Long-Wavelength-Absorbing and -Emitting Carbostyrils with High Fluorescence Quantum Yields

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Synthesis, absorption and fluorescence spectra, as well as quantum yields of a series of donor-acceptor-substituted carbostyrils (=quinolin-2(1*H*)-ones), are reported. Unprecedented strong absorption maxima ($\varepsilon =$ 10000–20000) close to the visible spectrum, large *Stokes* shifts up to 130 nm, and quantum yields up to 0.7 are obtained with derivatives containing donor substituents at C(6) and C(7), and either one Ph substituent at C(3) or one CF_3 residue at C(4). For analytical applications in biochemistry and medicine, *N*(1)-functionalization, or amidoacylation at C(3) in the case of the CF_3 derivatives, is possible without a concomitant hypsochromic shift of their absorption and emission maxima. Semiempirical molecular-orbital calculations (AM1 for structures, ZINDO for electronic transition energies) prove to be a suitable tool for the prediction of absorption properties of these compounds. The crystal-structure analysis of 6,7-dimethoxy-1-methyl-3-nitro-4-(trifluoromethyl)quinolin-2-(1*H*)-one (**7**) ($C_{13}H_{11}F_3N_2O_5$, monoclinic, $P2_1/c$, $a = 12.372(2)$, $b = 12.154(2)$, $c = 10.119(2)$Å, $\beta =$ $112.95(2)^\circ$) shows that the NO_2 group, squeezed between the CF_3 and the C=O group, is oriented almost perpendicularly ($87.8(4)^\circ$) to the ring plane. The intramolecular F···N distance between the CF_3 and the NO_2 group is only 2.513(4)Å.

Introduction. – In a previous publication [1], we described a fairly systematic investigation into the effect of substituents on the spectral-luminescent characteristics of quinolin-2(1*H*)-ones (carbostyrils). The aim of that work was to establish guidelines for the design of long-wavelength-absorbing and -emitting derivatives with potential analytic applications in biochemistry and medicine [2]. Such compounds are required to have high extinction coefficients ε and high fluorescence quantum yields Φ_F, ideally close to 1. Additionally, besides sufficiently large *Stokes* shifts, absorption maxima should be close to the visible spectrum. The latter requirement is also supported by the fact that reasonably priced light-emitting diodes (LED's) have become available [3] as excitation sources emitting at *ca.* 370 nm. A further feature to be fulfilled by compounds with potential application as, *e.g.*, fluorescence marker in biochemistry or medicine, is ready functionalization by simple chemical transformations.

Based on our results obtained previously [1], we now show that, by judiciously choosing the substituents, it is possible to obtain long-wavelength-absorbing and -emitting carbostyril derivatives with high quantum yields. Synthesis and spectral-luminescence characteristics of 19 selected candidates will be described. Since computational methods have proved to be useful tools to aid the design of dyes with special properties [1][4], the experimental results were complemented with semi-empirical molecular-orbital calculations (AM1 [5], ZINDO [6]). In some cases,

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calculations were performed prior to the synthesis, and experimental results obtained afterwards proved to be fairly similar to the theoretical predictions. In case of two potential structures, **21** and **22** (*Table 1*) the preparation could be even omitted, because the calculations did not indicate any advantages of these two compounds.

Table 1. *Photophysical Data for Carbostyrils* **1**–**22** (ν in cm^{-1}).

Compound	ν_{Abs} (exper.)	ε	ν_{abs} (calc.)	f	ν_{flu} (exper.)	Φ_F	$\Delta\nu$
1	28900	9000	28500	0.31	25500	0.09	3400
2	27200	10400	27200	0.36	22700	0.59	4500
3	27300	17400	26900	0.63	23000	0.23	4300
4	27200	20800	27000	0.68	23000	0.28	4200
5	28300	10200	28600	0.32	22400	0.04	5900
6	25500	8810	24700	0.41	[a])		
7	25400	7300	24700	0.40	[a])		
8	[b])		28400	0.38			
9	28600	15100	27500	0.44	23200	0.17	5400
10	28300	12800	27300	0.44	23200	0.20	5100
11	27100	13000	27200	0.41	22100	0.45	5000
12[c])	27700	17200	27200	0.30	25381	0.34	2319
13	27900	4100	27400	0.10	23500	0.05	4400
14	26100	3500	26400	0.11	20500	0.33	5600
15	29000	21100	28500	0.85	24200	0.30	4800
16	27200	9500	26700	0.35	22900	0.57	4300
17	27200	8100	27000	0.05	23100	0.12	4100
18	26800	7200	27400	0.22	22700	0.10	4100
19	28300	8000	27900	0.13	21100	0.10	7200
20	27100	5900	27100	0.20	21900	0.11	5200
21	[b])		26900	0.20			
22	[b])		27000	0.13			

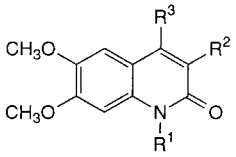
[a]) No fluorescence. [b]) Not prepared. [c]) Not a carbostyril.

