Pergamon

Tetrahedron Letters, Vol. 36, No. 1, pp. 83-86, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02156-2

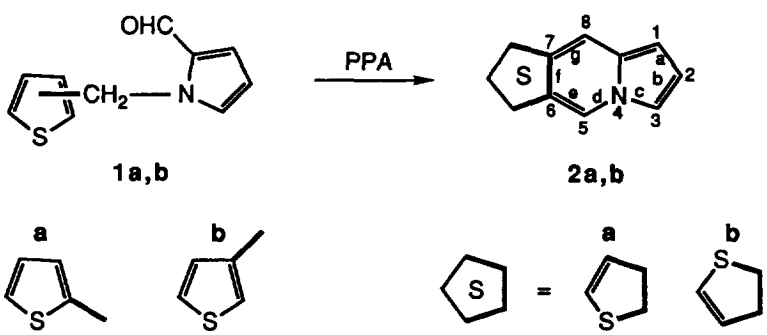
First Synthesis and Diels-Alder Reaction of Thieno[2,3(3,2)-f]Indolizines

Abdelali Daich, Philippe Ohier and Bernard Decroix*

Laboratoire de Chimie, Université Le Havre, 30 rue Gabriel Péri, 76600 Le Havre, France

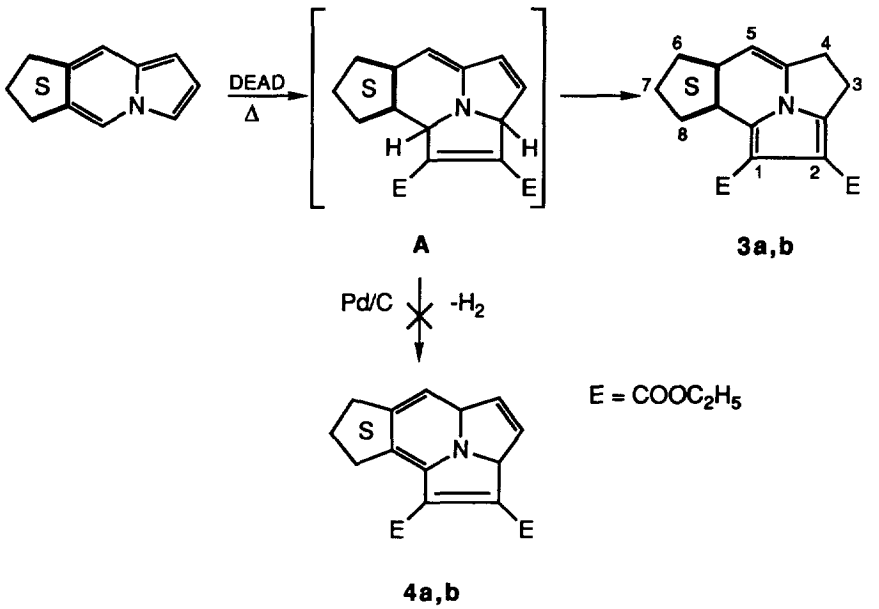
Abstract : Thieno[2,3(3,2)-f] indolizines were synthesized from 2-formyl-1-[thien-2(3)-ylmethyl]pyrrole. Under Diels-Alder reaction with diethyl acetylenedicarboxylate they led to cycl[3,2,2]azines fused to a thiophene ring.

Many approaches to indolizine nucleus synthesis are described in the literature[1-3]. Indolizines fused to an aromatic or heteroaromatic ring as thienoindolizines are theoretically interesting 14π-electron heteroaromatic systems. The thiophene ring can be fused to the indolizine on side a,b,e,f,g. Whereas the a,b,g junctions have been widely studied with either a 2,3 or 3,2 fused thiophene, the e and f junctions are at our knowledge not reported. Nevertheless, some derivatives with a saturated six membered ring are described in the literature[4-6]. Among these possibilities, ring system **2** is of special interest because it contains the somewhat unstable 2,3-dimethylenethiophene moiety[7,8].Cyclic analogues of 2,3-dimethylenethiophene have been already studied as thieno[2,3-c]furan[9-11] or benzodithiophene and derivatives[12]. In view of these results, we decided to investigate the preparation of the thieno[2,3(3,2)-f]indolizines (**2a,b**) and their Diels-Alder reaction.



Our strategy consisted of using the ready available 2-formyl-1[thien-2(3)-ylmethyl]pyrrole **1a,b**, previously reported by us[5], as starting materials. Actually, Castle synthesized polycyclic aromatic hydrocarbons having at least one fused thiophene ring from arylaldehydes[13] or arylacetaldehydes[14].

