Methyl 2-Benzoylamino-3-dimethylamonopropenoate in the Synthesis of Heterocyclic Systems. A Simple Synthesis of Amino Derivatives of Isomeric Naphthopyranones and Naphthodipyranones

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A simple synthesis of the amino derivatives of 3*H*-naphtho[2,1-*b*]pyran-3-one **5b-d**, **8**, **11**, and **20**, 2*H*-naphtho[1,2-*b*]pyran-2-one **14** and **19**, 2*H*,6*H*-naphtho[1,2-*b*:3,4-*b'*]dipyran-2,6-dione **9**, 2*H*,11*H*-naphtho[2,1-*b*:3,4-*b'*]dipyran-2,11-dione **12**, and 3*H*,9*H*-naphtho[1,2-*b*:5,6-*b'*]dipyran-3,9-dione **15** from the corresponding monohydroxynaphthalenes **2c,d**, dihydroxynaphthalenes **2b**, **7**, **10**, and **13**, and tetralones **16** and **17** with methyl 2-benzoylamino-3-dimethylaminopropenoate (**3**) in acetic acid is described.

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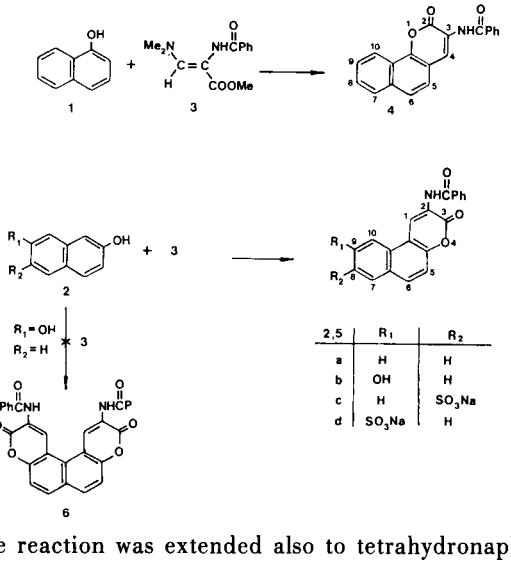
The naphthopyranones include 2*H*-naphtho[1,2-*b*]pyran, 3*H*-naphtho[2,1-*b*]pyran, naphtho[1,8-*bc*]pyran, and 1*H*,3*H*-naphtho[1,8-*cd*]pyran. There are many methods of preparation described in the literature, which are in principle very similar to those known in benzopyran series [1].

Methyl 2-benzoylamino-3-dimethylaminopropenoate [3] has been recently introduced in our laboratory for the synthesis of α-arylamino-α,β-dehydro-α-amino acid derivatives [2], β-heteroarylamino-α,β-dehydro-α-amino acids and dipeptides [3-6], and monocyclic, bicyclic and polycyclic systems, in which the α-amino acid structural element is incorporated in the ring system, such as pyranones [7], benzopyranones [8], pyranobenzopyranones [9], fused pyrimidines [8,10], pyranoazoles [8] and pyranoazines [8]. While unsubstituted phenol does not react with **3** in acetic acid, 1- and 2-naphthol have been found to give the corresponding 3-benzoylamino-2*H*-naphtho[1,2-*b*]pyran-2-one (**4**) and 2-benzoylamino-3*H*-naphtho[2,1-*b*]pyran-3-one (**5a**), respectively [9].

