^{1}H n.m.r. signals. The structure of the more stable *exo*-adduct (13) was confirmed by a single crystal *X*-ray analysis,§ which clearly revealed that the cycloaddition had occurred at the pyrrole ring (Figure 1).

In conclusion, although structure (3) has received much theoretical investigation, our experiments have shown that (3) is only a highly reactive tautomer of the parent compound (4). The direct spectroscopic observation of the parent system (3) would be rather difficult under normal conditions. However, *N*-substitution on the pyrrole ring of (3) might force the formation of (3) in the pyrrole form (A) containing a

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‡ Compound (5d) was prepared by the method of Gronowitz (ref. 4), using [$^2H_1$]acetic acid and D_2O in the zinc dust reduction step.

§ *Crystal data*, (13), $C_{16}H_{12}N_2O_2S$: *M* = 328.42, monoclinic, space group $P2_1/n$, *a* = 8.792(2), *b* = 17.644(3), *c* = 9.450(2) Å, β = 110.89(2)°, *Z* = 4, D_c = 1.59 g/cm^3. 2367 Independent reflections were measured of which 1700 were considered observed [$I > 3\sigma(I)$]. The structure was solved by direct methods to an *R* value of 0.034. All calculations were performed on a MicroVax II based Nicolet SHELXTL PLUS system. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

tetravalent sulphur atom. The synthesis of *N*-substituted compounds (**3**) is being investigated.

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