Benzopyrans. Part 43.[1] Reactions of some simple condensates of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde with ethyl β-aminocrotonate

J. Chem. Research (S), 2002, 311–313
J. Chem. Research (M), 2002, 0741–0751

Chandra Kanta Ghosh[a]*, Sumit Kumar Karak[a] and Amarendra Patra[b]

[a]*Organic Chemistry Laboratory, Department of Biochemistry, Calcutta University, Kolkata – 700 019, India*

[b]*Department of Pure Chemistry, Calcutta University, Kolkata – 700 009, India*

With ethyl β-aminocrotonate, the chromone **2A** (X = H(A), Me(B), Cl(C)) gives a mixture of the dihydropyridine **4A** and pyranopyridine **15A, 2B** gives **4B**, and **2C** gives varying amounts of the substituted enamine **3C**, pyridone **4C** and benzophenone **8**. 5-Hydroxy-5*H*-[1]benzopyrano-[4,3-*b*]pyridine **11** (< 3%) was obtained in each case. Palladised charcoal dehydrogenates dihydropyridines **4A** and **4B** to respectively **12A** and **12B** and ammonia converts **12A** into the diazanaphthalene **13**.

Keywords: 1-benzopyran-4-one, 5*H*-[1]-benzopyrano[4,3-*b*]pyridine, 1,4-dihydropyridine, ethyl β-aminocrotonate, benzophenone

Ethyl β-aminocrotonate (**1**) functioning as an enamine, may either undergo Michael addition to the exocyclic α,β-unsaturated carbonyl functionality (Scheme 1) or attack at the pyran 2-position (Scheme 2) of the condensates **2** of the title aldehyde. The mode of initial addition and further transformation of the adducts depends on the nature of R^1 and R^2 groups of the latter (**2**). The Michael adduct **3** (R^2 = Me) may cyclise to the dihydropyridine **4A,B** and **3** (R^1 = R^2 = OEt) to **4C** (Scheme 1 – path *a*). Elimination of $CH_2(COR^1)COR^2$ from **3** (retro Michael) (Scheme 1 – path *b*) leads to the imine **5** that may tautomerise to the enamine **6**. The latter two intermediates (**5** and **6**) can undergo intramolecular Michael addition or electrocyclisation with concomitant opening of the pyran ring to give the substituted pyridine **7** and benzophenone **8**, respectively. Transformation of **5** to the pyranopyridine **11** via **9** and **10** is also possible.

An alternative addition of the enamine **1** to the pyran 2-position with concomitant opening of the pyran ring, gives the intermediate **14** which by double cyclisation, forms the pyranopyridine **15** (Scheme 2 – path *a)*. If the conformation of this intermediate is as shown in **14**, its alternative cyclisation with elimination of $CH_2(COR^1)COR^2$ to **7** or/and **8** (path *b*) is unlikely.

The products obtained by heating a solution of **1** and **2** in DMF on a water bath are tabulated in Table 1. Formation of **4A**, **11** and **15A** from reaction of **1** with **2A** involves nearly all the plausible reaction courses as depicted in Schemes 1 and 2. The enamine **1** does not add to the pyran 2-position of **2B** and **2C** (Scheme 2) thereby precluding the formation of the pyranopyridines **15B** and **15C**, respectively. Facile cyclisation of **3A,B** to **4A,B** (Scheme 1 – path *a*) predominates over the reaction courses (path *b*) leading to **7, 8** and **11**. The adduct **3C**, obtained from **1** and **2C**, is comparatively stable as the cyclisation involving its amino and ester group leading to **4C** (path *a*) is not so facile. The lower nucleofugality of malonate anion apparently decreases its rate of conversion to **5** (path *b*). In fact we were able to isolate the adduct **3C** and benzophenone **8** in two cases and chromone linked pyridine **4C** in one case only (Table 1). A DMF solution of **3Cc** on further heating at 100°C gave a mixture of **8c** and **11c**. Reaction of **2Ca** with **1** in 1:1.5 molar proportion yielded the dihydropyridine **4Ba** in addition to **8a** and **11a** evidently via the intermediate **5a**. In no case could the pyridine **7**[1] be isolated.