In this communication we report a further application of this reagent for the preparation of some derivatives of 2*H*-naphtho[1,2-*b*]pyran-2-one and 3*H*-naphtho[2,1-*b*]pyran-3-one, 2*H*,6*H*-naphtho[1,2-*b*:3,4-*b'*]dipyran-2,6-dione, 2*H*,11*H*-naphtho[2,1-*b*:3,4-*b'*]dipyran-2,11-dione, and 3*H*,9*H*-naphtho[1,2-*b*:5,6-*b'*]dipyran-2,9-dione. The following naphthalene derivatives were selected: 2-hydroxy-6-sulphonic acid (**2c**) and 2-hydroxy-7-sulphonic acid (**2d**) in the form of their sodium salts, 1,3-dihydroxy- (**7**), 2,3-dihydroxy- (**10**), 1,5-dihydroxy- (**13**) and 2,7-dihydroxynaphthalene (**2b**). The compounds **2b,c,d** gave by heating in acetic acid the corresponding sodium 8- (**5c**) and 9-sulphonate (**5d**) and 9-hydroxy (**5b**) derivatives of 3*H*-naphtho[2,1-*b*]pyran-2-one. On the other hand, the dihydroxynaphthalenes **7**, **10**, and **13** afforded mixtures of naphthopyranones and naphthodipyrandiones. Thus, the compound **7** gave 3*H*-naphtho[2,1-*b*]pyran-3-one **8** and 2*H*,6*H*-naphtho[1,2-*b*:3,4-*b'*]dipyran-2,6-dione **9** in 35% and 6.3% yield, **10** was converted into 3*H*-naphtho[2,1-*b*]pyran-3-one **11** and 2*H*,11*H*-naphtho[2,1-*b*:3,4-*b'*]-dipyran-2,11-dione **12** in 48% and 13% yield, and from **13** a mixture of 2*H*-naphtho[1,2-*b*]pyran-2-one **14** and 3*H*,9*H*-naphtho[1,2-*b*:5,6-*b'*]dipyran-3,9-dione **15** in 25% and 13% yield were obtained, respectively. The only exception is 2,7-dihydroxynaphthalene (**2b**) from which the corresponding naphthodipyran derivative **6** was not formed most probably due to steric hindrance (Schemes 1 and 2).

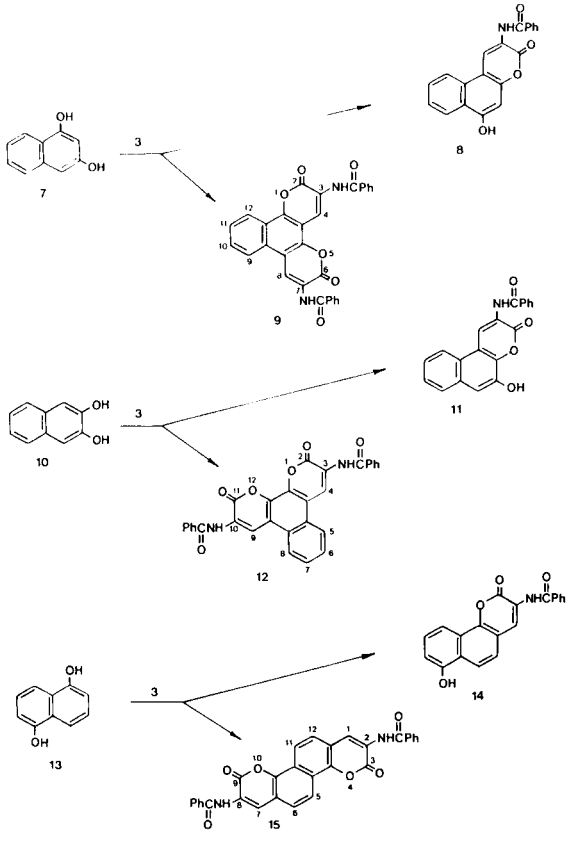
Scheme 1



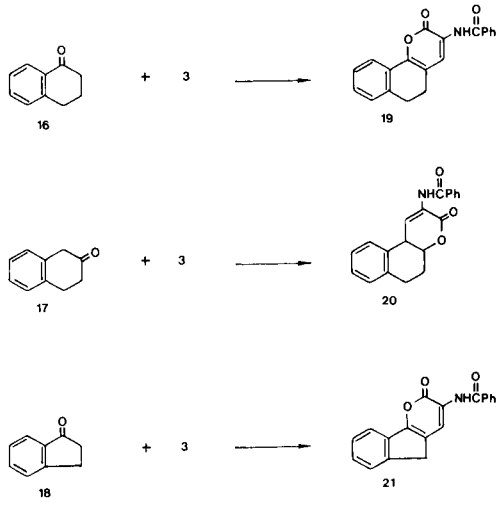
The reaction was extended also to tetrahydronaphthalene derivatives 1-tetralone (**16**) and 2-tetralone (**17**), and 1-indanone (**18**) to give the corresponding 5,6-dihydronaphtho[1,2-*b*]pyran-2-one derivative (**19**), 5,6-dihydronaphtho[2,1-*b*]pyran-3-one (**20**), and 5*H*-indano[1,2-*b*]pyran-2-one derivative (**21**) in 17%, 16%, and 24% yield, respectively (Scheme 3).

