26. The Reaction of 3-Formylchromone with *ortho*-Substituted Anilines. Preparation of a Tetraaza[14]annulene

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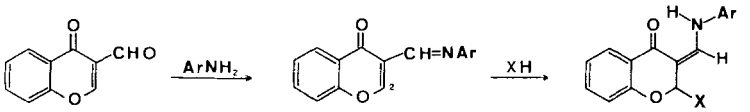
Summary

The reactions of 3-formylchromone (**1**) with 1,2-phenylenediamine, 2-aminodiphenylamine and 2-aminophenol were reinvestigated and shown to yield 1,8-dihydro-6, 13-di (2-hydroxybenzoyl)-dibenzo [*b, i*]-1, 4, 8, 11-tetraazacyclotetradeca-4,6,11,13-tetraene (**7**), 3-[2-(1-phenyl)benzimidazolyl]chromone (**10b**) and 3-(2-hydroxyphenyl)iminomethylchromone (**4**), respectively at variance with earlier reports. Compound **4** reacts with ethanol to give 2-ethoxy-3-[(2-hydroxyphenyl)-aminomethylidene]chroman-4-one (**5b**). Dehydrogenation of **7** produces 3-(2-benzimidazolyl)chromone (**10a**), also at variance with earlier reports. The structures have been elucidated with the aid of NMR. and mass spectra. The reaction mechanism is discussed.

Introduction. – 3-Formylchromone (**1**) reacts with primary aromatic amines to give the anils **2**, the C(2) atom of which is strongly activated towards nucleophilic substitution [1–4]. Compounds **2** react *e.g.* with alcohols, thiols, secondary amines, anilines and water [3] to form compounds of type **3**, some of which are rather unstable.



1 **2** **3**

X = OR, SR, OH, NR_2, NHAr

These compounds **3** show a characteristic *trans*-vicinal coupling of 12–13 Hz between the olefinic and the amino proton [1]. Compound **1** also reacts with aromatic amines carrying an additional reactive group in the *ortho*-position (*e.g.* OH, NH_2, NHC_6H_5, SH) [4] [5]. The reported [4] [5] structure of the reaction product of 1,2-phenylenediamine with **1**, however, differed from the results we obtained in the course of our studies on the synthesis of pyridines from **1** [6]. We

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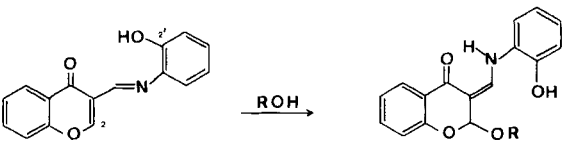
therefore also repeated the reaction of 2-aminophenol and 2-aminodiphenylamine with **1**, and we now report the structure of the products.

Results and discussion. – The reaction product with 2-aminophenol is **4**. The ^{1}H-NMR. spectrum shows two vinyl protons (2*s*) at 9.32 and 8.83 *(Exper. Part)*. If H_2O is added to a solution of **4** in D_6-DMSO, **5a** is obtained (6.17 ppm, $J = 5$ Hz for H–C(2) with H–O; $J(trans) = 13$ Hz between the olefinic proton and H–N). The ^{1}H-NMR. spectrum of **5a** is very similar to that of **4d** in [4] (= **8c**) except for the coupling between H–C(2) and H–O, which is easily averaged out with a trace of acid.

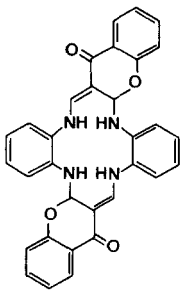


4 **5**

a R = H
b R = Et

Recrystallization of **4** in ethanol affords **5b**. The ethoxy group appears as a ABX_3-system in the ^{1}H-NMR. spectrum owing to the chiral center at C(2) proving that the ethoxy group is indeed part of the molecule. Ethanol is easily split off again upon heating **5b**, so that **4** and **5b** have apparently the same melting point, identical with that of **4d** in [4] (**8c**). In the field desorption (FD.) mass spectrum, the molecular ion of **5b** ($m/z = 311$) can be observed besides the *M*-EtOH peak ($m/z = 265$). The compounds **4a**, **4b**, **4e** and **4f** in [4] (= **8a**, **8b**, **8d**, **8e**) are reported to have a coupling constant of 12–13 Hz between olefinic and amino protons and have, therefore, probably the analogous structures of type **5**. This coupling requires a *trans*-arrangement of the two protons since the *cis*-coupling is considerably smaller (*cf. e.g.* [7]).

