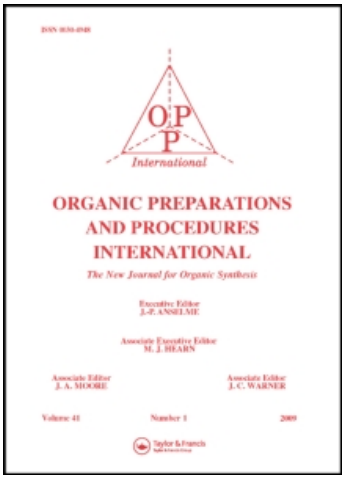


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF [1]BENZOPYRANO[3,4-h]BENZO[b]-1,6-NAPHTHYRIDINE-6-ONES

K. Rajendra Prasad[a]; Malleshwar Darbarwar[a]
[a] Department of Chemistry, Osmania University, Hyderabad, INDIA

To cite this Article Prasad, K. Rajendra and Darbarwar, Malleshwar(1995) 'SYNTHESIS OF [1]BENZOPYRANO[3,4-h]BENZO[b]-1,6-NAPHTHYRIDINE-6-ONES', Organic Preparations and Procedures International, 27: 5, 547 — 550
To link to this Article: DOI: 10.1080/00304949509458496
URL: http://dx.doi.org/10.1080/00304949509458496

OPPI BRIEFS

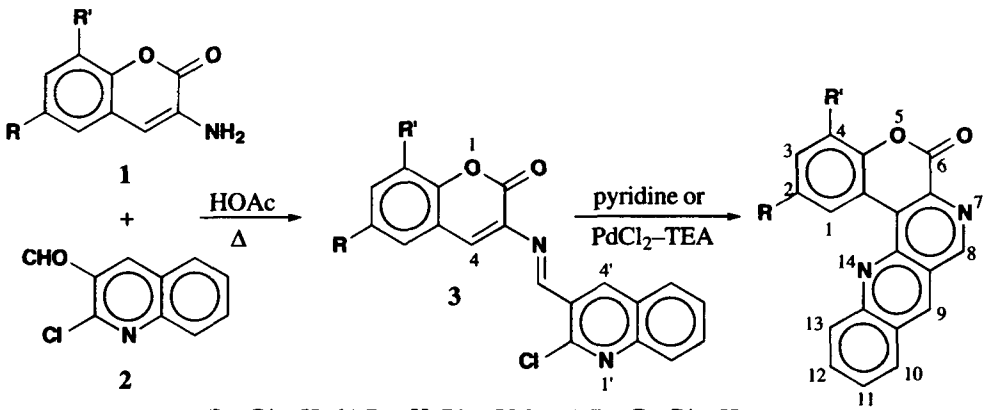
SYNTHESIS OF [1]BENZOPYRANO[3,4-h]BENZO[b]-1,6-NAPHTHYRIDINE-6-ONES

Submitted by K. Rajendra Prasad and Malleshwar Darbarwar*
(10/06/94)

Department of Chemistry, Osmania University
Hyderabad-500007, INDIA

In continuation of our efforts[1] to construct a heterocyclic ring system involving the 3,4-positions of 3-amino-2H-1-benzopyran-2-one and to evaluate their physiological activity, we report herein the synthesis of new heterocyclic systems, [1]benzopyrano[3,4-h]-benzo[b]-1,6-naphthyridine-6-ones (**4**), from 3-aminocoumarins (**1a-f**)[2,3] and 2-chloro-3-formylquinoline[4] (**2**).

In a representative experiment, 3-aminocoumarin (**1a**) and 2-chloro-3-formylquinoline (**2**) were heated in glacial acetic acid on a steam bath for 6 hrs. The crude compound was chromatographed over neutral alumina using a benzene-ethyl acetate (1:1) mixture as an eluent to obtain a brown crystalline compound, mp. 239-241° (**3a**). Its IR spectrum showed characteristic absorptions at 1725 cm^{-1} and 1605 cm^{-1} which are attributed to the lactone carbonyl and C=N functions respectively. Its ^1H NMR spectrum (DMSO-d_6), displayed signals at δ 8.71 (s, 1H) assigned for C_4-H of quinoline ring, 8.55 (s, 1H, C_4-H of 2H-[1]-benzopyran-2-one ring), 8.1 (s, 1H, azomethine, N=CH), and 7.0-8.0 (m, 8H) for the aromatic protons. The mass spectrum of the compound showed the molecular ion at m/z 334 and the percentage of P+2 peak supports the presence of one chlorine atom. Based on the spectral data and elemental analysis, the compound was assigned as 3-{[(2′-chloroquinolinyl)methylene]amino}-2H-benzopyran-2-one (**3a**). The mass fragmentation pattern of



a) R = R' = H b) R = H, R' = OMe c) R = Br, R' = H
d) R = Br, R' = OMe d) R = R' = Br f) R = Cl, R' = H