The reaction proceeds as a nucleophilic attack of the anion, formed from the hydroxynaphthalene derivative to the protonated form of the reagent, followed by elimina-

Scheme 2



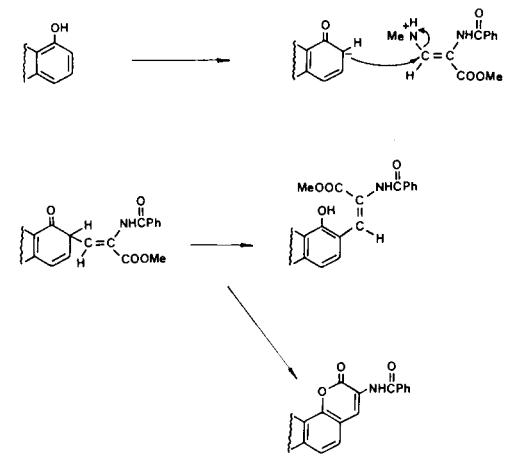
Scheme 3



tion of dimethylamine and further cyclization of the tautomeric form of the intermediate into the fused pyranone system (Scheme 4).

The structure of 3*H*-naphtho[2,1-*b*]pyran-3-ones derived from 2-hydroxynaphthalenes is unambigous, according to the evidence published previously for unsubstituted system [9].

Scheme 4



The structure of naphthodipyrandiones **9**, **12**, and **15** are also clear, since there are no other possibilities. On the other hand, in the formation of monopyrano fused systems, derived from dihydroxynaphthalenes, the question arises, which position is more reactive and which hydroxy group is involved in the cyclization. The answer to this question was obtained from the chemical shifts of proton at position 4 (*para* position) in respect to oxygen atom in the pyranone ring. Namely, the chemical shift of this proton is strongly dependent upon the type of ring fusion. When the proton is in the amphi position, such as in the systems **5**, **8**, and **11** it appears at δ = 9.07-9.60 ppm, when this proton is in peri position such as in systems **4**, and **14**, it appears at δ = 8.60-8.90 ppm (Table 1).

Table 1

Compound	δH [ppm] peri		amphi	
4	H_4	8.80 [9]		
5a			H_1	9.43 [9]
5b			H_1	9.30
5c			H_1	9.60
5d			H_1	9.47
8			H_1	9.20
9	H_4	8.90	H_8	9.13
11			H_1	9.34
12			H_4	9.07
			H_9	9.07
14	H_4	8.77		
15	H_1	8.63		
	H_7	8.63		

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a JEOL JNM FX 90Q FT or VARIAN EM-360 L instruments and microanalyses for C, H, and N on

a Perkin-Elmer Analyser 2400.

Methyl 2-benzoylamino-3-dimethylaminopropenoate (**3**) was prepared according to the procedure described previously [5].

The following compounds were prepared according to essentially the same procedure as described in the literature for compounds **4** and **5a** [9]:

2-Benzoylamino-9-hydroxy-3*H*-naphtho[2,1-*b*]pyran-3-one (**5b**).

This compound was prepared from **2b** and **3** in 73% yield, mp >320° (from a mixture of DMF, ethanol and water); ^{1}H nmr (DMSO-d_6): δ 7.07-8.10 (m, 10H, H_5, H_6, H_7, H_8, H_{10}, PhCO), 9.30 (s, 1H, H_1), 9.67 (br s, 1H, NHCO), 10.20 (br s, 1H, OH).

Anal. Calcd. for $C_{20}H_{13}NO_4$: C, 72.50; H, 3.95; N, 4.23. Found: C, 72.17; H, 4.07; N, 4.16.

Sodium 2-Benzoylamino-3*H*-naphtho[2,1-*b*]pyran-2-one-8-sulphonate (**5c**).

This compound was prepared from **2c** and **3** in 8% yield, mp >310° (from a mixture of ethanol and water); ^{1}H nmr (DMSO-d_6): δ 7.63-8.50 (m, 10H, H_5, H_6, H_7, H_8, H_{10}, PhCO), 9.60 (s, 1H, H_1), 9.90 (br s, 1H, NHCO).

Anal. Calcd. for $C_{20}H_{12}NO_6SNa$: C, 57.56; H, 2.90; N, 3.36. Found: C, 57.37; H, 3.24; N, 3.25.

