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STUDIES ON DOUBLE ACYLATION OF AROMATIC HYDROCARBONS. VIII. APPLICATION TO HETEROCYCLIC SYSTEMS - TOTAL SYNTHESIS OF DIBENZOTHIOPHENE

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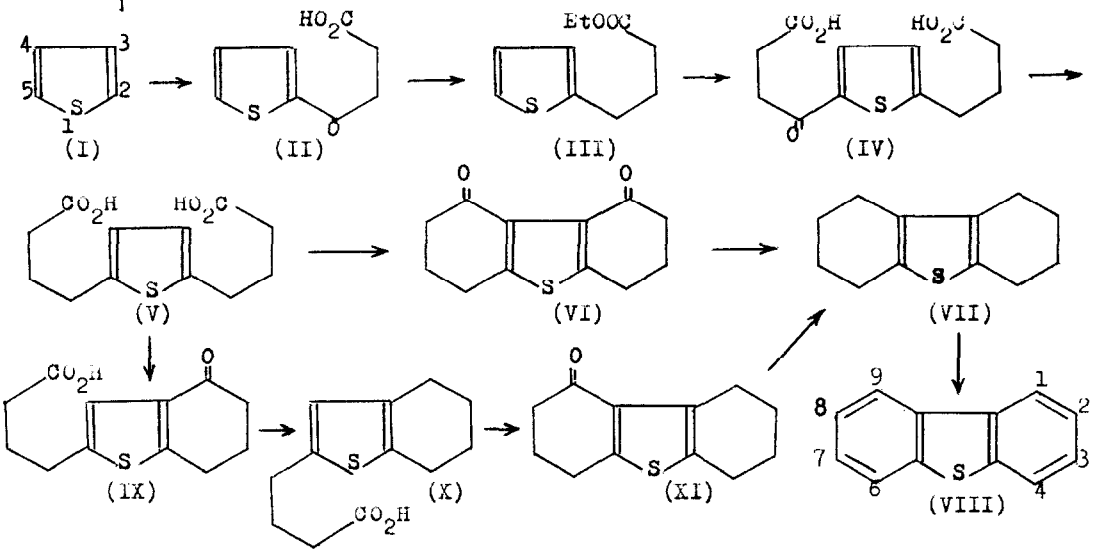
Several applications of a new general route to the total syntheses of polycyclic hydrocarbons - based on the Friedel-Crafts double acylation - in which two new benzene rings (or a benzene and a cyclopentene ring) are fused on to the acylating aromatic substrate, have been reported earlier (1). In these syntheses, the novel dibasic acid of the type Ar-$[(CH_2)_3CO_2H$ - R-CH $(CH_2)_nCO_2H]$, R=H, n=2; R=CH_3, n=1, where Ar represents the aromatic radical, constitutes the key compound.

The present communication reports the first application of the said synthesis to a heterocyclic system, in this case to thiophene (I). It was considered that acylation of (I) invariably results in α- or 2-substitution and that in 2-alkyl thiophenes (2,3), the acyl group enters the equivalent 5-position, due to the still dominant directing effect of the sulphur atom, a fact which should make possible the double succinoylation of thiophene - in two stages - leading ultimately to the synthesis of dibenzothiophene (VIII) via the key dibasic acid (V).

In effect, the ethyl ester (III) of γ-(2-thienyl)-butyric acid (4), prepared in its turn by the succinoylation of (I) and the subsequent reduction of β-(2-thenoyl)-propionic acid (4)(II) so obtained, was succinoylated (80% yield) in nitrobenzene solution, to give via the keto acid (IV), m.p. 138-38.5° (EtOH) (Found: C, 53.75; H, 5.24. $C_{12}H_{14}O_5S$ requires C, 53.38; H, 5.23), the key dibasic acid 2,5-di-(γ-carboxypropyl)-thiophene (V), m.p. 109.5-10° (C_6H_6)(Found: C, 56.43; H, 6.37; S, 12.28. $C_{12}H_{16}O_4S$ requires C, 56.30; H, 6.30; S, 12.53). The reduction of (IV) to (V) was accomplished by Huang-Minlon method in 70% yield.

A double cyclization of the dibasic acid (V), accomplished earlier in similar cases (1b-e), employing PCl_5 in conjunction with anhydrous $SnCl_4$ or $AlCl_3$ or using $SOCl_2$ and $AlCl_3$ resulted in the formation of a neutral product (40-60% yield)(presumably the diketone VI), which could not be obtained in the crystalline form. Its direct conversion to 1,2,3,4,6,7,8,9-octahydrodibenzothiophene (VII) and aromatization of the latter gave a product which although could not be

crystallised, showed the characteristic absorption maxima in the ultraviolet for dibenzothiophene at 290, 280, 264 and 248 mμ (Lit. (5), 289, 280, 264, 258 and 237 mμ).



Considering the possible deteriorating effect of $AlCl_3$ on sulphur and thiophene, cyclization was repeated with orthophosphoric acid (with added P_2O_5)(6), which gave γ-2-(4-keto-4,5,6,7-tetrahydro)-thianaphthenyl butyric acid (IX) in 74% yield, m.p. 114-15° (benzene-petr.ether)(Found: C, 60.08; H, 6.13; S, 13.22. $C_{12}H_{14}O_3S$ requires C, 60.55; H, 5.93; S, 13.47). The reduction of (IX) gave γ-2-(4,5,6,7-tetrahydro)-thianaphthenyl butyric acid (X), m.p. 60-61° (Kofler hot stage)(EtOH) λ max 235 mμ (ε = 5600) in the ultraviolet, ν CO (carboxyl) at 5.90 μ (1695 cm^{-1}). The same acid (X) m.p. 60°, was obtained by Cagniant and Cagniant (7) by succinoylation of 4,5,6,7-tetrahydrothianaphthene and the reduction of the keto acid β-2-(4,5,6,7-tetrahydro)-thianaphthenoyl propionic acid so obtained. These authors cyclised (X) to (XI) which was then reduced to (VII) and finally dehydrogenated by heating to 340°, with Se, obtaining presumably dibenzothiophene (VIII)(only the m.p. of the styphnate, 161° has been mentioned by the authors (7)).

The formation of (IX) as a result of the monocyclization of the key dibasic acid (V) of the present synthesis, and its conversion to (X), obtained in its turn by another direct route (7), confirms the feasibility of the synthesis of dibenzothiophene herein proposed.

In fact, the formation of the octahydro compound of the type (VII), on the

one hand by direct reduction of the diketones of the type (VI) and on the other, from the monocyclised product of the type (IX), has constituted in case of other syntheses (1b-e) accomplished by our method, the unequivocal nature of the same.

Further work on the preparation of the diketone (VI), in the pure form, and its conversion to (VII) and (VIII), is in progress and the details will be published elsewhere.

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