Results. – The structures investigated in the present paper are depicted below. The choice of these molecules was guided by the following previous findings: *i*) a MeO group at C(7) leads to relatively high absorption intensities; *ii*) the largest bathochromic shifts are found for 6-MeO derivatives; *iii*) high-fluorescence quantum yields are shown by 3-aryl derivatives; *iv*) linear benzo annulation has a bathochromic effect comparable to MeO substitution at C(6). Consequently, 6,7-dimethoxy derivatives, *e.g.*, **1**–**11**, were promising compounds. Additionally, the CF_3 group has proved to be beneficial for long-wavelength-absorbing and -emitting coumarins [7]. This structural feature, thus, was also incorporated into most of the investigated compounds. Functionalization was accomplished either by alkylation at N(1) or *via* alkylation or acylation of the 3-NH_2 derivatives **8**–**10** (obtainable from the NO_2 compounds **6** and **7**). The strongly fluorescent compound **12**, which is not a carbostyril, was formed by coincidence in an attempt to synthesize **11**.

Absorption Spectra. For solubility reasons, dimethyl sulfoxide (DMSO) and not hexane was used throughout as the solvent. Even in this polar medium, most of the investigated compounds show at least partly resolved vibrational fine structure in their UV spectra. In the long-wavelength region, usually three peaks were discernible with a

	1	2	3	4	5	6	7	8	9	10	11
R^1	H	H	H	H	H	H	Me	H	H	Me	H
R^2	H	H	Ph	Ar*	H	NO_2	NO_2	NH_2	NH_2	NH_2	NHAc
R^3	Me	CF_3	H	H	Ph	CF_3	CF_3	CH_3	CF_3	CF_3	CF_3

* Ar = 4-MeO-Phe



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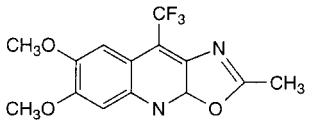

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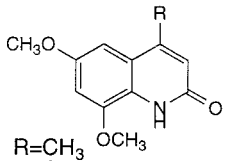
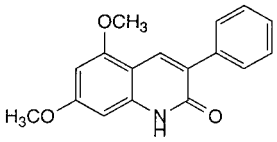


13 R=CH_3
14 R=CF_3



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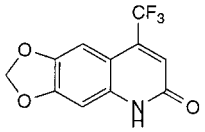

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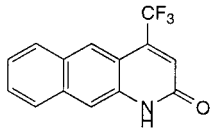

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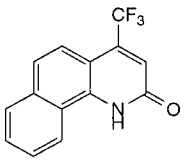

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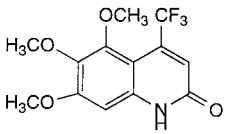

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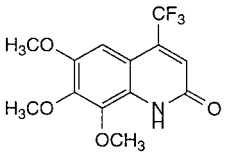

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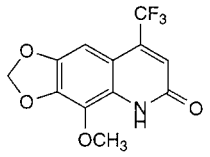

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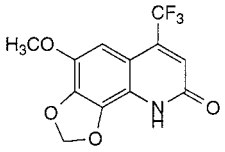

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most intense central absorption or one central peak with two shoulders. Therefore, the data in *Table 1* (ν_{Abs}(exper.) and ε) refer to these central peaks.

First of all, replacement of the Me group at C(4) by CF_3 has a profound (1200–1800 cm^{-1}) bathochromic effect (*e.g.*, **1** *vs.* **2**, **13** *vs.* **14**, **18** *vs.* its CH_3 derivative (ν = 28000 cm^{-1} [1]), whereas this structural modification has little effect on ε. As anticipated, the NO_2 derivatives **6** and **7** (*i.e.*, acceptor at C(3)) are characterized by absorption at the longest wavelength among all investigated compounds even – as

evidenced by both the calculations and the X-ray structure determination – for a nearly perpendicular arrangement of NO_2 with respect to the heterocyclic ring. Reduction of NO_2, yielding the NH_2 derivatives **9** and **10**, leads to a significant hypsochromic effect (*e.g.*, **9** *vs.* **2**). Acetylation of **9**, giving **11**, results in a bathochromically shifted absorption maximum at the desired value of *ca.* 27000 cm^{-1}. In addition, **11** has a reasonably high extinction coefficient ($\varepsilon = 13000$). Interestingly, introduction of a third MeO group has either no effect (**20**) or results in a blue shift (**19**). Compounds **1** and **2** demonstrate the importance of the MeO group at C(7) for high absorption intensities (compare ε of these two compounds with those of **13** and **14**, resp.). Constraining the two donor groups at C(6) and C(7) by incorporation into a five-membered ring system has little effect (**16** *vs.* **2**). Methylation at N(1) (**9** *vs.* **10**) causes no hypsochromic shift at all. Finally, also included in *Table 1* are the calculated transition energies ν (cm^{-1}) and oscillator strengths *f*. Not surprisingly, the largest deviations of calculated from experimental transition energies are found for compounds **9** and **10**, *i.e.*, NH_2-substituted derivatives. In our experience, the effect of NH_2 groups on absorption spectra is significantly underestimated by the ZINDO method [4]. Generally, apart from **9** and **10**, the calculated transition energies closely match the experimental data. Excluding these two molecules, the mean deviation between experimental and calculated wave numbers is *ca.* 400 cm^{-1}. In contrast, as has also been observed in our previous paper, oscillator strengths *f* are only moderately correlated with extinction coefficients. Nevertheless, *f* still appears to be a useful quantity for a rough estimate of absorption intensities. Clearly, the computational procedure used is of predictive value for absorption spectra. Thus, synthesis of compounds **21** and **22** was not attempted, since according to the calculations (see *Table 1*) these two molecules are not expected to be superior to **20**.

