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BIOTIN SYNTHESIS. I.[1a-f] SYNTHESIS OF 4-(4-CARBOXYBUTYL)-1,2-DIHYDROTHIENO[3,4-d]IMIDAZOL-2-ONE

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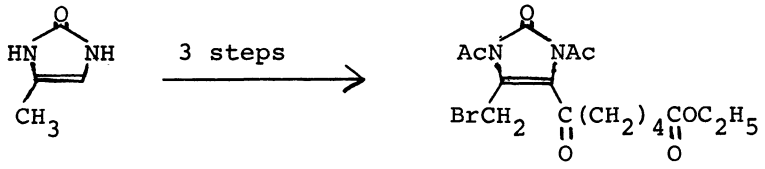
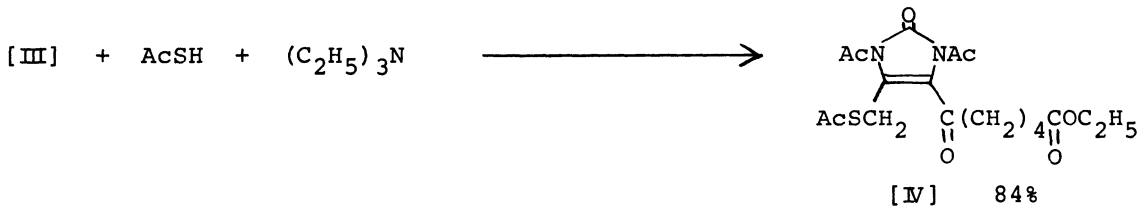
4-(4-Carboxybutyl)-1,2-dihydrothieno[3,4-d]imidazol-2-one [I], a precusor of dl-biotin, was synthesized via 6 steps starting from 4-methyl-2(1H)-imidazolone.

In the previous paper, a convenient method for the preparation of 2(1H)-imidazolone derivatives by the reactions of the potassium salt of benzyl cyanocarbamate or ethyl cyanocarbamate with α-halo carbonyl compounds was reported.[2] This prompted us to investigate a synthesis of dl-biotin starting from 4-methyl-2(1H)-imidazolone.

In this communication, a synthesis of 4-(4-carboxybutyl)-1,2-dihydrothieno-[3,4-d]imidazol-2-one [I], a precusor of dl-biotin, starting from 4-methyl-2(1H)-imidazolone via 6 procedures is described. 1,3-Diacetyl-4-bromomethyl-5-(ω-ethoxycarbonylvaleryl)-2(1H)-imidazolone [III] was prepared in good yield via 3 steps starting from 4-methyl-2(1H)-imidazolone [II] according to the literature method.[3] Then the bromide [III] was treated with an equimolar amount of thioacetic acid in the presence of an equimolar amount of triethylamine in acetonitrile at -30~0° for 2 hr and the corresponding thiolester [IV] was obtained in 84% yield [mp. 85~86° Anal. Found: C, 52.65 ; H, 5.89; N, 6.85; S, 7.85. Calcd. for $C_{18}H_{24}O_7N_2S$, C, 52.41; H, 5.86; N, 6.79; S, 7.78. λ_{max}(95%-EtOH): 227nm(ε 8.37×10^3), 267nm(ε 7.25×10^3)].

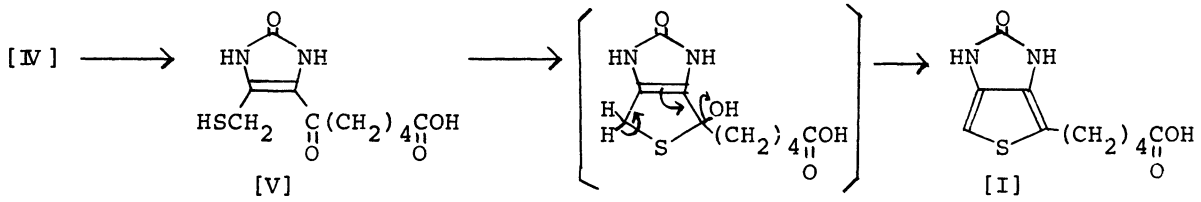


[II] [III]



[IV] 84%

It is expected that the desired thiophene [I] would be produced through an intramolecular nucleophilic addition of thiol group, formed by hydrolysis of the thiolester [IV], to the carbonyl group, followed by the subsequent dehydration accompanying the migration of double bond of the imidazolone ring as sketched below.



Expectedly, the thiophene [I] was obtained in 84% yield by the treatment of the thiol ester [IV] with 4 equimolar amounts of potassiun hydroxide in methanol at room temperature for 2 hr and the subsequent treatment of the crude hydrolyzed product[V] with dry hydrogen chloride in acetic acid at 20~25° for 2 hr [mp. 250~253° (dec), lit. 253~254° (dec)[1c] Anal. Found: C, 50.27; H, 5.09; N, 11.31; S, 13.16. Calcd. for $C_{10}H_{12}O_3N_2S$, C, 50.00; H, 5.04; N, 11.66; S, 13.32. ir (KBr) 3400, 3200, 1730, 1670, 740, 715 cm^{-1}. nmr (DMSO-d_6): δ 1.56 (m 4H), 2.30 (m 2H), 2.60 (m 2H), 6.17 (s 1H), 10.17 (broad 3H). λ max (95%-EtOH): 260nm (ε 1.37×10^4)].

It has been already reported that [I] is reduced to dl-biotin by hydrogenation on MoS_3-Al_2O_3 under high pressure at an elevated temperature.[1c] More effective procedure for the reduction of thiophene [I] is now under investigation.

REFERENCES

1) a) S. A. Harris, D. E. Woff, R. Mozingo, and K. Folkers, J. Amer. Chem. Soc., 67, 2096 (1945); b) B. R. Baker, J. Org. Chem., 12, 186 (1947); c) L. C. Cheney and J. R. Piening, J. Amer. Chem. Soc., 67, 2252 (1945); idem, U.S. 2,466,004 (1949); Chem. Abstr., 44, 3532 (1950); L. C. Cheney, U.S. 2,052,422 (1950); Chem. Abstr., 44, 6440 (1950); d) M. W. Goldberg and L. H. Sternbach, U.S. 2,489,232 (1949); Chem. Abstr., 45, 184 (1951); e) C. A. Grob and H. von Sprecher, Helv. Chim. Acta, 35, 885 (1952); f) A. Grüssrer, J. P. Bourguin, and O. Schnider, ibid., 28, 517 (1945).
2) T. Taguchi, Y. Sato, K. Watanabe, and T. Mukaiyama, Chem. Lett., in press.
3) R. Duschinsky and L. A. Dolan, J. Amer. Chem. Soc., 70, 657 (1948).

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