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INTRAMOLECULAR NITRENE INSERTION REACTIONS INTO THIOPHENE RINGS

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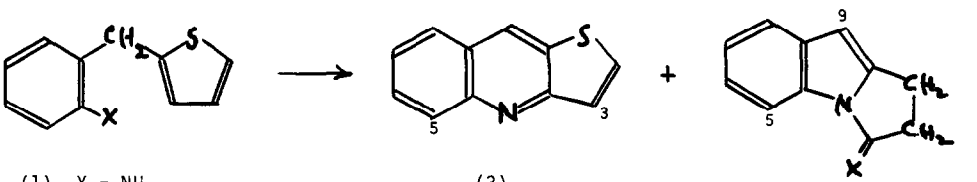
We have shown that intramolecular insertion of an intermediate nitrene occurs readily when 2-azidodiphenylmethanes are heated at 180-200° in trichlorobenzene[1-3]. We have now extended this study to the decomposition of 2-azidobenzyl heterocyclic systems; the 2-azidobenzylthiophenes have shown new decomposition routes, which are reported here.



(1) X = NH_2

(2) X = N_3

(3)

+ (1)

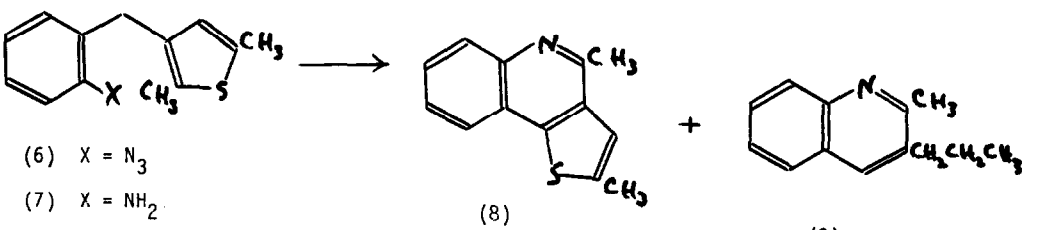
(4) X = S

(5) X = O

2-(2-Aminobenzyl)thiophene(1) was prepared from 2-(2-nitrobenzoyl)thiophene by sequential catalytic and Huang-Minlon reduction. Diazotisation and treatment with azide ion gave 2-(2-azidobenzyl)thiophene(2), which decomposed (4 hr.) in trichlorobenzene at 190°. The decomposition produced much tar; separation by a combination of acid extraction and column chromotography, followed by p.l.c., gave three major products. The first major component was thieno[3,2-b]quinoline(3), (5%) m.p. 113° [4]. Two 1H signals showed large shifts when the n.m.r. solution was treated with $Eu(fod)_3$ shift reagent. One signal

had J 7Hz (H5), and the other J 3.5Hz (H3). This evidence excludes the isomeric thieno-[2,3-b] quinoline structure; the thieno [3,2-b] quinoline(3) was synthesized unambigously by dehydrogenation of 2,3-dihydrothioeno[3,2-b]quinoline, m.p. 75-76°, and the two specimens were shown to be identical. The second decomposition product was the amine(1), identical with a synthetic specimen. The third decomposition produced was 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-thione,(4), (3%), m.p. 103°. The thione (4) showed absorption at δ2.85 (2H,t,H2), 3.35 (2H,t,H1), 6.15 (1H,s,H9), 7.1 to 7.4 (3H,m), and 8.8 p.p.m. (1H,m,H5); m/e 187(100%), 154, 130; λ_{max} (EtOH) 233, 273, and 310 nm ($\log_{10}$ ε 4.00, 4.09, 4.00). A minor component, m.p. 147-149°, was identical with a sample of 1,2-dihydro-3H-pyrrolo-[1,2-a] indol-3-one,(5), supplied by Professor R.W. Franck; since oxygen was not excluded from the work-up this probably arises by oxidation of compound (4).

3-(2-Azidobenzyl)-2,5-dimethylthiophene(6) was synthesised by a route similar to that used for compound (2). Decomposition of the azide(6) gave a much cleaner reaction mixture, yielding two major products, and a number of minor components. One of the major products (15%) was 3-(2-aminobenzyl)-2,5-dimethylthiophene(7), m.p. 55°, identical with a synthetic specimen. The second major component (34%) was 2,4-dimethylthieno [3,2-c]quinoline,(8), m.p. 71.5-72.5°. The n.m.r. spectrum showed two non-equivalent methyl signals at δ2.72 and 2.6 p.p.m. (CCl_4); the latter showed long-range coupling (J 1.5Hz) to a signal (1H) at δ6.95 p.p.m.. Addition of $Eu(fod)_3$ to the n.m.r. solution caused large downfield shifts in a doublet (1H,J7Hz) and in the coupled methyl group. The identification of a minor component as 2-methyl-3-n-propylquinoline[5], (9), (3%), narrowed the possibilities to two. The structure (8) was confirmed by synthesis; 2,3-dihydro-2,4-dimethylthieno[3,2-c]quinoline[6] was dehydrogenated using Pd/C at 310-320°.