the compound is in agreement with the assigned structure [m/z (%): 336(7), 334(20), 306(45), 299(8), 290(15), 188(25), 118 (100),76(25)]. Compound **3a** was subsequently subjected to cyclodehydrochlorination reaction in dry pyridine. After work-up and chromatographic purification (benzene-ethyl acetate, 1:1), a colorless crystalline compound, mp 281-282°, was obtained. Its IR spectrum exhibited absorptions at 1720 cm^{-1} and 1600 cm^{-1} which may be attributed to the lactone carbonyl and C=N groups respectively and its ^1H NMR spectrum displayed signals at δ 8.85 (s, 1H, C_9-H), 8.2 (s, 1H, C_8-H) and at 7.2-8.1 (m, 8H). The fact that there is no signal for C_4-H of the coumarin moiety in the product clearly indicates the formation of **4a** by cyclodehydrochlorination involving position 4 of **3a**. The mass spectrum of **4a** gives the molecular ion at m/z 298. Based on the spectral data and elemental analysis, the compound was assigned as [1]benzopyrano[3,4-h]benzo[b]-1,6-naphthyridine-6-one (**4a**). The mass fragmentation pattern is consistent with this structure. This procedure was extended to five other 3-aminocoumarins (**1b-f**) and 2-chloro-3-formylquinoline (**2**) in order to ascertain the generality of the reaction and the product obtained in each case has been characterized as corresponding **3b-f** and **4b-f** (Table 1). The conversion of **3a** to **4a** was also carried out, albeit in poor yields (30%), by reflux in the presence of triethylamine $PdCl_2$.

EXPERIMENTAL SECTION

Melting points were taken on a Hoover capillary melting point apparatus and are uncorrected. IR spectra were recorded in KBr on a Schimadzu-435 spectrometer. PMR spectra were obtained on Varian A-60D, Jeol or Brucker spectrometers using TMS as an internal standard; mass spectra were carried out on Perkin-Elmer Hitachi RMU-6L and Ms-30 instruments. Elemental analyses were performed by Central Drug Research Institute (CDRI), Lucknow, India.

General Procedure for the Preparation of 3.- A mixture of the appropriate 3-aminocoumarin (**1a-f**, 0.002 mol) and 2-chloro-3-formylquinoline (**2,** 0.002 mol) were heated in glacial acetic acid (10 mL) on a steam bath. The progress of the reaction was monitored by tlc. The product was collected, washed with petroleum ether, dried and chromatographed over a neutral alumina. Elution with benzene-ethyl acetate (1:1) mixture afforded the corresponding 3-{[(2′-chloroquinolinyl)methylene]-amino}-2H-[1]benzopyran-2-ones (**3a-f**).

[1]-Benzopyrano[3,4-h]benzo[b]-1,6-naphthyridine-6-ones (4a-f).- 3{[(2′-Chloroquinolinyl)methylene]amino}-2H[1]benzopyran-2-ones (**3a-f**, 0.0015-0.002 mol) were heated in dry pyridine (15-20 mL). The reaction was monitored by tlc. After the completion of the reaction, the entire reaction contents were poured over crushed ice. The product that separated was collected and chromatographed over neutral alumina. Elution with benzene-ethyl acetate mixture yielded the corresponding [1]-benzopyrano[3,4-h]benzo[b]-1,6-naphthyridine-6-one (**4a-f**) as a crystalline compound.

Acknowledgements.- One of the authors (K. R. Prasad) is grateful to the UGC, New Delhi, for the award of a Fellowship.

TABLE 1. Yields, Physical Constants, Analytical and Spectral Data of Compounds **3** and **4**.