Thus, the aldehydes **1a,b** treated with polyphosphoric acid at 100°C led respectively to thieno[2,3-f]indolizine (**2a**) (69 %) and thieno[3,2-f]indolizine (**2b**) (65 %). They are yellow-green crystalline solids which exhibit the expected spectroscopic properties[15]. The chemical shifts and coupling constants are in agreement with those reported as well as for indolizine[16] than 2,3-dimethylenethiophene[17]. As already observed with 1,2,6,7-dibenzopyrrocoline[18], compounds **2a,b** are so sensitive to oxygen that satisfactory analyses could be obtained only difficultly.



Several indolizines[19-21] are known to undergo[8+2]π cycloadditions with electron-deficient alkynes to afford [3,2,2]cyclazines. Thus, when heated with diethyl acetylenedicarboxylate (DEAD) in toluene, compounds **2a,b** gave the preferential 3,5 adduct **A** which immediately tautomerize into the tetracyclic compounds **3a,b** in good yields (63 %, 53 % respectively). The structures of **3a,b** were supported by their spectroscopic data [22]. Whatever the conditions, in the presence or the absence of a dehydrogenation catalyst (5 % palladium on charcoal), the only products isolated were the hydrogenated compounds **3a,b**. The possible dehydrogenated compounds **4a,b** were not identified. It seem that the dimethylenethiophene moiety was not stable enought to facilitate the dehydrogenation of the intermediate **A**. In constrast, the good conjugation of **A** in the thiophene ring promote the tautomerization leading to the hydrogenated compound **3a,b**.

In summary, we reported the first and efficient synthesis and the Diels-Alder reaction of the thieno[f]indolizine ring system. Since the 5,8 adduct was not observed, this result confirmed the 3,5 regiospecificity of the addition. So, we intend to investigate the Diels-Alder reaction on 3-substituted (or not) indolizines [6,7] annelated to a thiophene ring or other heterocycles.

REFERENCES AND NOTES :

1. Borrows, E. T.; Holland, D. O. *Chem. Rev.* **1948**, *42*, 638-643.
2. Mosby, W.L. *in Chemistry of Heterocyclic Compounds*, part 1, Weissberger, A. Ed, Interscience Publishers, New York, **1961**, p 325.
3. Uchida, T.; Matsumoto, K. *Synthesis* **1976**, 209-236.
4. Maffrand, J. P. *Heterocycles* **1981**, *16*, 35-37.
5. Decroix, B.; Morel, J. *J. Heterocycl .Chem.* **1991**, *28*, 81-87.
6. Verboom, W.; Verboom, C.; Eissink, I. M.; Lammerink, B. H. M.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas*, **1990**, *109*, 481-488.
7. Jackson, P. M.; Moody, C. J. ; Shah, P. *J. Chem. Soc. Perkin Trans 1*, **1990**, 2909-2918.
8. Van Den Berg, K. J.; Van Leusen, A. M. *Recl. Trav. Chim.* Pays-Bas, **1993**, *112*, 7-14.
9. Friedrichsen, W.; Schoening, A. *Heterocycles*, **1986**, *24*, 307-308.
10. Schoening, A.; Friedrichsen, W. *Tetrahedron Letters* **1988**, *29*, 1137-1140.
11. Schoening, A.; Friedrichsen, W. *Liebigs Ann. Chem.* **1989**, 405-409.
12. Bradsher, C. K. *Chem. Rev.*, **1987**, *87*, 1277-1297.
13. Tedjamulia, M. L.; Tominaga, Y.; Castle, R. N. *J. Heterocycl. Chem.* **1983**, *20*, 861-866.
14. Thompson, R.D.; Iwao, M.; Lee, M. L.; Castle, R. M. *J. Heterocycl. Chem.* **1981**, *18*, 981-984.
15. **2a** : mp 172-3°C ; ^{1}H NMR ($CDCl_3$) : 6.37 (dd, J = 1.2, 3.5 Hz, 1H, H_1), 6.85 (d, J = 6.6 Hz, 1H, H_8), 6.89 (dd, J = 2.2, 3.5 Hz, 1H,H_2), 7.02 (d, J = 6.6 Hz, 1H, H_7), 7.36-7.40 (m, 1H, H_3), 7.66 (s, 1H, H_9), 8.38 (s, 1H, H_5) ; ^{13}C NMR ($CDCl_3$): 95.3 (C_1), 110.4 (C_3), 110.6 (C_2), 115.1 (C_6), 119.1 (C_9), 120 (C_7), 126.8 (C_8), 128.0 (C_{8a}), 130.4 (C_{5a}), 132.5 (C_{9a}) ; Analyse : $C_{10}H_7NS$, calcd% : C = 69.33, H = 4.07, N = 8.09, found : C = 68.89, H = 3.68, N = 7.81.

