Tetrahedron Letters No.18, pp. 1953-1958, 1966. Pergamon Press Ltd.
Printed in Great Britain.

A NEW SYNTHESIS OF BENZO-c-THIOPHENES

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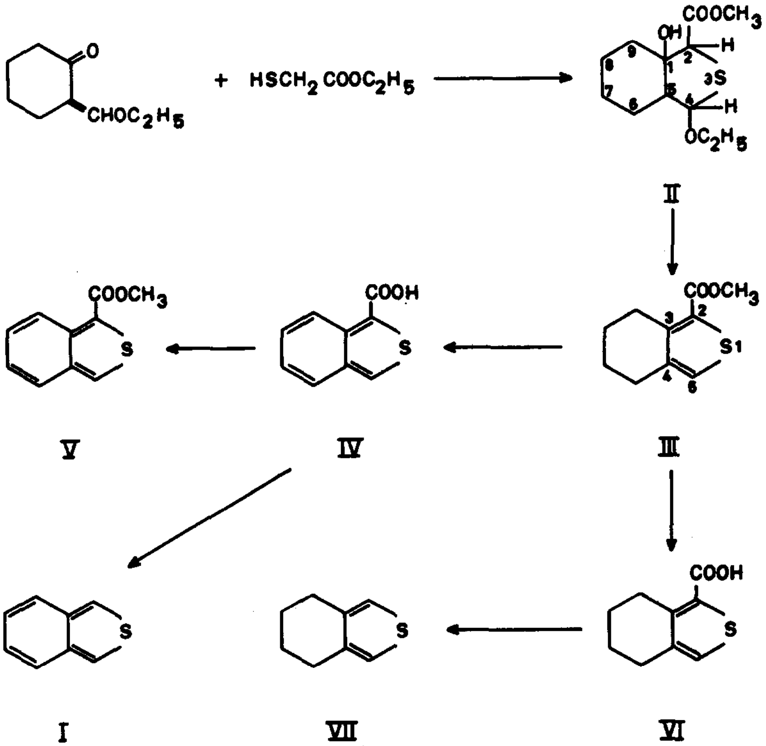
(Received 1 March 1966)

Although benzo-b-thiophene and its derivatives are well known the synthesis of benzo-c-thiophene (I) has been reported only recently[1]. Whereas the latter is unstable, several of its derivatives have been reported[2]. We wish now to report a new synthesis of (I) by an extension of the thiophene synthesis reported recently by us[3].



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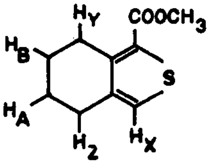
Condensation of ethyl mercaptoacetate with ethoxymethylenecyclohexanone in the presence of sodium ethoxide yielded in one step 2-carbomethoxy-4-ethoxy-1-hydroxybicyclo-(4.3.0)-3-thianonane (II), a pale yellow liquid, b.p. 110°/0.002 mm (yield, 46%). No UV absorption beyond 220 mμ; IR bands:- OH, 2.88, ester CO, 5.75μ. (Found: C, 55.6; H, 7.8; S, 12.4. $C_{12}H_{20}O_4S$ requires: C, 55.4; H, 7.8; S, 12.3%).

Dehydration of (II) with p-toluenesulfonic acid afforded 2-carbomethoxytetrahydrobenzo-c-thiophene (III) as a colourless liquid, b.p. 118°/2.5 mm (yield, 82%); UV λ_{max}^{EtOH} (log ϵ):- 263 (4.0); IR:- no OH absorption, ester CO at 5.85μ. (Found: C, 61.1; H, 6.5; S, 15.7. $C_{10}H_{12}O_2S$ requires: C, 61.2; H, 6.2; S, 16.3%).

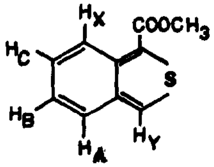
NMR spectrum of III in CCl_4:-



A singlet at 6.9 ppm indicated the single thiophene proton Hx; a sharp methyl peak at 3.775 ppm for the methyl group of the ester; a broad two proton multiplet centred at 3 ppm for Hy protons and a similar multiplet centered at 2.675 ppm for H_Z protons; the four H_A and H_B protons are given by a multiplet at 1.75 ppm.