Sodium 2-Benzoylamino-3*H*-naphtho[2,1-*b*]pyran-2-one-9-sulphonate (**5d**).

This compound was prepared from **2d** and **3** in 11% yield, mp >310° (from a mixture of DMF, ethanol and water); ^{1}H nmr (DMSO-d_6): δ 7.57-8.23 (m, 9H, H_5, H_6, H_7, H_8, PhCO), 8.63 (s, 1H, H_{10}), 9.47 (s, 1H, H_1), 9.83 (br s, 1H, NHCO).

Anal. Calcd. for $C_{20}H_{12}NO_6SNa$: C, 57.56; H, 2.90; N, 3.36. Found: C, 57.49; H, 3.14; N, 3.21.

2-Benzoylamino-6-hydroxy-3*H*-naphtho[2,1-*b*]pyran-3-one (**8**) and 3,7-Dibenzoylamino-2*H*,6*H*-naphtho[1,2-*b*:3,4-*b'*]dipyran-2,6-dione (**9**).

A mixture of **7** (480 mg, 0.003 mole) and **3** (2.232 g, 0.009 mole) in acetic acid (10 ml) was heated under reflux for 2 hours. The solid separated after cooling to room temperature was collected by filtration to give 535 mg of **8** and **9**. The mixture was added to the boiling DMF during vigorous stirring. The remaining solid was collected by filtration to give **9** (95 mg, 6.3%), mp >320° (from DMF); ^{1}H nmr (deuteriosulfuric acid): δ 7.17-8.33 (m, 14H, H_9, H_{10}, H_{11}, H_{12}, 2 x PhCO), 8.90 (s, 1H, H_4), 9.13 (s, 1H, H_8).

Anal. Calcd. for $C_{30}H_{18}N_2O_6$: C, 71.71; H, 3.61; N, 5.57. Found: C, 71.90; H, 3.65; N, 5.50.

To the filtrate water (5 ml) was added and the precipitate was collected by filtration to give **8**, (344 mg, 35%), mp >320° (from a mixture of DMF, ethanol and water); ^{1}H nmr (deuteriosulfuric acid): δ 7.10-8.13 (m, 14H, H_5, H_6, H_7, H_8, 2 x PhCO), 9.07 (br s, 2H, H_4, H_9).

Anal. Calcd. for $C_{20}H_{13}NO_4$: C, 72.50; H, 3.95; N, 4.23. Found: C, 72.79; H, 4.03; N, 4.26.

Compound **8** can be prepared in the following way:

A mixture of **7** (0.8 g, 0.005 mole) and **3** (1.24 g, 0.005 mole) in acetic acid (10 ml) was heated under reflux for 30 minutes. The precipitate was, after cooling to room temperature, collected by filtration to give **8** (1.60 g, 97%), mp 320° (from a mixture of DMF, ethanol and water). The compound was identical with that obtained above.

2-Benzoylamino-5-hydroxy-3*H*-naphtho[2,1-*b*]pyran-3-one (**11**) and 3,10-Dibenzoylamino-2*H*,11*H*-naphtho[2,1-*b*:3,4-*b'*]dipyran-2,11-dione (**12**).

A mixture of these two compounds was prepared from **10** and **3**, yield 798 mg. The mixture was suspended in DMF (15 ml) and during vigorous stirring compound **11** was dissolved. The residue was collected by filtration to give **12** (193 mg, 13%), mp >320° dec (from DMF); ^{1}H nmr (deuteriosulfuric acid): δ 7.10-8.13 (m, 14H, H_5, H_6, H_7, H_8, 2 x PhCO).

Anal. Calcd. for $C_{30}H_{18}N_2O_6 \cdot H_2O$: C, 69.23; H, 3.87; N, 5.38. Found: C, 69.32; H, 3.61; N, 5.52.

To the DMF solution obtained above water (30 ml) was added. The precipitate was collected by filtration to give **11** (478 mg, 48%), mp 245° dec (from a mixture of DMF and ethanol); ^{1}H nmr (DMSO-d_6): δ 7.43-8.17 (m, 10H, H_6, H_7, H_8, H_9, H_{10}, PhCO), 9.34 (s, 1H, H_1), 9.78 (br s, 1H, NHCO).

Anal. Calcd. for $C_{20}H_{13}NO_4$: C, 72.50; H, 3.95; N, 4.23. Found: C, 72.13; H, 4.25; N, 3.98.