(6) X = N_3

(7) X = NH_2

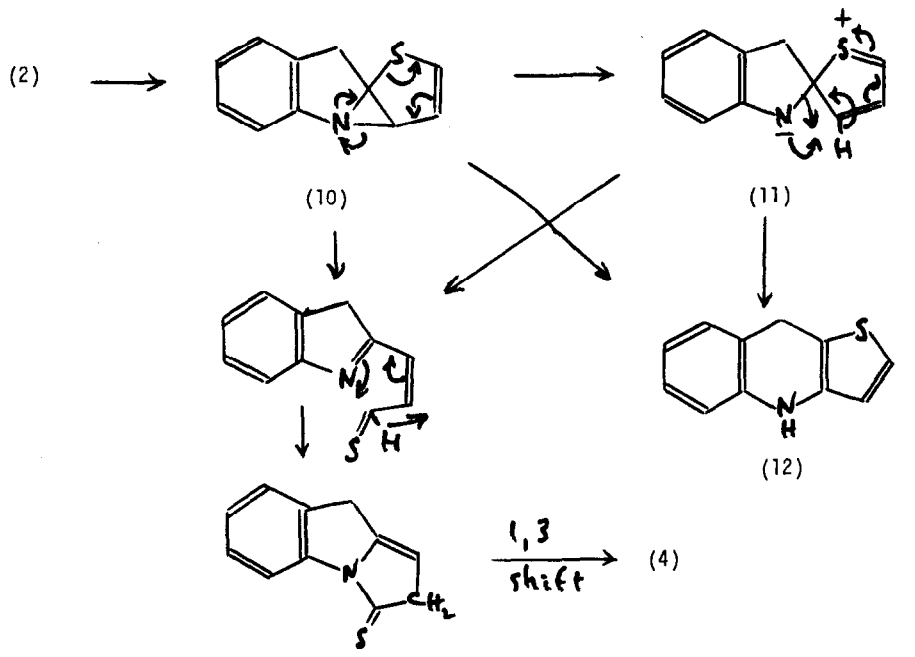
(8)

+ (7)

(9)

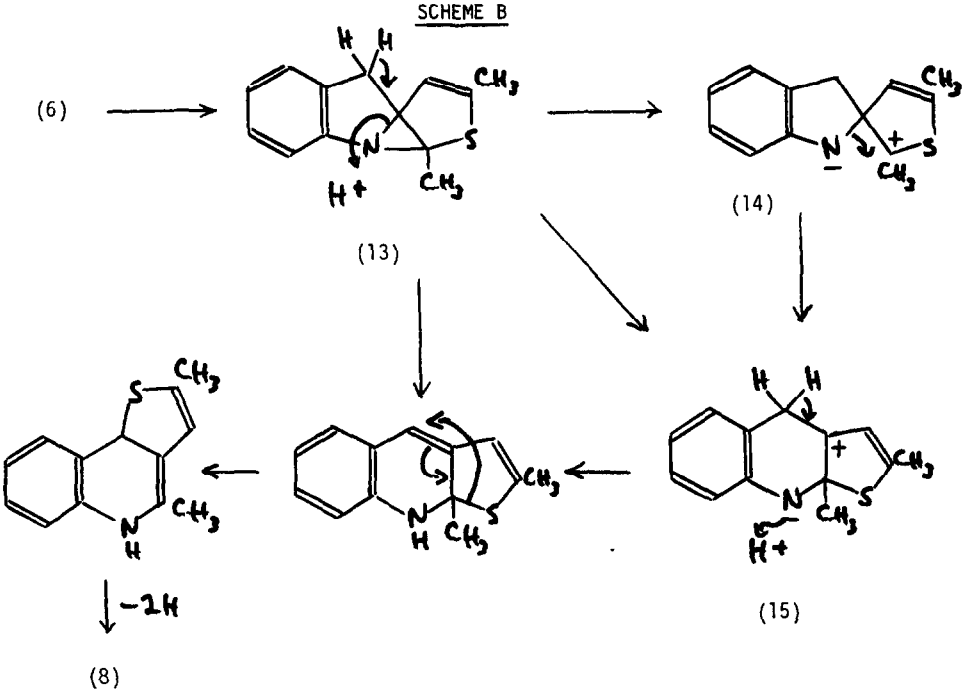
Both these reactions show interesting departures from previous nitrene insertion pathways. From the 2-substituted thiophene(2) the thieno[3,2-b]-quinoline(3) can arise either via an aziridine intermediate(10) or a spirodiene(11), in the latter case by migration of the anionic nitrogen-SCHEME A. The expected product is the dihydrothienoquinoline(12) but the presence of the amine(1) indicates the possibility of dehydrogenation by nitrene/hydrogen abstraction. The more interesting product is the pyrroloindolothione(4) which probably arises by opening of the thiophene ring with subsequent re-cyclisation. A possible route is shown in Scheme A.

SCHEME A



In the case of the 3-substituted thiophene either the aziridine(13) or the spiro compound(14) can re-arrange as shown (SCHEME B) but the sp^3 carbon between nitrogen and sulphur prevents aromatisation. Loss of a proton from intermediate(15) can be followed by a 1,3-sulphur shift to give a dihydrothienoquinoline; again the presence of a considerable amount of amine(7) indicates the mode of dehydrogenation to give compound(8).

SCHEME B



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