Fluorescence Spectra. Experimental fluorescence maxima ν, quantum yields Φ_F as well as *Stokes* shifts $\Delta\nu$ are also collected in *Table 1*. Most important, for several of the investigated compounds, fluorescence quantum yields above 0.5 are obtained. Low values for Φ_F are shown by compounds containing H or Me instead of CF_3 at C(4), *e.g.*, **1**, **5**, and **13**, those lacking the 7-MeO substituent (**13** and **14**), or benzo-annulated derivatives **17** and **18**. The bathochromic shift induced by CF_3 groups on fluorescence maxima is even more pronounced (2000 – 3000 cm^{-1}) than for absorption spectra. *Stokes* shifts are in the range 4000 – 5000 cm^{-1}. Unusually large *Stokes* shifts are found for 4-Ph derivative **5**, which may be caused by a reduction of the Ph torsion in the first electronic excited state, and, especially, for trimethoxy derivative **19**. Thus, in contrast to the absorption maximum, introduction of the third MeO group significantly shifts the emission to longer wavelengths. Unfortunately, this substitution leads to a substantial loss in fluorescence quantum yields. Introduction of an NH_2 group at C(3) causes not only a hypsochromic shift, but also a reduction in Φ_F (compare **2** with **9**). An unusually low *Stokes*' shift, of 2300 cm^{-1} is found for accidentally prepared, strongly fluorescent compound **12**, which is, however, not a carbostyril.

Crystal and Molecular Structure of **7**. The NO_2 group is squeezed between the CF_3 group and the C=O group, and is thereby oriented almost perpendicularly (87.8(4)°) to the ring plane (see *Fig.*) and is not coplanar as observed in nitrobenzene [8] or in other *ortho*-unsubstituted aromatic NO_2 compounds. By the CF_3 group, the NO_2 group is strained towards the C=O group: the bonding angle C(2)–C(3)–N(3) is

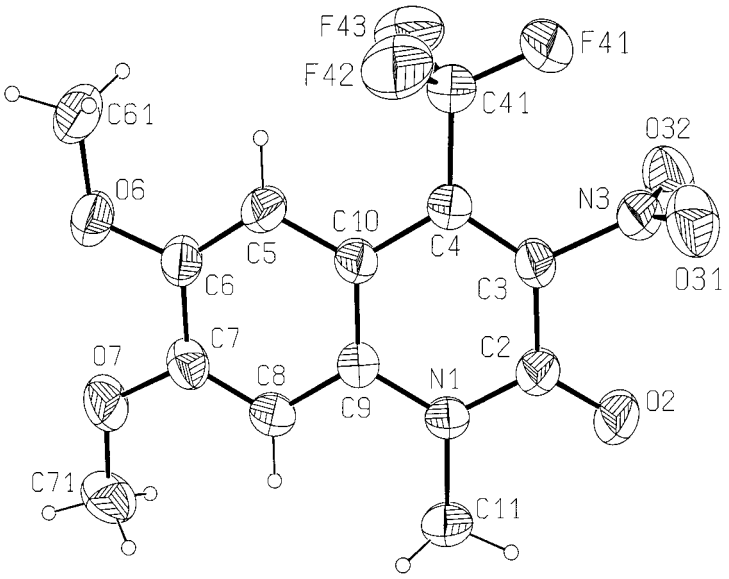

Figure. *Plot of a molecule of compound* **7** *showing the atomic numbering scheme.* The probability ellipsoids are drawn at the 50% probability level, the H-atoms are drawn with arbitrary radii (ORTEP [31]).

diminished from 116.8° in quinolin-2(1*H*)-one [9] to 111.3(2)° in **7**, the intramolecular F(41)···N(3) contact is only 2.513(4)Å compared to the sum of the *van der Waals* radii of 3.02Å [10]. The corresponding calculated (AM1) structural parameters closely match the experimental ones (C(2)–C(3)–N(3)–O(31) = – 89.0°, F(41)–C(41)–C(4)–C(3) = – 0.6°, C(2)–C(3)–N(3) = 113.4°, F(41)···N(3) = 2.514 Å). Selected bonding parameters are given in *Table 2*.

A search in the Cambridge Crystallographic Database [11] for *ortho*-substituted nitro-trifluoromethyl compounds yielded 5 hits with the following torsion angles τ corresponding to F(41)–C(41)–C(4)–C(3) in **7**: if the CF_3 group is encompassed by two NO_2 groups, $|\tau|$ ranges from 91.4 to 95.9° [12][13]; in one compound, the CF_3 group is *cis*-oriented with a C–F bond towards the NO_2 group ($\tau = -7.9°$ [14]) as in **7** [$\tau = -1.6(5)°$], in one compound *trans* with $\tau = 178.4°$ [14], and in one compound $\tau = 80.9°$ [15]. In these compounds, the torsion angles corresponding to O(31)–N(3)–C(3)–C(4) in **7** range from 36.2 to 53.3° if the ring is unsubstituted at the other side of the NO_2 group [12][13][15], but range from 90.2 to 91.4° if the ring is substituted at both sides of the NO_2 group [14].