3-Benzoylamino-7-hydroxy-2*H*-naphtho[1,2-*b*]pyran-2-one (**14**) and 2,8-Dibenzoylamino-3*H*,9*H*-naphtho[1,2-*b*:5,6-*b'*]dipyran-3,9-dione (**15**).

A mixture of these two compounds was obtained from **13** and **3**, yield 785 mg. The mixture was suspended in DMF (15 ml) and during vigorous stirring compound **14** was dissolved. The solid residue was collected by filtration to give **15** (105 mg, 7%), mp >320° (from DMF); ^{1}H nmr (deuteriosulfuric acid): δ 7.30-8.40 (m, 14H, H_5, H_6, H_{11}, H_{12}, 2 x PhCO), 8.63 (s, 2H, H_1, H_7).

Anal. Calcd. for $C_{30}H_{18}N_2O_6$: C, 71.71; H, 3.61; N, 5.57. Found: C, 71.95; H, 3.58; N, 5.54.

To the DMF solution obtained above water (30 ml) was added and the precipitate was collected by filtration to give **14** (422 mg, 43%), mp >275° dec (from ethanol); ^{1}H nmr (DMSO-d_6): δ 7.00-8.14 (m, 10H, H_5, H_6, H_8, H_9, H_{10}, PhCO), 8.77 (s, 1H, H_4), 9.73 (br s, NHCO).

Anal. Calcd. for $C_{20}H_{13}NO_4$: C, 72.50; H, 3.95; N, 4.23. Found: C, 72.40; H, 4.13; N, 4.21.

3-Benzoylamino-2(5*H*)-indano[1,2-*b*]pyranone (**21**).

To a mixture of **18** (661 mg, 0.005 mole) and **3** (1.24 g, 0.005 mole) in dry DMF (25 ml) zinc chloride (2 g) was added and the solution was heated under reflux for 1 hour. The precipitate, formed after standing for 24 hours at room temperature, was collected by filtration to give **21** (132 mg). Water was added to the filtrate, and the precipitate was collected by filtration to give additional 252 mg of **21**, combined yield 24%, mp 243-244° (from methanol); ^{1}H nmr (DMSO-d_6), 150°, δ 3.73 (s, 2H, 5-CH_2), 7.23-7.63 (m, 7H, H_6, H_7, H_8, H_9, $H_{3'}$, $H_{4'}$, $H_{5'}$, (PhCO)), 7.76-8.00 (m, 2H, $H_{2'}$, $H_{6'}$ (PhCO)), 8.43 (s, 1H, H_4), 9.00 (br s, 1H, NHCO).

Anal. Calcd. for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.19; H, 4.29; N, 4.28.

In the same manner the following compounds were obtained:

3-Benzoylamino-2(5*H*,6*H*)-naphtho[1,2-*b*]pyranone (**19**).

This compound was obtained from **16** and **3** in 17% yield, mp 188-191° (from a mixture of ethanol and water); ^{1}H nmr (DMSO-d_6): δ 2.72-3.02 (m, 4H, $-CH_2CH_2O$), 7.37-8.13 (m, 9H, H_7, H_8, H_9, H_{10}, PhCO), 8.23 (s, 1H, H_4), 9.58 (br s, 1H, NHCO).

Anal. Calcd. for $C_{20}H_{15}NO_3$: C, 75.69; H, 4.76; N, 4.41. Found: C, 75.44; H, 4.80; N, 4.46.

2-Benzoylamino-3(5*H*,6*H*)-naphtho[2,1-*b*]pyranone (**20**).

This compound was prepared from **17** and **3** in 66% yield, mp 204-207° (from a mixture of DMF, ethanol and water); ^{1}H nmr (DMSO-d_6), 150°, δ 2.85-2.95 (m, 4H, $-CH_2CH_2-$), 7.17-7.60 (m, 7H, $H_{3'}$, $H_{4'}$, $H_{5'}$ (PhCO), H_7, H_8, H_9, H_{10}), 7.83-8.00 (m, 2H, $H_{2'}$, $H_{6'}$ (PhCO)), 8.60 (s, 1H, H_1), 9.07 (br s, 1H, NHCO).

Anal. Calcd. for $C_{20}H_{15}NO_3$: C, 75.69; H, 4.76; N, 4.41. Found: C, 75.39; H, 4.83; N, 4.39.

Acknowledgement.

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