Tetrahedron Letters 52 (2011) 1946–1948

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

An organocatalytic rearrangement of 2-(*N*-alkyl-/aryl-)amino-4-oxo-4*H*-1-benzopyran-3-carbaldehyde

Sourav Maiti, Suman Kalyan Panja, Chandrakanta Bandyopadhyay *

Department of Chemistry, R. K. Mission Vivekananda Centenary College, Rahara, Kolkata 700 118, West Bengal, India

ARTICLE INFO

Article history:
Received 21 January 2011
Revised 10 February 2011
Accepted 12 February 2011
Available online 17 February 2011

Keywords:
Rearrangement
Organocatalysis
Chromone-3-carbanilide
2-Aminochromone-3-carbaldehyde
Chroman-2,4-dione
1-Benzopyran

ABSTRACT

2-(Arylamino)-4-oxo-4*H*-1-benzopyran-3-carbaldehyde rearranges to 4-oxo-4*H*-1-benzopyran-3-carbanilide when treated with glycine in the presence of formalin, but under similar conditions 2-(alkylamino)-4-oxo-4*H*-1-benzopyran-3-carbaldehyde rearranges to 3-alkylaminomethylenechroman-2,4-dione.

1. Introduction

Organocatalysis reaction is a rapidly growing area in the field of synthetic organic chemistry. The advantage is that metal is excluded which often causes toxicity. Iminium ion catalysed organic reactions and rearrangements have gained significance in the last decade.[1] Isomerisation of retinals which are the key reactions in vision can be catalysed by iminium ion.[2] It also catalyses asymmetric vinylogous α-ketol rearrangements.[3] Conversion of *O*-allylated salicylaldehyde to chromanone using thiazolidine salt as organocatalyst has been accomplished.[4] Recently, a study has been made on asymmetric organocatalytic rearrangement reactions.[5]

2-Alkyl/arylaminochromone-3-carbaldehyde (**1**) has been reported to be a very good building block for the synthesis of various heterocycles.[6] It has been synthesized by selective rearrangement of nitrone **2**.[7] Compound **1** reacts with formalin and secondary amine to produce 3,3′-methylenebis(2-alkyl/arylaminochromone) using deformylative Mannich reaction.[8] Primary amines (both aliphatic and aromatic) convert **1** to **3**.[9] We report herein a rearrangement reaction of **1** catalysed by the combined action of formalin and primary amine.

In continuation of our earlier studies on double deformylative Mannich reaction on 3-formylchromone using formalin and glycine as the reagent to form *N*,*N*-di(chromon-3-ylmethyl)glycines,[10] compound **1a** was heated in methanol with equimolar amount of glycine in the presence of excess formalin for 10 h. After usual work-up, the reaction mixture produced a white solid, which was found to be **4a** (Table 1, entry 1). The structure of the compound was established on the basis of ^{1}H NMR and mass spectral analysis and finally confirmed by comparing with an authentic sample.[11] Similar results were obtained from the reactions of **1b–d** (entries 2–4). The structure of **4** clearly rules out the possibility of incorporation of formaldehyde and glycine in the product,[12] but in their absence no change was observed when **1** was heated in methanol for 15 h. As 1°-amine reacts with **1** to produce **3**,[9] catalytic activity of either CH_2O or combined effect of formalin and 1°-amine was examined. Compound **1** was heated with formalin alone in methanol for 16 h, but no change in **1** was observed (entry 5). To check the combined effect of CH_2O and 1°-amine, glycine was substituted by alanine and compound **1a** produced **4a** in good yield (entry 6). Assuming amine moiety of aminoacid to be responsible for the rearrangement, an equimolar amount of **1a** and ethyl amine was heated in methanol in the presence of excess formalin. Surprisingly, the same transformation takes place although in lower yield (entry 7). Methyl amine or benzyl amine was also employed, but yields are poor compared to that of glycine (entries 8 and 9). It should be mentioned that the above rearrangement does not take place in the presence of formaldehyde and liquor ammonia (entry 10). When the amine component is changed from aliphatic to aromatic, no rearranged product was isolated even after heating for 18 h (entry 11). Use of paraformaldehyde in place of formalin takes a longer reaction time and gives a poor yield (entry 12).