Cmpd.	Time (hrs)	Yield (%)	mp (°C)	Elemental Analysis Calcd. (Found) C	H	N	IR(cm^{-1}) C=O C=N	^1H NMR (δ)
3a	6	66	239-241	68.27 (68.33)	3.24 (3.32)	8.44 (8.39)	1725 1605	8.71 (s, 1H, C_4-H); 8.55(s, C_4-H); 8.1(s, -N=CH); 7.01-8.0 (m, 8H, ArH
3b	8	62	256-258	65.91 (65.99)	3.65 (3.60)	7.66 (7.69)	1730 1600	8.8 (s, 1H, C_4-H); 8.6 (s, 1H, C_4-H); 8.0 (s,1H, -N=CH); 7.1-7.8 (m, 7H, ArH); 3.8 (s,3H, -OMe)
3c	10	60	266-268	55.47 (55.40)	2.52 (2.45)	6.88 (6.80)	1720 1605	8.79 (s,1H, C_4-H); 8.66 (s, 1H, C_4-H); 7.01-8.0 (m, 8H ArH and -N=CH)
3d	8	59	251-253	54.41 (54.35)	2.67 (2.74)	6.39 (6.34)	1715 1610	8.76 (s,1H, C_4-H); 8.5 (s, 1H, C_4-H); 7.1-8.02 (m, 7H, ArH and -N=CH); 3.84 (s,3H , OMe)
3e	11	56	262-264	46.64 (46.57)	1.91 (1.85)	5.63 (5.72)	1705 1600	8.75 (s,1H, C_4-H); 8.6 (s, 1H, C_4-H); 6.9-8.0 (m, 7H, ArH and -N=CH)
3f	9	59	269-271	62.12 (62.01)	2.81 (2.74)	7.55 (7.61)	1720 1605	8.81 (m,1H, C_4-H); 8.6 (s, 1H, C_4-H); 7.2-8.2 (m, 8H, ArH and -N=CH)
4a	11	60	281-282	76.54 (76.59)	3.44 (3.39)	9.36 (9.40)	1720 1600	8.85(s, 1H, C_9-H); 8.2 (s, 1H, C_8-H); 7.2-8.1 (m, 8H, ArH)
4b	14	58	276-278	73.18 (73.23)	3.59 (3.69)	8.61 (8.54)	1720 1605	8.75 (s, 1H, C_9-H); 7.1-8.1 (m, 8H, ArH and -N=CH); 4.1 (s, 3H, OMe)
4c	13	55	289-291	60.77 (60.70)	2.36 (2.41)	7.51 (7.45)	1715 1590	8.74 (s, 1H, C_9-H); 7.2-8.3 (m, 8H, ArH and -N=CH)
4d	17	56	292-294	59.22 (59.16)	2.77 (2.73)	6.84 (6.90)	1705 1600	8.8 (s,1H,C_9-H); 7.3-8.2 (m, 7H, ArH and -N=CH); 3.9 (s, 3H, OMe)
4e	15	54	310-212	49.88 (49.82)	1.67 (1.76)	6.03 (6.11)	1725 1595	8.74 (s, 1H, C_9-H); 7.1-8.1 (m, 7H, ArH and -N=CH)
4f	11	50	302-204	68.79 (68.74)	2.64 (2.83)	8.35 (8.43)	1720 1610	8.76 (s,1H, C_9-H); 7.1-8.2 (m, 8H, ArH and -N=CH)

REFERENCES

1. K. Rajendra Prasad and D. Malleshwar, *Synth. Commun.*, **22**, 2479 (1992).

2. D. Chakravarthi and R. Das, *J. Ind. Chem. Soc.*, **48**, 371 (1971).

3. C. M. Brewster, *J. Am. Chem. Soc.*, **46**, 2463 (1924).

4. O. Meth-Cohn, N. Brahma and B. Tarnowski, *J. Chem. Soc. Perkin I*, 1523 (**1981**).

****

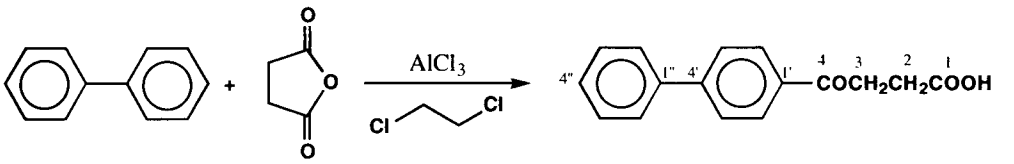
AN IMPROVED SYNTHESIS OF FENBUFEN

Submitted by (11/14/94)

Rafael Castillo*, Margarita Suárez-Herrera, Mayra Aparicio, Francisco Hernández-Luis and Alicia Hernández

Departmento de Farmacia, División de Bioquímica y Farmacia
Facultad de Química, UNAM, México D.F. 04510, MEXICO

Nitrobenzene is a very useful solvent in Friedel-Crafts acylations.[1] Some advantages of this solvent are: its inertness, its high polarity which facilitates the dissolution of the usual catalyst $AlCl_3$ to form a homogeneous reaction medium, and its ability to form a bulky complex with $AlCl_3$-acylating reagent which these leading to the formation of regiospecific products from substitution in the less sterically hindered positions of the substrate. However, nitrobenzene is not always an ideal solvent, since it is toxic and its recovery requires a steam distillation at the end of the reaction. Clearly then, in those Friedel-Crafts acylation reactions where orientation of the acyl group is not a problem, it is preferable to use a solvent which is easier to recover. This paper reports a simple and a convenient synthesis of the antiinflammatory agent *fenbufen*, (3-(4-biphenylcarbonyl)propionic acid).[2] This drug has been synthesized from biphenyl and succinic anhydride using nitrobenzene as solvent and $AlCl_3$ as catalyst, a process that takes from four to six days.[3]



If we assume that biphenyl has the 2,6- and 2´,6´-positions sterically hindered, we can expect that only the equivalent positions 4 and 4´ will be available for substitution.Thus, nitrobenzene is not needed in this reaction. Therefore, a solvent with a lower boiling point, e. g., as 1,2-