Conclusion. – Although carbostyrils offer the advantage of greater thermal and chemical stability over the corresponding coumarins, they have attracted considerably less interest as potential analytical reagents. Their major disadvantages were their shorter-wavelength absorption and emission, diminished sensitivity to substituents, and their comparatively low fluorescence quantum yields [16]. In the present paper, we have shown that it is possible, by judiciously choosing the nature and position of substituents, to synthesize long-wavelength-absorbing and -emitting carbostyril deriv-

Table 2. *Selected Bond Lengths* [Å] *and Bond Angles* [°] *for* **7** (for numbering of atoms, see the *Figure*)

N(1)–C(2)	1.377(3)	C(2)–C(3)	1.450(4)
C(3)–C(4)	1.359(4)	C(4)–C(10)	1.444(4)
C(10)–C(5)	1.420(4)	C(5)–C(6)	1.368(4)
C(6)–C(7)	1.420(4)	C(7)–C(8)	1.372(4)
C(8)–C(9)	1.411(4)	C(9)–C(10)	1.406(4)
N(1)–C(9)	1.404(3)	N(1)–C(11)	1.470(3)
C(2)–O(2)	1.233(3)	C(3)–N(3)	1.481(3)
N(3)–O(31)	1.218(3)	N(3)–O(32)	1.223(3)
C(4)–C(41)	1.509(4)	C(41)–F(41)	1.328(3)
C(41)–F(42)	1.328(4)	C(41)–F(43)	1.335(4)
C(6)–O(6)	1.362(3)	O(6)–C(61)	1.425(3)
C(7)–O(7)	1.358(3)	O(7)–C(71)	1.434(4)
C(2)–N(1)–C(9)	123.4(2)	C(2)–N(1)–C(11)	116.7(2)
C(9)–N(1)–C(11)	119.8(2)	N(1)–C(2)–C(3)	114.5(2)
N(1)–C(2)–O(2)	123.2(3)	C(3)–C(2)–O(2)	122.3(2)
C(2)–C(3)–C(4)	125.0(2)	C(2)–C(3)–N(3)	111.3(2)
C(4)–C(3)–N(3)	123.7(2)	C(3)–C(4)–C(10)	118.1(2)
C(3)–C(4)–C(41)	121.9(2)	C(10)–C(4)–C(41)	120.0(2)
C(5)–C(6)–O(6)	125.8(3)	C(7)–C(6)–O(6)	115.0(2)
C(6)–O(6)–C(61)	117.5(2)	C(6)–C(7)–O(7)	114.5(3)
C(8)–C(7)–O(7)	125.1(3)	C(7)–O(7)–C(71)	118.7(2)
C(3)–N(3)–O(31)	118.2(3)	C(3)–N(3)–O(32)	116.5(3)
O(31)–N(3)–O(32)	125.2(3)	C(4)–C(41)–F(41)	113.9(3)
C(4)–C(41)–F(42)	111.6(3)	C(4)–C(41)–F(43)	111.7(3)
C(11)–N(1)–C(2)–O(2)	0.8(4)	O(2)–C(2)–C(3)–N(3)	1.3(4)
C(2)–C(3)–N(3)–O(31)	– 87.3(3)	C(2)–C(3)–N(3)–O(32)	89.0(3)
N(3)–C(3)–C(4)–C(41)	– 4.1(4)	C(3)–C(4)–C(41)–F(41)	– 1.6(5)
C(5)–C(6)–O(6)–C(61)	– 6.8(4)	C(8)–C(7)–O(7)–C(71)	– 6.2(5)

atives with sufficiently high absorption intensities (extinction coefficients ε) and fluorescence quantum yields Φ_F. Specifically, derivatives containing a CF_3 group at C(4) and MeO groups at C(7) show excellent photophysical properties. In addition, the MeO substituent at C(6) is required for absorption and emission at sufficiently long wavelengths. Evidently, compound **2**, analogue type **16**, and especially compounds of type **11**, derived from precursor **9**, ideally fulfill the requirements outlined in the introduction ($\lambda_{abs} \geq 370$ nm; $\lambda_F \geq 450$ nm; sufficiently high absorption intensity and fluorescence quantum yield, possibility to form linkages without decrease in wavelength). However, it should also be noted that carbostyrils with substitution patterns as in **4** and **15** exhibit outstanding photophysical data (see *Table 1*) which could be used for further exploration.

Experimental Part

General. Chemicals and reagents were purchased from *Aldrich* or *Fluka*, and used without further purification. M.p.: *Gallenkamp Melting Point Apparatus*, model *MPD-350*, in open capillary tubes. IR Spectra: *Perkin-Elmer 298* spectrophotometer, in KBr pellets. ^{1}H-NMR Spectra: *Varian XL-200* at 200 MHz or a *Bruker* at 360 MHz, in the solvents indicated, chemical shifts (δ) in ppm rel. to internal TMS. Microanalyses were performed on a *Fisons* elemental analyzer model *EA 1108*.

