Pergamon

Tetrahedron Letters, Vol. 37, No. 15, pp. 2641-2642, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

S0040-4039(96)00349-8

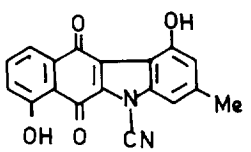
The First Approach to Kinamycin Antibiotics : Synthesis of Kinafluorenone Scaffold

Dipakranjan Mal * and Nirmal K. Hazra

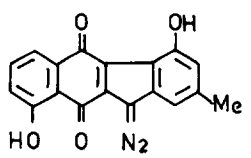
Department of Chemistry, Indian Institute of Technology, Kharagpur : 721302

Abstract : Annulation of indenone **5** with phthalide sulfone **6** has been successfully performed to furnish model benzo [*b*] fluorenone **7**, illustrating a potential route to kinamycin antibiotics.
Copyright © 1996 Elsevier Science Ltd

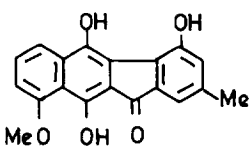
Occurrence of 6-6-5-6 or 6-6-5 carbocyclic frameworks among the polyketide antibiotics is a rarity[1]. Except for fredericamycin[2], such skeletons are found only in kinamycins, a small group of metabolites whose structures, after 25 years of their isolation, have recently been revised. For example, prekinamycin is proposed to possess structure **2**[3]. While kinamycins have enjoyed considerable attention, the synthetic studies[4] reported so far have dealt with the prerevised structures e.g. **1** for prekinamycin. In recent years, newer members of kinamycin group, with 6-6-5-6 ring system have been isolated[5], kinafluorenone **3**[1] being a major metabolite of a mutant strain of Streptomyces murayamaensis.



1



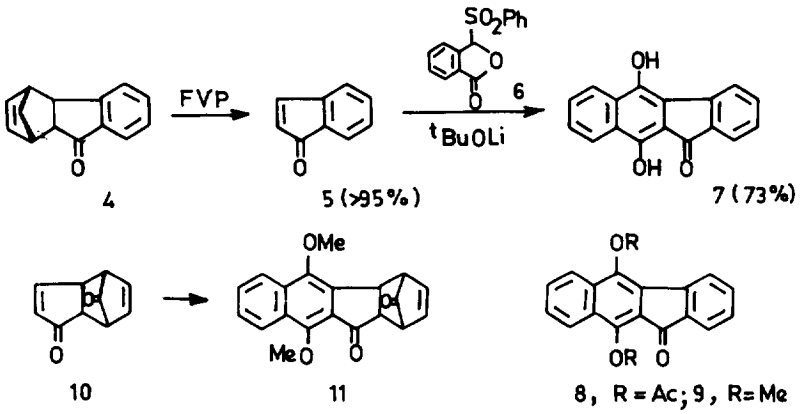
2



3

Inspection of the structure **3** led us to consider extension of Hauser's annulation strategy[6], previously successful with cyclohexenones, to indenones. But, the major practical hurdle was to obtain indenone **5** in pure form on a preparative scale, despite the availability of many methods[7] for its preparation. Moreover, we were apprehensive that indenone would undergo polymerisation in the Hauser's basic condition, like cyclopentenone[8], a notorious Michael acceptor. However, we could develop an efficient preparative method for indenone **5**, based on flash vacuum pyrolysis (FVP) of adduct **4**.

Treatment of yellow phthalide sulfone anion, prepared by deprotonation of **6** by ^{t}BuOLi at -60°C, with a solution of **5** in THF, followed by acidic work-up resulted in a red amorphous solid of quinol **7** (73%) (Scheme 1). Without attempting purification, it was subjected to acetylation (Ac_2O / Py) to produce benzo [*b*] fluorenone **8**[9]. It is worth noting that kinafluorenone **3** was not characterisable as such due to its poor solubility in common



Scheme I

organic solvents. Quinol **7** was further characterised by its conversion to dimethyl ether **9**. Alternatively, compound **9** was prepared from the cyclocondensed adduct of **6** and **10**, via methylation, cheletropic elimination and aromatisation.

Thus, the annulation of **5** with **6**, constituting the first report of an indenone undergoing annulation, represents a potential solution to the synthesis of kinamycins. Further work is in progress to accomplish the total syntheses of kinafluorenone **3** and prekinamycin **2**.

Acknowledgement : The authors are grateful to DST, New Delhi for financial support of the project.

References and Notes

1 Conc, M.C.; Melville, C.R.; Gore, M.P.; Gould, S.J. *J. Org. Chem.* **1993**, 58, 1058.

2 Misra, R.; Pandey, R.C.; Silverton, J.V. *J. Am. Chem. Soc.* **1982**, 104, 4478.

3 Gould, S.J.; Tamayo, N.; Melville, C.R.; Conc, M.C. *J. Am. Chem. Soc.* **1994**, 116, 2207.

4 (a) Mithani, S.; Weertunga, G., Taylor, N.J; Dmitrienko, G.I. *J. Am. Chem. Soc.* **1994**, 116, 2209. (b) Knolker, H-J.; Sullivan, N.O'. *Tetrahedron,* **1994**, 50, 10893 and the references therein.

5 Volkmann, C.; Rossner, E.; Metzler, M.; Zahner, H.; Zeeck, A. *Liebigs Ann. Chem.* **1995**, 1169.

6 Hauser, F.M.; Prasanna, S. *J. Org. Chem.* **1981**, 103, 6378.

7 Szmant, H.H.; Nanjundiah, R. *J. Org. Chem.*, **1978**, 43, 1835.

8 (a) Mal, D.; Murty, K.V.S.N.; Datta, K. *Tetrahedron Lett.* **1994**, 35, 9617. (b) Boger, D.L.; Zhang, M. *J. Org. Chem.* **1992.** 57, 3974.

9 Data for **8**: 244-245°C; light yellow, 73% ; υ_{max}/cm^{-1} 1765, 1707, 1637, 1596, 1357, 1197; δ_H 8.06(brd, 1 H, J 8), 7.8-7.45 (m, 6H), 7.36(dt, 1 H, J 1, 1.7), 2.62(s, 3 H), 2.59(s, 3 H). δ_C(d_6-DMSO, δ_C 39.6), 188.80, 169.24, 168.38, 142.81, 141.04, 138.55, 136.23(CH), 135.24, 132.03, 130.86(CH), 130.26(CH), 128.81, 128.55(CH), 127.66, 124.4(CH), 124.12(CH), 122.85(CH), 121, 20.77, 20.61.

11: 167-168°C; υ_{max}/cm^{-1} 1784, 1705, 1354, 716; δ_H 8.36(d, 1 H, J 8.5), 8.09(d, 1 H, J 8.2), 7.67(dt, 1 H, J 1.4, 8), 7.55(dt, 1 H, J 1.2, 8), 6.32-6.26(m, 1 H), 6.00-5.95(m, 1 H), 4.11(s, 3 H), 4.16-4.10(m, 1 H), 4.06(s, 3 H), 3.74-3.69(m, 1 H), 3.59-3.54 (m, 1 H), 3.37(dd, 1 H, J 5,8); δ_C 201.61, 200.77, 152.02, 148.62, 136.13, 132.62, 130.84, 130.09, 129.41, 128.89, 126.75, 126.51, 125.06, 121.76, 63.19, 61.66, 50.46, 49.89, 46.74, 35.84.

(*Received in UK* 5 *January* 1996; *revised* 19 *February* 1996; *accepted* 23 *February* 1996)