To verify the extent of catalytic activity of the amine component, glycine was used in the reaction mixture in varying amounts keeping formalin in excess (Table 2). It was observed that the

* Corresponding author.
E-mail address: kantachandra@rediffmail.com (C. Bandyopadhyay).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.02.053

Table 1
Rearrangement of **1** using a primary amine and formalin

Entry	R^1	R^2	Amine component	Additive	Time (h)	Product (% yield)	Mp (°C)
1	H	Ph	Glycine	CH_2O	8	**4a** (70)	214–216 (215–217)[11]
2	Me	Ph	Glycine	CH_2O	7	**4b** (72)	188–190
3	H	Ar[a]	Glycine	CH_2O	8	**4c** (70)	220–222
4	Me	Ar[a]	Glycine	CH_2O	10	**4d** (74)	218–220
5	H	Ph	––	CH_2O	16	85% recovery of **1a**	
6	H	Ph	Alanine	CH_2O	10	**4a** (72)	214–216
7	H	Ph	$EtNH_2$	CH_2O	10	**4a** (40)	214–216
8	H	Ph	$MeNH_2$	CH_2O	10	**4a** (35)	214–216
9	Me	Ph	$PhCH_2NH_2$	CH_2O	14	**4b** (60)	188–190
10	H	Ph	NH_4OH	CH_2O	15	70% recovery of **1a**	
11	H	Ph	$PhNH_2$	CH_2O	18	60% recovery of **1a**	
12	Me	Ph	Glycine	$(CH_2O)_n$	13	**4b** (40)	188–190
13	H	Me	Glycine	CH_2O	8	**5e** (55) (*E*/*Z*:1/2)	198–200 (194–96)[7]
14	Me	Et	Glycine	CH_2O	10	**5f** (52) (*E*/*Z*:2/5)	184–186
15	H	Et	Glycine	CH_2O	10	**5g** (60) (*E*/*Z*:2/5)	184–186
16	H	Ph	$AlCl_3$ in benzene		5	65% recovery of **1a**	
17	H	Ph	BF_3 in CH_2Cl_2		6	60% recovery of **1a**	

[a] Ar stands for 4-MeC_6H_4.

reaction time increases with decrease in the concentration of glycine (Table 2, entries 1–5). Use of 26 mol% of glycine gives 72% yield in 14 h (entry 3), on further decreasing the concentration of glycine, the yield decreases even with longer reaction hours.