The reaction of **1** with 1,2-phenylenediamine does not yield the anil analogous to **4** but the dihydrotetraaza[14]annulene **7**. Its structure is proven mainly by its simple ^{1}H-NMR. spectrum. The six protons of the 14-membered ring form two identical A_2X systems, *i.e.* two olefinic protons of the same chemical shift couple with the same coupling constant (6.5 Hz) with one amino proton forming a triplet. This is characteristic for such a ring system [8]. There are only two different chemical shifts for the two phenylenediamine aromatic rings and only four for the salicyloyl aromatic rings. Compound **7** is, therefore, highly symmetrical (D_{2h}) in the NMR. time scale. Structure **7** is proven, furthermore, by the ready formation of its Ni, Cu and Zn complexes, a well known [9] reaction of this ring system (the ^{1}H-NMR. spectrum of the Zn complex is given in the *Exper. Part*). The molecular ion ($m/z = 528$) is present in the FD. mass spectrum. Treatment of **7** with acetic acid according to [5] yields **10a** (see below) *inter alia*, which has the same melting point as **8a** in [5] (= **11a**). Since all the data presented are in disagreement with the diazepinone structure **8** (no chromane CH, no *AX*-system of olefinic and NH proton *etc.*), **4g** in [4] (= **8f**) and **4a** in [5] (= **2**, Ar = *o*-$NH_2C_6H_4$) must be assigned



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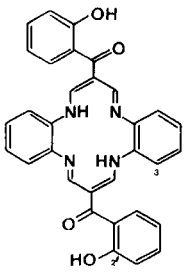
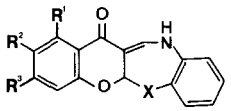


7



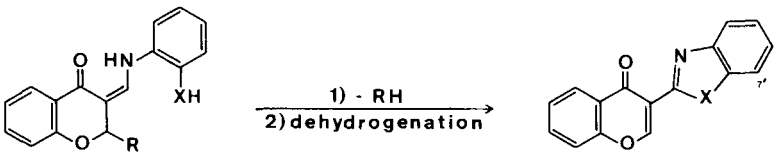
8

a X = S, $R^1 = R^2 = R^3 = H$ (corresponds to (**4a**) in [4])
b X = S, $R^1 = R^3 = CH_3$, $R^2 = H$ (corresponds to (**4b**) in [4])
c X = O, $R^1 = R^2 = R^3 = H$ (corresponds to (**4d**) in [4])
d X = O, $R^1 = R^3 = H$, $R^2 = CH_3$ (corresponds to (**4e**) in [4])
e X = O, $R^1 = R^3 = CH_3$, $R^2 = H$ (corresponds to (**4f**) in [4])
f X = NH, $R^1 = R^2 = R^3 = H$ (corresponds to (**4g**) in [4])

structure **7**. Similar tetraaza[14]annulenes have been prepared from 1,2-phenylenediamine and propynal [9]. Corresponding metal complexes are also known [9] [10]. A general template reaction of 1,2-phenylenediamine and 1,3-dicarbonyl compounds produces the metal complexes directly [11].

Compound **7** is presumably formed *via* **6** which is analogous to **5** and can be formed by a nucleophilic substitution at C(2) of one anil by the free amino group of another. This reaction corresponds to that of the anil **2** with anilines. The reversibility of the reaction at C(2) [3] and the insolubility of the tetraaza[14]annulenes [9] favors the formation of **7** which is thereby continuously removed from the equilibrium and is formed in high yield.

The adducts of type **9** form the corresponding benzoheteroazoles **10** under dehydrogenation (*cf.* [4]).



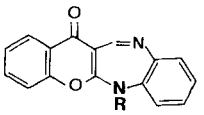
9
R: *cf.* X in **3**

10
a X = NH
b X = NØ

The structure elucidation of **10a** is especially straightforward since the benzimidazole part of the molecule appears as an *AA'BB'*-system in the ^{1}H-NMR. spectrum in CD_3OD precluding any dissymetric structure. In D_6-DMSO, however, the NH side exchange is slow, and an *ABMN*-system is obtained. The solubility of **10b** enabled us also to measure the ^{13}C-NMR. spectrum. The atom C(7') is found at

110.3 ppm, a value typical for a benzimidazole [12]. This high field shift as compared to 1,2-phenylenediamine (115.6 ppm) is caused by the annelation of a five-membered ring [13]. The corresponding C-atom in larger annelated rings has a signal at much lower field (~121 ppm) (*cf. e.g.* [14]). Having shown that the compounds formulated as **7g** and **7l** in [4] (= **11a**, **11b**) are in fact the benzimidazoles **10a** and **10b**, we suggest on the basis of the similarity of the reported UV. spectra of the remaining compounds of type **7** in [4], that they also possess a benzoheteroazole structure.