General Procedure for the Synthesis of Compounds **1**, **2**, **13**, **14**, **16**–**20**. Substances were prepared according to the *Knorr* synthesis [17]. Ethyl 3-oxobutanoate (2 equiv.) was heated in an open flask to the boiling point, and the primary arylamine (1 equiv.) was added slowly. The contents of the flask were stirred occasionally to

facilitate removal of the alcohol formed, and heating was continued for 30 min after all of the arylamine had been added. On cooling the mixture, a dark liquid formed, which was concentrated under reduced pressure to remove the excess of ester. The residual oil, representing the corresponding 3-oxo-arenecarboxamide, was not crystallized, but used directly for the ring closure. To this oil, 76% H_2SO_4 or 10% P_2O_5 in $MeSO_3H$ was added, and the mixture was heated carefully to 90–95°. Fumes developed at this temp., indicating that the reaction had begun. After the reaction subsided (the temp. of the mixture must not exceed 95°), the mixture was heated at 95° for 10 min, then cooled to 60° and poured into H_2O. The precipitate formed was isolated and finally recrystallized from alcohol.

*6,7-Dimethoxy-4-methylquinolin-2(1*H*)-one* (**1**): obtained from ethyl acetoacetate and 3,4-dimethoxyaniline. Yield: 88%. Colorless prisms. M.p. 240° (MeOH) ([18]: m.p. 236–237°).

*6,7-Dimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**2**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 3,4-dimethoxyaniline. Yield: 50%. Colorless prisms. M.p. 272° (EtOH). IR: 1675, 1625, 1560, 1520, 1460, 1430, 1320, 1270, 1245. ^{1}H-NMR ((D$_6$)DMSO): 3.80 (*s*, MeO–C(6)); 3.85 (*s*, MeO–C(7)); 6.80 (*s*, H–C(3)); 7.00 (*m*, H–C(5), H–C(8)); 12.15 (*s*, NH). Anal. calc. for $C_{12}H_{10}F_3NO_3$: C 52.75, H 3.69, N 5.13, O 17.57, F 20.86; found: C 52.95, H 3.50, N 5.07.

*6,8-Dimethoxy-4-methylquinolin-2(1*H*)-one* (**13**): obtained from ethyl acetoacetate and 2,4-dimethoxyaniline. Yield: 47%. Brown prisms. M.p. 231–233° (EtOH). IR: 1645, 1620, 1605, 1460, 1395, 1380, 1360, 1275, 1215. ^{1}H-NMR ((D$_6$)DMSO): 2.40 (*s*, Me–C(4)); 3.85 (*s*, MeO–C(6)); 3.90 (*s*, MeO–C(8)); 6.45 (*s*, H–C(3)); 6.75 (*s*, H–C(5)); 6.80 (*s*, H–C(7)); 10.50 (*s*, NH). Anal. calc. for $C_{12}H_{13}NO_3$: C 65.74, H 5.98, N 6.39, O 21.89; found: C 65.41, H 6.00, N 6.36.

*6,8-Dimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**14**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 2,4-dimethoxyaniline. Yield: 88%. Yellow prisms. M.p. 196° (EtOH). IR: 1675, 1615, 1465, 1410, 1360, 1320, 1275. ^{1}H-NMR ((D$_6$)DMSO): 3.85 (*s*, MeO–C(6)); 4.00 (*s*, MeO–C(8)); 6.70 (*s*, H–C(3)); 7.05 (*s*, H–C(5)); 7.10 (*s*, H–C(7)); 11.55 (*s*, NH). Anal. calc. for $C_{12}H_{10}F_3NO_3$: C 52.75, H 3.69, N 5.13, O 17.57, F 20.86; found: C 52.60, H 3.48, N 5.01.

*6,7-(Methylenedioxy)-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**16**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 3,4-methylenedioxyaniline. Yield: 58%. Colorless prisms. M.p. 288–290° (DMSO). IR: 1665, 1565, 1500, 1475, 1450, 1430, 1405, 1360, 1315. ^{1}H-NMR ((D$_6$)DMSO): 6.18 (*s*, OCH_2O); 6.80 (*s*, H–C(3)); 6.95 (*s*, H–C(5)); 7.05 (*s*, H–C(8)); 12.22 (*s*, NH). Anal. calc. for $C_{11}H_6F_3NO_3$: C 51.38, H 2.35, N 5.45, O 18.66, F 22.16; found: C 51.31, H 2.18, N 5.37.

*4-(Trifluoromethyl)benzo[*g*]quinolin-2(1*H*)-one* (**17**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 2-naphthylamine. Yield: 48%. Colorless prisms. M.p. 274–276° (EtOH). IR: 1670, 1585, 1545, 1525, 1485, 1465, 1425, 1400, 1310, 1265, 1250. ^{1}H-NMR ((D$_6$)DMSO): 7.20 (*s*, H–C(3)); 7.50–7.80 (*m*, H–C(7), H–C(9), H–C(10)); 8.05 (*m*, H–C(8)); 8.20 (*m*, H–C(6)); 8.40 (*m*, H–C(5)); 12.80 (*s*, NH). Anal. calc. for $C_{14}H_8F_3NO$: C 63.88, H 3.06, N 5.32, O 6.08, F 21.65; found: C 63.75, H 2.96, N 5.25.