Dehydrogenation of (III) with palladised carbon, selenium and chloranil under various conditions was unsuccessful. Finally interaction of (III) with N-bromosuccinimide followed by treatment with sodium methoxide gave 2-carboxybenzo-c-thiophene (IV), a pale brown crystalline solid, m.p. 198° (yield, 78%). UV λ_{max}^{EtOH} (log ϵ):- 237 (4.27), S 286 (3.41), 299 (3.59), 313 (3.66), 352 (3.81).

(Found: C, 59.8; H, 3.7; S, 18.3.$C_9H_6O_2S$ requires: C, 60.7; H, 3.4; S, 18.0%). Interaction of (IV) with diazomethane gave 2-carbomethoxybenzo-c-thiophene (V), a pale yellow liquid, b.p. 110°/0.01 mm. UV $\lambda_{\text{max}}^{\text{EtOH}}$ (log ϵ):- 244 (4.32), S 287 (3.51), 300 (3.71), 314 (3.82), 356 (3.88). (cf. Mayer[1] for I). (Found: C, 62.0; H, 4.4; S, 16.2. $C_{10}H_8O_2S$ requires: C, 62.5; H, 4.2; S, 16.7%).



The structure of (V) was confirmed by its NMR spectrum. The low field doublet displaying fine structure at 8 and 8.5 ppm represents Hx; the singlet single proton resonance that comes next at 7.875 ppm for H_y; the remaining three protons give a complex ABC spectrum centered at 7.3 ppm; the methyl group of the ester is shown by a single sharp peak at 3.875 ppm.

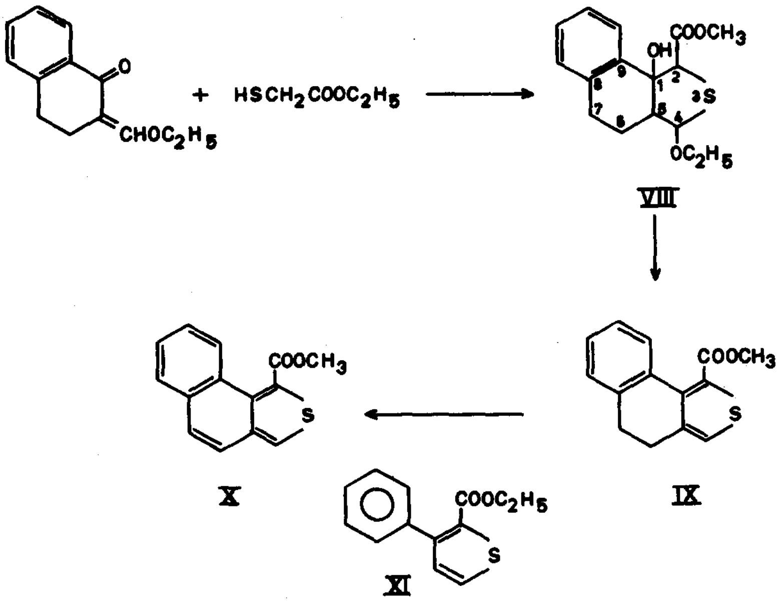
Decarboxylation of the acid (IV) by treatment with copper-quinoline at 110° for 15 minutes gave (I) as a pale yellow liquid with naphthalene like odour. The UV spectrum of the latter showed characteristic absorption bands (278, 283, 305, 333 $m\mu$) which were identical with that reported earlier by Mayer[1]. UV spectrum $\lambda_{\text{max}}^{\text{EtOH}}$ (log ϵ):- 272 (3.34), 278 (3.34), 283 (3.31), 290 (3.28), 305 (3.16), 313 (3.01), 318 (3.06), 322 (3.08), 328 (3.13), 333 (3.15), 343 (3.05), 347 (3.05). The above extinction values were lower than that cited by Mayer who has described (I) as a colourless solid, m.p. 50-51°. The product obtained above was unstable and could not be purified further.

Compound (III) was hydrolyzed by baryta when it gave 2-carboxytetrahydrobenzo-c-thiophene (VI) which crystallized from ethanol in colourless cubes, m.p. 203° (yield, 92%). (Found: C, 59.7; H, 6.0;

S, 18.0 · $C_9H_{10}O_2S$ requires: C, 59.3; H, 5.5; S, 17.6%).