Diethyl 1,4-dihydro-2,6-dimethyl-3,5-dicarboxylate (Hantzsch ester) when dissolved in chloroform is gradually dehydrogenated at ambient temperature[5], but the dihydropyridines **4A** and **4B** like their 4-aryl analogues survived even prolonged digestion in chloroform. **4A** and **4B** were dehydrogenated to respectively to **12A** and **12B** by refluxing with palladised charcoal in xylene. Refluxing **12A** with liquor ammonia in ethanol afforded the diazanaphthalene **13**. In ^{1}H NMR spectra, the ethoxymethylene protons of the pyridines **4** and **12** appear as quartets of quartets. The appearance of 3- and 4-H of **4Cb** (at δ 3.82 and 4.81) as two slightly broadened singlets is compatible with the dihedral angle of 91.2° between these two vicinal protons in the global energy minimised structure of the compound. For the dihydropyridine **4B**, quaternary carbon peak at *ca* δ 98 is attributable to its pyridyl 3-, 5-C and that at δ 147 to 2-, 6-C. The reverse assignment of the above two peaks in isomeric diethyl 1,4-dihydro-2,6-dimethyl-4-(4-oxo-4*H*-1-benzopyran-2-yl)pyridine-3,5-dicarboxylate[8] is wrong.

Table 1 Yields (%) of the products obtained from ethyl β-aminocrotonate (**1**) and chromones **2** in DMF at water bath temperature

Substrate	Products[a]			
2	**3**	**4**	**8**	**15**
Aa	—	47	—	8
Ab	—	52	—	6
Ac	—	37	—	18
Ba	—	51	—	—
Bb	—	32	—	—
Bc	—	26	—	—
Ca	—	—	32	
Cb	15	8	—	—
Cc	14	—	15	—

[a]Each member of the chromones **2** gave in < 3% yield the corresponding 1-benzopyrano[4,3-*b*]pyridine **11** identical with an authentic sample[1]. The same reaction for **2A** and **2B** in refluxing ethanolic solution gave a higher yield (10–15%) of **11** but a lower yield (~ 25%) of **4**.