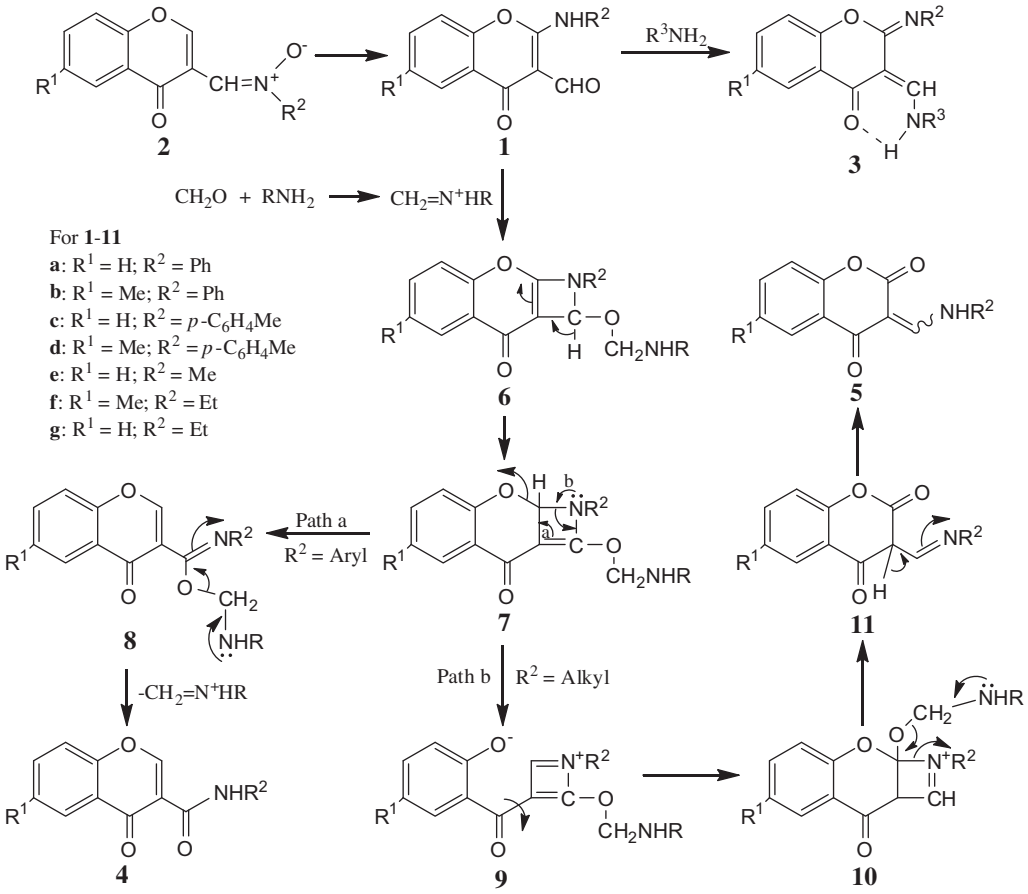
Table 2
Catalytic effect of glycine on the rearrangement of **1** to **4**

Entry	R^1	R^2	Glycine (mol%)	Time (h)	Product	Yield (%)
1	Me	Ph	100	7	**4b**	72
2	Me	Ph	40	14	**4b**	72
3	Me	Ph	26	14	**4b**	72
4	Me	Ph	12	24	**4b**	60
5	Me	Ph	6	40	**4b**	40

The reaction was then extended using 2-(alkylamino)-4-oxo-4*H*-1-benzopyran-3-carbaldehyde **1** (R^2 = alkyl). When **1e–g** was heated with equimolar amounts glycine in methanol in the presence of excess formalin for 7–10 h, it produced **5** (Table 1, entries 13–15). Compound **5** appeared as a diastereomeric mixture of *E* and *Z* forms.[7]

The above observations may be rationalized as follows: initial formation of iminium ion from 1°-amine and CH_2O catalyses the intramolecular attack of NHR^2 group of **1** on the CHO function to form **6**, where 1,3-H shift takes place to produce **7**. Electrocyclic ring opening of **7** (R^2 = aryl) (path a) leads to **8**, which forms **4** with the expulsion of iminium ion. But in **7** when R^2 = alkyl, NR^2 group becomes more nucleophilic and facilitates the pyran ring opening to **9** (path b), which recyclises to **10**. Expulsion of iminium ion from **10** leads to the opening of azetinium ring to form **11**, which finally tautomerises to **5** (Scheme 1).

It may be predicted that the formation of iminium ion is responsible in catalysing the reaction. Among the different amines used in the rearrangement, aminoacids have the highest and the aromatic amine has the lowest tendency to form the iminium ion. The yields



Scheme 1. Rearrangement of **1**–**4** and **5** using a primary amine and formalin.

of rearrangement products also corroborate the above prediction. It is to be mentioned here that anhydrous $AlCl_3$ or BF_3 failed to carry out this rearrangement (entries 16 and 17).