*4-(Trifluoromethyl)benzo[*h*]quinolin-2(1*H*)-one* (**18**): obtained from ethyl 4,4,4-trifluoroacetoacetate and naphthalen-1-amine. Yield: 75%. Yellow prisms. M.p. 288° (MeOH) ([19]: m.p. 304–305°).

*5,6,7-Trimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**19**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 3,4,5-trimethoxyaniline. Yield: 44%. Grey prisms. M.p. 231–233° (EtOH). IR: 1675, 1615, 1550, 1500, 1480, 1445, 1415, 1385, 1365. ^{1}H-NMR ((D$_6$)DMSO): 3.87 (*s*, MeO–C(6)); 3.94 (*s*, MeO–C(5), MeO–C(7)); 6.88 (*s*, H–C(3)); 6.90 (*s*, H–C(8)); 12.08 (*s*, NH). Anal. calc. for $C_{13}H_{12}F_3NO_4$: C 51.48, H 4.00, N 4.62, O 21.10, F 18.80; found: C 51.42, H 3.90, N 4.57.

*6,7,8-Trimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**20**): obtained from ethyl 4,4,4-trifluoroacetoacetate and 2,3,4-trimethoxyaniline. Yield: 43%. Grey prisms. M.p. 242–244° (EtOH). IR: 1675, 1615, 1500, 1465, 1420, 1355, 1320, 1275. ^{1}H-NMR ($CDCl_3$): 3.90 (*s*, MeO–C(7)); 3.97 (*s*, MeO–C(6)); 4.08 (*s*, MeO–C(8); 6.90–7.05 (*m*, H–C(3), H–C(5)); 10.00 (*s*, NH). Anal. calc. for $C_{13}H_{12}F_3NO_4$: C 51.48, H 4.00, N 4.62, O 21.10, F 18.80; found: C 51.38, H 3.89, N 4.55.

*6,7-Dimethoxy-3-phenylquinolin-2(1*H*)-one* (**3**): obtained from 2-chloro-6,7-dimethoxy-3-phenylquinoline (0.72 g, 2.4 mmol) in glacial AcOH and H_2O according to the procedure described in [20]. Yield: 0.45 g (66%). Colorless prisms. M.p. 242–244° ([21]: m.p. 264°).

*6,7-Dimethoxy-3-(4-methoxyphenyl)quinolin-2(1*H*)-one* (**4**): obtained from 2-chloro-6,7-dimethoxy-3-(4-methoxyphenyl)quinoline (0.72 g, 2.4 mmol) in glacial AcOH and H_2O according to the procedure described in [20]. Yield: 0.53 g (87%). Colorless prisms. M.p. 247–249° ([22]: m.p. 250°).

*6,7-Dimethoxy-4-phenylquinolin-2(1*H*)-one* (**5**): obtained from 3,4-dimethoxyaniline (2.4 g, 16 mmol) and ethyl 3-oxo-3-phenylpropanoate (3.7 g, 19 mmol) according to the procedure described in [23]. Yield: 0.15 g (30%). Colorless prisms. M.p. 262° (EtOH). IR: 1655, 1515, 1440, 1415, 1355, 1260, 1230, 1210, 1120. ^{1}H-NMR

((D$_6$)DMSO): 3.60 (*s*, MeO–C(6)); 3.85 (*s*, MeO–C(7)); 6.25 (*s*, H–C(3)); 6.80 (*s*, H–C(8)); 6.95 (*s*, H–C(5)); 7.40–7.65 (*m*, H–C(2), H–C(3), H–C(4), H–C(5), H–C(6) of Ph); 11.70 (*s*, NH). Anal. calc. for $C_{17}H_{15}NO_3$: C 72.58, H 5.37, N 4.98, O 17.06, found: C 72.48, H 5.40, N 4.94.

*6,7-Dimethoxy-3-nitro-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**6**). First 35 ml of cooled 40% HNO_3 and then 17.5 ml of a cold soln. containing HNO_3/H_2SO_4 1.0 : 1.2 were added dropwise to 3.50 g (12.81 mmol) of 6,7-dimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one under N_2 while cooling with an ice-water bath. The mixture was warmed and stirred 35 min at r.t., then poured into 175 ml of cold H_2O. After 25 min at 0°, the formed precipitate was isolated and washed with H_2O. The product was purified by flash column chromatography (silica gel *60* from *Fluka*, particle size 35–70 μm; CH_2Cl_2/acetone 9 : 1). Yield: 2.57 g (8.08 mmol; 63%). Yellow solid. M.p. 270° (acetone). IR: 1670, 1625, 1550, 1515, 1460, 1430, 1360, 1310, 1295, 1260, 1250, 1210, 1180. ^{1}H-NMR ((D$_6$)DMSO): 3.80 (*s*, MeO–C(6)); 3.85 (*s*, MeO–C(7)); 7.00 (*s*, H–C(5), H–C(8)); 12.15 (*s*, NH). Anal. calc. for $C_{12}H_9F_3N_2O_5$: C 45.29, H 2.85, N 8.80, O 25.14, F 17.91; found: C 45.52, H 2.59, N 8.55.