The acid (VI) on decarboxylation by copper-quinoline at 110° for 30 minutes gave tetrahydrobenzo-c-thiophene (VII) as a colourless liquid, b.p. 75°/5 mm (yield, 86%). (Found: C, 69.2; H, 7.3, S, 23.2. $C_8H_{10}S$ requires: C, 69.6; H, 7.2; S, 23.2%). Compound (VII) however, could not be dehydrogenated by N-bromosuccinimide and sodium methoxide. Similarly (V) could also not be decarbomethoxylated by treatment with lithium iodide in boiling collidine (cf. Eschenmoser[4]).

Starting from polycyclic o-ethoxymethylene ketones and ethyl mercaptoacetate more complex thiophenes of the type I appear synthesizeable. Thus condensation of 2-ethoxymethylene-1-tetralone with ethyl mercaptoacetate gave 8,9-benzo-2-carbomethoxy-4-ethoxy-1-hydroxybicyclo-(4.3.0)-3-thia-8-nonene (VIII) as a colourless liquid, b.p. 80°/0.03 mm (yield, 35%). UV spectrum λ_{max}^{EtOH} ($\log\epsilon$):- 228 (4.03), S 268 (3.31); IR bands for OH, 2.90 and ester CO, 5.75μ. (Found: C, 61.9; H, 6.4; S, 10.5. $C_{16}H_{20}O_4S$ requires C, 62.3; H, 6.5; S, 10.4%).



On dehydration of (VIII) by treatment with p-toluenesulfonic acid 1-carbomethoxy-4,5-dihydro-6,7-naphtho-c-thiophene (IX) was obtained which was repeatedly distilled (ten times) and finally collected as a thick yellow coloured liquid, b.p. 90°/0.006 mm (yield, 80%). (Found: C, 68.5; H, 5.5; S, 12.5. $C_{14}H_{12}O_2S$ requires C, 68.8; H, 5.0; S, 13.1%). IR:- no OH; aromatic ester CO at 5.85μ; UV spectrum λ_{max}^{EtOH} (log ϵ):- 259 (4.00). The UV absorption was similar to that of (III) described above. The UV spectrum of compound (IX) was also compared with 2-carboethoxy-3-phenylthiophene (XI) prepared by us earlier. The latter gave the following characteristic absorption λ_{max}^{EtOH} (log ϵ):- 273 (4.55). The compound (XI) absorbed at a longer wavelength (273) as compared to (III) and (IX) (263 and 259 respectively). An atomic model of (IX) shows that the thiophene and benzene rings are noncoplanar.

Dehydrogenation of (IX) by treatment with chloranil or N-bromosuccinimide and sodium methoxide proved unsuccessful. Analysis of the treated products revealed that desulfurization had occurred. Treatment of (IX) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in benzene at reflux also lead to desulfurization. When the latter reaction was carried out in benzene solution at room temperature a product was obtained which decomposed partially on vacuum distillation. Chromatographic purification (alumina, benzene as a solvent) of the crude product gave a yellow oil (A) which probably contains 1-carbomethoxynaphtho-c-thiophene (X) as revealed by its UV absorption spectrum. The values for UV absorption spectrum for (A) and 1,3-dimethylnaphtho-c-thiophene[5] are given below: Product A λ_{max}^{EtOH} (log ϵ):- 225 (4.06), 265 (4.11), 275 (4.00), 282 (4.02), 304 (4.05), 316 (4.03). 1,3-Dimethylnaphtho-c-thiophene λ_{max}^{EtOH} (log ϵ):- 229 (4.3), 254 (4.43), 265 (4.5), 272 (4.45), S 280 (4.4), 335 (3.9), S 350 (3.75).

All liquids were distilled under vacuum in bulb tubes and the b.p. refer to the bath temperature.

Acknowledgement

This research was supported by a grant from the Petroleum Research Fund administered by American Chemical Society. Grateful acknowledgement is hereby made to the donors of the Fund. We are grateful to Dr. Madhavan Nair for a study of NMR spectra and Dr. T. S. Gore for microanalysis.

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