In conclusion, we have reported a combined organocatalytic effect of formaldehyde and glycine in the rearrangement of 2-(*N*-alkyl-/aryl-)amino-4-oxo-4*H*-1-benzopyran-3-carbaldehyde (**1**). The differential effect of alkyl and aryl group in the amine function of **1** in this rearrangement has also been rationalized.

Acknowledgements

We gratefully acknowledge Department of Biotechnology (DBT), India (No. BT/PR8217/Med/14/1239/2006) for financial assistance; IICB, Jadavpur for spectral analysis and finally the college authorities for providing research facilities.

References and notes

1. Erkkila, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470.
2. (a) Ouellet, S. G.; Tuttle, J. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 32–33; (b) Yang, J. W.; Hechavarria Fonseca, M. T.; Vignola, N.; List, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 108–110.
3. Zhang, E.; Fan, C. A.; Tu, Y. Q.; Zhang, F. M.; Song, Y. L. *J. Am. Chem. Soc.* **2009**, *131*, 14626–14627.
4. (a) Enders, D.; Breuer, K.; Runsink, J. *Helv. Chim. Acta* **1996**, *79*, 1899–1902; (b) Aupoix, A.; Vo-Thanh, G. *Synlett* **2009**, 1915–1920.
5. Moyano, A.; El-Hamdouni, N.; Atlamsani, A. *Chem. Eur. J.* **2010**, *16*, 5260–5273.
6. (a) Singh, G.; Singh, L.; Ishar, M. P. S. *Tetrahedron* **2002**, *58*, 7883–7890; (b) Sattofattori, E.; Anzaldi, M.; Balbi, A.; Artali, R.; Bombieri, G. *Helv. Chim. Acta* **2002**, *85*, 1698–1705; (c) Singh, G.; Singh, G.; Ishar, M. P. S. *Synlett* **2003**, 256–258; (d) Singh, G.; Singh, G.; Ishar, M. P. S. *Helv. Chim. Acta* **2003**, *86*, 169–180.
7. Ghosh, T.; Bandyopadhyay, C. *Tetrahedron Lett.* **2004**, *45*, 6169–6172.
8. Maiti, S.; Panja, S. K.; Bandyopadhyay, C. *Tetrahedron Lett.* **2009**, *50*, 3966–3969.
9. Maiti, S.; Panja, S. K.; Bandyopadhyay, C. *Indian J. Chem.* **2009**, *48B*, 1447–1452.
10. Panja, S. K.; Maiti, S.; Drew, M. G. B.; Bandyopadhyay, C. *Tetrahedron* **2009**, *65*, 1276–1280.
11. Klutchko, S.; Cohen, M. P.; Shavel, Jr. J.; von Strandtmann, M. *J. Heterocycl. Chem.* **1974**, *11*, 183–188.
12. *General procedure for the rearrangement of* **1**: To a solution of **1b** (140 mg, 0.5 mmol) in methanol (5 mL), formalin (0.3 mL) and glycine (10 mg, 0.13 mmol, 26 mol%) were added. The resulting mixture was heated under reflux. A solid began to separate after 4.5 h and heating was continued for 14 h when the absence of **1b** was observed by TLC. The reaction mixture was cooled and deposited solid was filtered out. The solid was further crystallized from benzene–light petroleum to afford **4b** (100 mg, 72%) as a white crystalline solid. IR (KBr) ν_{max}: 3124, 3048, 2758, 1678, 1615, 1558 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.51 (3 H, s, CH_3), 7.14 (1 H, br t, J = 7.5 Hz, ArH), 7.34–7.39 (2 H, m, ArH), 7.47 (1 H, d, J = 8.4 Hz, 8-H), 7.57 (1 H, br d, J = 8.4 Hz, 7-H), 7.73 (2 H, br d, J = 7.8 Hz, ArH), 8.09 (1 H, br s, 5-H), 9.04 (1 H, s, 2-H), 11.44 (1 H, br s, exchangeable, NH); mass m/z: 280 (M^++H), 302 (M^++Na).