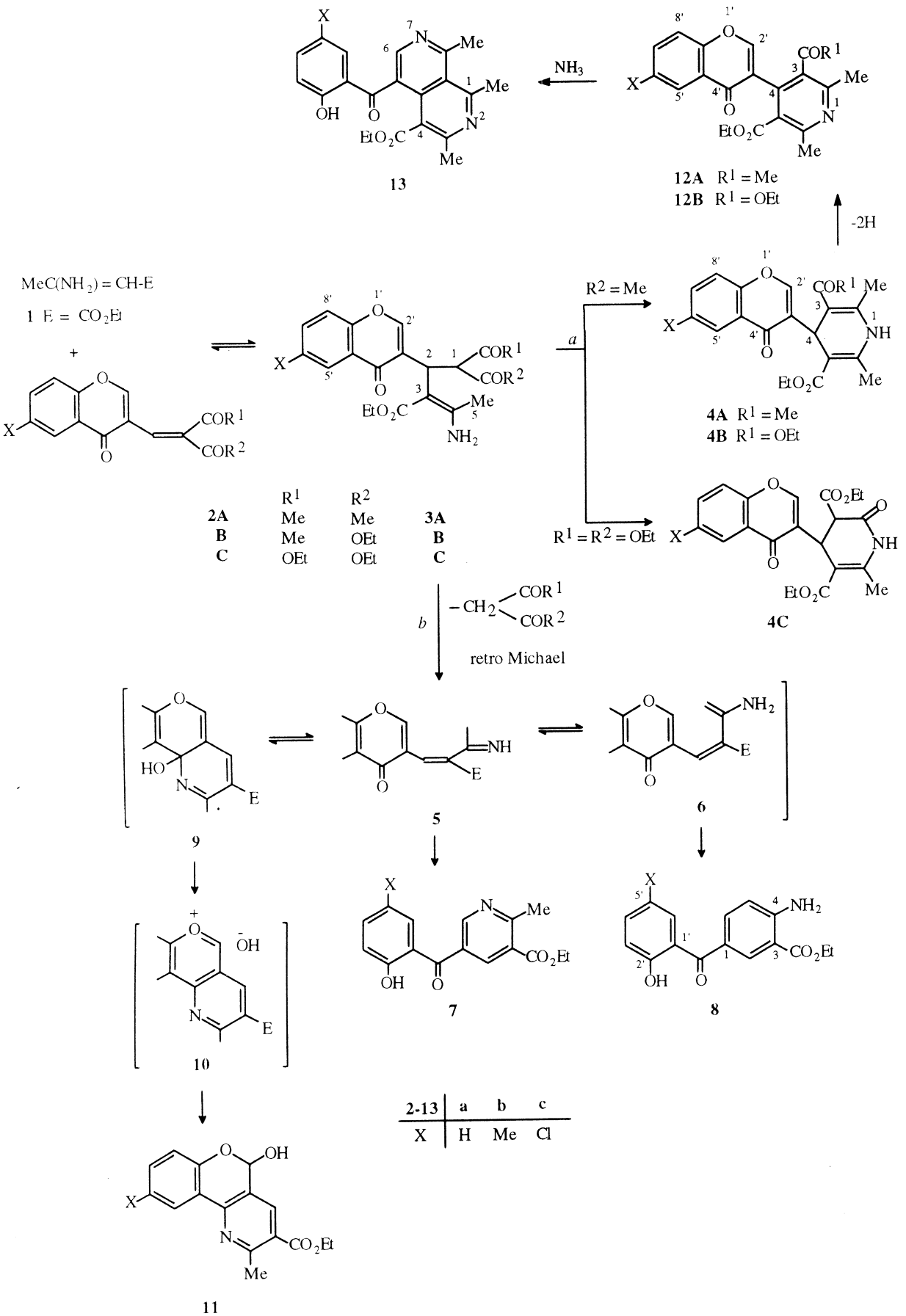
We thank CSIR, New Delhi for financial support and Dr. (Mrs.) C. Mukherjee, Department of Pure Chemistry, Calcutta University for help with molecular modeling studies.

Techniques used: ^{1}H and ^{13}C NMR, elemental analysis, IR, molecular modeling

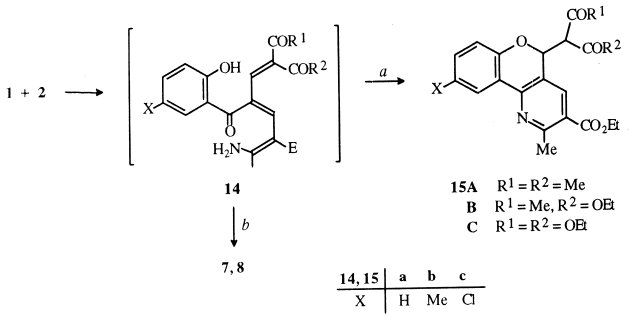
References: 9

Schemes: 2

* To receive any correspondence. E-mail: amarendra@satyam.net.in


NH3
13
12A R1 = Me
12B R1 = OEt
-2H
MeC(NH2) = CH-E
1 E = CO2Et
2A
B
C
R1 R2
Me Me
Me OEt
OEt OEt
3A
B
C
a
R2 = Me
4A R1 = Me
4B R1 = OEt
R1 = R2 = OEt
4C
b
retro Michael
5
6
9
10
7
8
11
2-13 a b c
X H Me Cl

Scheme 1



Scheme 2

Table 1: Yields of the products obtained from the enamine **1** and chromones **2**

Table 2: Analytical and ^{1}H NMR spectral data for the pyridines **4** and **12**

Table 3: ^{13}C NMR spectral data for **4** and **12**.

Received 22 January 2002; accepted 24 April 2002
Paper 02/1210

References cited in this synopsis

1 C.K. Ghosh, A. Ray and A. Patra, *J. Heterocycl. Chem.*, 2001, **38**, 1459.
5 C.K. Ghosh, unpublished results.
8 S.G. Jagadeesh, G.L. David Krupadanam and G. Srimannarayana, *Ind. J. Chem.*, 1997, **36B**, 965.