A ring closure starting from **9** is a favored '5-*exo*-trig' process [15] and not a disfavored '5-*endo*-trig' process as the authors [4] assumed on the basis of a different structure.



11a (corresponds to **7g** in [4] and to **8a** in [5] for R = H)
11b (corresponds to **7l** in [4] for R = C_6H_5)

Experimental Part

General remarks: see [16].

The preparations of **4**, **7**, **10a** and **10b** have been reported [4] [5].

Preparation of 2-ethoxy-3-[(2-hydroxyphenyl)aminomethylidene]chroman-4-one (**5b**). After refluxing a solution of 10 g **4** in 500 ml of ethanol for 10 min the reaction mixture was cooled to 0°, and the precipitated **5b** was filtered off (6 g, 39%); m.p. 217–219°.

$C_{18}H_{17}NO_4$ Calc. C 69.44 H 5.51 N 4.50% Found C 69.58 H 5.39 N 4.69%

Preparation of metal complexes of 1,8-dihydro-6,13-di(2-hydroxybenzoyl)-dibenzo[b,i]-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraene (**7**). A hot solution of 4 g **7** in 60 ml dry. *N,N*-dimethylformamide was added to a hot solution of 1.9 g nickel(II) acetate aq. in 20 ml of the same solvent. The precipitated nickel complex of **7** was filtered off, washed with ethanol and ether and vacuum-dried (3.5 g of red crystals, 76%): m.p. > 300°.

$C_{32}H_{22}N_4NiO_4$ Calc. C 65.67 H 3.79 N 9.57 Ni 10.03%
Found „ 65.55 „ 3.93 „ 9.64 „ 9.76%

By the same procedure **7** and copper (II) acetate-aq. or zinc-acetate-aq. yielded brown copper-complex of **7** (89%), m.p. > 300°.

$C_{32}H_{22}N_4O_4Cu$ Calc. Cu 10.77% Found Cu 10.80%

Red zinc-complex of **7** (62%), m.p. > 300°.

$C_{32}H_{22}N_4O_4Zn.\ 1/2\ H_2O$ Calc. Zn 10.87% Found Zn 10.60%

Spectra. The ^{1}H-NMR. spectra were recorded with a *Bruker* HX 360 and a WM 250 spectometer, the ^{13}C-NMR. spectra with a *Varian* XL 100 and a *Bruker* WM 250 spectometer.

Spectral data of 3-(2-hydroxyphenyl)iminomethylchromone (**4**). ^{1}H-NMR. (D_6-DMSO): 9.32 (*s*, N=CH); 9.05 (br. *s*, OH); 8.83 (*s*, H–C(2)); 8.19 (*d*×*d*, H–C(5)); 7.87 (*t*×*d*, H–C(7)); 7.76 (*d*, H–C(8)); 7.57 (*t*×*d*, H–C(6)); 7.24 (*d*×*d*, H–C(6′)); 7.12 (br. *t*, H–C(4′)); 6.86 (*m*, H–C(3′,5′)). – ^{1}H-NMR. ($CDCl_3$): 9.09 (*s*, N=CH); 8.83 (*s*, H–C(2)); 8.37 (*d*×*d*, H–C(5)); 7.75 (*t*×*d*, H–C(7)); 7.56 (*d*, H–C(8)); 7.50 (*t*×*d*, H–C(6)); 7.37 (*d*×*d*, H–C(6′)); 7.23 (*t*×*d*, H–C(4′)); 7.11 (br. *s*, OH); 7.02 (*d*×*d*, H–C(3′)); 6.93 (*t*×*d*, H–C(5′)). – MS. *m/z* (int): 266 (18), 265 (100, M), 264 (88), 247 (14), 236 (28), 172 (16), 160 (13), 146 (23), 121 (18), 120 (35), 105 (15), 104 (13).

Spectral data of 2-hydroxy-3-[(2-hydroxyphenyl)aminomethylidene]chroman-4-one (**5a**). ^{1}H-NMR. (D_6-DMSO): 11.98 (*d*, *J* = 13, NH); 10.32 (br. *s*, phenol OH); 8.04 (*d*, *J* = 13, =CH–N); 7.83 (*d*×*d*, H–C(5)); 7.46 (*t*×*d*, H–C(7)); 7.23 (*d*, *J* = 5, HO–C(2)); 6.8–7.1 (remaining arom. H); 6.17 (*d*, *J* = 5, H–C(2)).