   2b : mp 134-5°C ; ^{1}H NMR ($CDCl_3$) : 6.41 (dd, J = 1.1, 4.0 Hz, 1H, H_1), 6.90 (d, J = 5.6 Hz, 1H, H_6), 6.93 (dd, J = 2.6, 4.0 Hz, 1H, H_2), 7.07 (d, J = 5.6 Hz, 1H, H_7), 7.43-7.45 (m, 1H, H3), 7,72 (s, 1H, H_9), 8.45 (s, 1H, H_5) ; ^{13}C NMR ($CDCl_3$) : 95.4 (C_1), 110.5 (C_3), 110.7 (C_2), 115,2 (C_9), 119.2 (C_5), 120.0 (C_7), 126.9 (C_6), 128.1 (C_{5a}), 130.5 (C_{8a}), 132.5 (C_{9a}) ; Analyse : $C_{10}H_7NS$, calcd% : C = 69.33, H = 4.07, N = 8.09, found : C = 68.93, H = 3.81, N = 7.79.
16. Matsumoto, K.; Uchida, T.; Ikemi, Y.; Tanaka, T.; Asahi, M.; Kato, T.; Konishi, H. *Bull. Chem. Soc. Jpn*, **1987**, *60*, 3645-3653.
17. Ahmed, M.; Ashby, J.; Ayad, M.; Meth-Cohn, O. *J. Chem. Soc. Perkin I*, **1973**, 1099-1103.
18. Godfrey, J. C. *J. Org. Chem.* **1959**, *24*, 581.
19. Acheson, R. M. *Advances in Heterocyclic Chemistry, vol I, Academic Press*, New York and London, **1963**, p 125.
20. Matsumoto, K.; Uchida, T.; Aoyama, K.; Nishikawa, M.; Kuroda, T.; Okamoto, T. *J. Heterocyclic Chem.* **1988**, *25*, 1793-1801.
21. Matsumoto, K.; Uchida, T.; Yoshida, H.; Toda, M.; Kakehi, A. *J. Chem. Soc. Perkin Trans I, 1992*, 2437-2441.
22. **3a** : mp 151-2°C (ether-ligroine) ; IR : 1715, 1680 (CO) ; ^{1}H ($CDCl_3$) : 1.28 (t, J = 7.1 Hz, 3H, CH_3), 1.37 (t, J = 7.1 Hz, 3H, CH_3), 3.57-3.63 (m, 2H, H_4), 4.11-4.20 (m, 2H, H_3), 4.21 (q, J = 7,1 Hz, 2H, CH_2), 4.35 (q, J = 7.1 Hz, 2H, CH_2), 5.53-5.62 (m, 1H, H_5), 7.12 (d, J = 5.3 Hz, 1H, H6), 7,58 (d, J = 5.3 Hz, 1H, H_7) ; ^{13}C NMR ($CDCl_3$) : 12.3 (CH_3), 12.5 (CH_3), 22.5 (CH_3), 32.2 (CH_2), 57,9

(C_3), 58.9 (C_4), 107.3 (C_{2a}), 109.5 (C_5), 109.9 (C_2), 119.7 (C_1), 122,3 (C_7), 122,7 (C_6), 124.7 (C_{8a}), 129.9 (C_{5a}), 130.3 (C_{4a}), 137.3 (C_{8b}), 161.8 (CO), 163,4 (CO) ; Analyse : $C_{18}H_{17}NO_4S$, calcd% : C = 62.96, H = 4.99, N = 4.08, found : C = 62.79, H = 4.80, N = 3.91.

3b : mp 144-5°C (ether-ligroine) ; IR : 1715, 1680 (CO) ; ^1H NMR ($CDCl_3$) : 1.28 (t, J = 7.0 Hz, 3H, CH_3), 1.36 (t, J = 7.0 Hz, 3H, CH_3), 3.35-3.65 (m, 2H, H_4), 3.95-4.17 (m, 2H, H_3), 4.22 (q, J = 7.0 Hz, 2H, CH_2), 4.35 (q, J = 7.0 Hz, 2H, CH_2), 5.41-5.62 (m, 1H, H_5), 7.11 (d, J = 5.1 Hz, 1H, H_8), 7.57 (d, J = 5.1 Hz, 1H, H_7) ; ^{13}C NMR ($CDCl_3$) : 14.2 (CH_3), 14.4 (CH_3), 24.3 (CH_2), 34.1 (CH_2), 59.7 (C_4), 60.5 (C_3), 109.0 (C_{2a}), 111.3 (C_5), 111.6 (C_2), 121.5 (C_1), 124.0 (C_7), 124.4 (C_8) 124.7 (C_{6a}), 132.0 (C_{4a}), 139.1 (C_{8b}), 163.5 (CO), 165.2 (CO) ; Analyse $C_{18}H_{17}NO_4S$, calcd% : C = 62.96, H = 4.99, N = 4.08, found : C = 62.56, H = 5.00, N = 4.11.

(*Received in France* 15 *September* 1994; *accepted* 2 *November* 1994)