*6,7-Dimethoxy-1-methyl-3-nitro-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**7**). Compound **6** (400 mg, 1.26 mmol), dimethyl sulfate (212 mg; 1.68 mmol), and K_2CO_3 (3.0 g, 22 mmol) were refluxed in acetone (120 ml) for 4 h. Filtration and evaporation of the solvent gave a mixture of *N*- and *O*-methylated products (80 : 20), which were separated by flash column chromatography (silica gel *60* from *Fluka*, particle size 35–70 μm; CH_2Cl_2/acetone 9 : 1). Yield: 230 mg (0.69 mmol; 55%) of **7** (the *O*-methylated product was not further investigated). M.p. 254° (CH_2Cl_2/acetone 9 : 1). IR: 1650, 1615, 1550, 1520, 1460, 1430, 1390. ^{1}H-NMR ($CDCl_3$): 3.85 (*s*, MeO–C(6)); 3.95 (*s*, MeO–C(7)); 4.10 (*s*, Me–N); 6.87 (*s*, H–C(8)); 7.28 (*s*, H–C(5)). Anal. calc. for $C_{13}H_{11}F_3N_2O_5$: C 47.00, H 3.34, N 8.43; found: C 47.12, H 3.31, N 8.40.

*3-Amino-6,7-dimethoxy-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**9**). A suspension of 1.08 g (3.39 mmol) of **6** in 200 ml of abs. EtOH was reduced by shaking with H_2 at 50 psi (3.4 bar, $3.4 \cdot 10^5$ Pa) and 50° for 24 h, in the presence of PtO_2 (50 mg). The soln. was filtered, evaporated, and the residue was recrystallized from toluene. Yield: 0.83 g (2.88 mmol; 85%). Yellow solid. M.p. 221° (EtOH). IR: 3520, 3405, 1620, 1615, 1580, 1515, 1470, 1430, 1375, 1345, 1275, 1230, 1140, 1095. ^{1}H-NMR ((D$_6$)DMSO): 3.75 (*s*, MeO–C(6)); 3.80 (*s*, MeO–C(7)); 6.15 (*s*, NH_2–C(3)); 6.90 (*s*, H–C(8)); 6.95 (*d*, H–C(5)); 12.10 (*s*, NH). Anal. calc. for $C_{12}H_{11}F_3N_2O_3$: C 50.01, H 3.85, N 9.72, O 16.65, F 19.77; found: C 50.28, H 3.79, N 9.49.

*3-Amino-6,7-dimethoxy-1-methyl-4-(trifluoromethyl)quinolin-2(1*H*)-one* (**10**). A suspension of 230 mg (0.69 mmol) of **7** in 40 ml of abs. EtOH was reduced by shaking with H_2 at 50 psi (3.4 bar, $3.4 \cdot 10^5$ Pa) and 50° for 24 h, in the presence of PtO_2 (10 mg). The soln. was filtered and evaporated. Yield: 200 mg (0.66 mmol; 96%). Yellow solid. M.p. 191° (EtOH). IR: 3490, 3390, 1620, 1555, 1530, 1470, 1450, 1410, 1365, 1300, 1270, 1235, 1160. ^{1}H-NMR ((D$_6$)DMSO): 3.81 (*s*, MeO–C(6)); 3.90 (*s*, MeO–C(7)); 3.96 (*s*, Me–N(1)); 5.48 (*s*, NH_2–C(3)); 6.80 (*s*, H–C(8)); 7.18 (*d*, H–C(5)). Anal. calc. for $C_{13}H_{13}F_3N_2O_3$: C 51.66, H 4.34, N 9.27; found: C 51.75, H 4.32, N 9.35.

N-*[6,7-dimethoxy-2-oxo-4-(trifluoromethyl)-1*H*-quinolin-3-yl]acetamide* (**11**). A mixture of 50 mg (0.17 mmol) of **9** and 35 mg (0.35 mmol) of Ac_2O in 2 ml of abs. pyridine was refluxed in the presence of 4-pyrrolidinopyridine (10 mg) under Ar for 1 h. The formed precipitate was washed with CH_2Cl_2 and dried at 60°. Yield: 35 mg (0.11 mmol; 61%). Yellow solid. M.p.: dec. above 320° (CH_2Cl_2). IR: 3250, 1655, 1520, 1450, 1420, 1365, 1325, 1290, 1270, 1250. ^{1}H-NMR ((D$_6$)DMSO): 2.10 (*s*, Me–CO); 3.82 (*s*, MeO–C(6)); 3.88 (*s*, MeO–C(7)); 6.97 (*s*, H–C(8)); 7.09 (*s*, H–C(5)); 9.60 (*s*, NH–C(3)); 12.50 (*s*, NH). Anal. calc. for $C_{14}H_{13}F_3N_2O_4$: C 50.91, H 3.97, N 8.48; found: C 51.01, H 3.89, N 8.43.