Spectral data of 2-ethoxy-3-[(2-hydroxyphenyl)aminomethylene]chroman-4-one (**5b**). ^{1}H-NMR. (D_6-DMSO): 12.0 (*d*, *J* = 13, NH); 10.3 (br. *s*, OH); 8.12 (*d*, *J* = 13, =CH–N); 7.83 (*d*×*d*, H–C(5)); 7.48 (*t*×*d*, H–C(7)); 6.8–7.15 (remaining aromatic H); 5.95 (*s*, H–C(2)); 3.75 and 1.15 (*ABX*$_3$, Et). – ^{13}C-NMR. (D_6-DMSO) (multiplicities given for the proton-coupled spectrum): 179.5 (C(4)); 155.4 (C(8a); 146.0 (C(2′)); 144.0 (*d*×*d*, *C*H–C(3)); 134.0 (C(7)); 127.7 (C(1′)); 125.5 and 124.1 (C(5,6)); 122.8 (C(4a)); 121.7, 119.8, 117.8, 115.5 and 114.1 (other aromatic CH); 103.3 (C(3)); 100.1 (br. *d*, C(2)); 62.8 (CH_2); 14.9 (CH_3). – FD.-MS. *m/z*: 311 (M), 265 (M-EtOH). Molecular weight determination ($CDCl_3$): Calc. 311, Found 329.

Spectral data of compound **7**. ^{1}H-NMR. (D_6-DMSO): 14.3 (*t*, *J* = 6, NH); 10.15 (*s*, OH); 8.54 (*d*, *J* = 6, =CH–N); 7.35 (*m*, H–C(4′,6′)); 7.29 and 7.15 (*AA′BB′* of H–C(3,6) and H–C(4,5)); 6.98 (H–C(3′)); 6.95 (H–C(5′)). – ^{1}H-NMR. ($CDCl_3$): 14.57 (*t*, *J* = 6.5, NH); 11.4 (*s*, OH); 8.60 (*d*, *J* = 6.5, =CH–N); 7.59 (*d*×*d*, H–C(6′)); 7.49 (*d*×*d*×*d*, H–C(4′)); 7.27 and 7.16 (*AA′BB′*, H–C(3,6) and H–C(4,5)); 7.09 (d×d, H–C(3′)); 6.95 (*d*×*d*×*d*, H–C(5′)). – EI.-MS. *m/z* (int.): 420 (7) (M – $C_6H_4(NH_2)_2$), 300 (12), 264 (48), 263 (76), 262 (100), 235 (26), 119 (56). – FD.-MS. (*m/z*): 528, 420, 264.

Spectral data of the Zn-complex of **7**. ^{1}H-NMR. (D_6-DMSO): 10.06 (br. *s*, OH); 8.59 (*s*, =CH–N); 7.33 (H–C(4′)); 7.27 (H–C(6′)); 7.19 and 7.07 (*AA′BB′*, H–C(3,6) and H–C(4,5)); 6.94 (H–C(3′)); 6.91 (H–C(5′)).

Spectral data of 3-(2-benzimidazolyl)chromone (**10a**). ^{1}H-NMR. (D_6-DMSO): 12.55 (br. *s*, NH); 9.34 (*s*, H–C(2)); 8.28 (H–C(5)); 7.91 (H–C(7)); 7.79 (H–C(8)); 7.68 and 7.63 (H–C(4′,7′)); 7.62 (H–C(6)); 7.2 (H–C(5′,6′)). – ^{1}H-NMR. (CD_3OD): 9.19 (*s*, H–C(2)); 8.36 (H–C(5)); 7.89 (H–C(7)); 7.73 (H–C(8)); 7.60 (H–C(6)); 7.67 and 7.29 (*AA′XX′*, H–C(4′,7′) and H–C(5′,6′). – MS. *m/z* (int.): 263 (22), 262 (100, M), 205 (9), 194 (7), 142 (19), 131 (6).

Spectral data of 3-[2-(1-phenyl)benzimidazolyl]chromone (**10b**). ^{1}H-NMR. (D_6-DMSO): 8.82 (*s*, H–C(2)); 7.92 (H–C(5)); 7.84 (H–C(7)); 7.80 (H–C(4′)); 7.71 (H–C(8)); 7.49 (H–C(6)); 7.3–7.5 (remaining aromatic H). – ^{13}C-NMR. (D_6-DMSO): 173.5 (C(4)); 158.8 (C(2)); 155.6 (C(8a)); 146.0 (C(2′)); 142.4 (C(3a′)); 136.1 and 135.9 (C(1″,7a′)); 134.7 (C(7)); 129.4, 128.2, 126.2 (C(3″,4″,5″,6″ and 5)); 125.1 and 123.5 (C(6,6′)); 123.2 (C(4a)); 122.5 (C(5′)); 119.4 (C(4′)); 118.6 (C(8)); 116.6 (C(3)); 110.3 (C(7′)).

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