*6,7-Dimethoxy-2-methyl-9-(trifluoromethyl)[1,3]oxazolo[5,4-*b*]quinoline* (**12**): obtained from **9** (100 mg, 0.35 mmol), Ac_2O (2.0 ml, 21 mmol), and I_2 (5 mg) according to the procedure described in [24]. Yield: 90 mg (0.29 mmol, 83%). Colorless solid. M.p. 231° (DMSO). IR: 1625, 1580, 1490, 1435, 1350, 1335, 1280, 1255, 1225, 1215. ^{1}H-NMR ((D$_6$)DMSO): 2.70 (*s*, Me–C(2)); 3.92 (*s*, MeO–C(7)); 3.98 (*s*, MeO–C(6)); 7.35 (*s*, H–C(5)); 7.60 (*s*, H–C(8)). Anal. calc. for $C_{14}H_{11}F_3N_2O_3$: C 53.85, H 3.55, N 8.97; found: C 53.86, H 3.52, N 8.92.

*5,7-Dimethoxy-3-phenylquinolin-2(1*H*)-one* (**15**): obtained from 2-chloro-5,7-dimethoxy-3-phenylquinoline (0.20 g, 0.67 mmol) in glacial AcOH and H_2O according to the procedure described in [20]. Yield: 0.14 g (74%). Colorless prisms. M.p. 243° ($CHCl_3$/acetone 7 : 3). IR: 2930, 2840, 1660, 1630, 1615, 1570, 1515, 1475, 1455, 1440, 1410, 1395. ^{1}H-NMR ((D$_6$)DMSO): 3.85 (*s*, MeO–C(5)); 3.95 (*s*, MeO–C(7)); 6.40 (*s*, H–C(6)); 6.50 (*s*, H–C(8)); 7.30–7.50 (*m*, H–C(3), H–C(4), H–C(5) of Ph); 7.70 (*d*, H–C(2), H–C(6) of Ph); 8.05 (*s*, H–C(4)); 11.85 (*s*, NH). Anal. calc. for $C_{17}H_{15}NO_3$: C 72.59, H 5.37, N 4.98, O 17.06, found: C 72.47; H 5.30; N 4.88.

Absorption and Fluorescence Spectra. Solvents for UV and fluorescence spectra were purified by distillation. UV/VIS Spectra were recorded on a *Shimadzu* UV/VIS scanning spectrophotometer *UV-2101PC*. Excitation and emission spectra were obtained with a *Shimadzu RF-5001PC* spectrofluorophotometer. It is

fitted with a 150-W Xe lamp operated as a continuous wave source, slits selectable in 6 steps to produce spectral bandwidths of 1.5, 3, 5, 10, 15, and 20 nm, and an *R452-01* photomultiplier. Excitation and emission monochromators: ion-blazed holographic concave grating *F*/2.5.

UV Spectra were recorded at a concentration of 10 μg/ml, excitation and emission spectra at a concentration of 1 μg/ml. For the determination of quantum yields, emission signals were set in relation to the emission signal of **3** under the same conditions (slit, solvent, temp., and concentration). Compound **3** has a quantum yield, according to [25], of 0.020. Emission spectra are uncorrected.

X-Ray Crystal-Structure Determination of **7**. Crystal data and measurement conditions are summarized in *Table 3*. The diffraction data were collected by ω scans on a modified *Stoe* four-circle diffractometer at r.t. The structure was solved by direct methods (SHELXS-97 [26]) and refined by full-matrix least-squares techniques against F^2 (SHELXL-97 [27]) until the parameter shifts became zero. The non-H-atoms were refined with anisotropic displacement parameters. The H-atoms of the Me groups were refined with common isotropic displacement parameters for the H-atoms of the same group and idealized geometry with C–H distances of 0.96 Å.

Table 3. *Crystallographic Data for Compound* **7**

Formula	$C_{13}H_{11}F_3N_2O_5$
Formula weight [g/mol]	332.24
Temperature [K]	298
Crystal size [mm]	$0.55 \times 0.50 \times 0.10$
Crystal system	monoclinic
Space group	$P2_1/c$ (No. 14)
a [Å]	12.372(2)
b [Å]	12.154(2)
c [Å]	10.119(2)
β [°]	112.95(2)
V [Å^3]	1401.1(4)
Z	4
$F(000)$	680
ρ_{calc} [g cm^{-3}]	1.575
λ [Å]	0.71069
μ (MoK_α) [mm^{-1}]	0.146
Θ_{max} [°]	25
No. of measured reflections	3169
No. of independent reflections	2457
No. of observed reflections	1573
Criterion for observed reflections	$I > 2\sigma(I)$
Refinement (on F^2)	Full-matrix
No. of parameters refined	213
$R1 = \Sigma \parallel F_o \mid - \mid F_c \parallel / \Sigma \mid F_o \mid$	0.0544
$wR = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$	0.1269
$S = \{\Sigma[w(F_o^2 - F_c^2)^2]/(N_{ref} - N_{par})\}^{1/2}$	1.073
Max. and min. $\Delta\rho$ [eÅ^{-3}]	0.158, −0.161

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-118478. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 (1223) 336033; e-mail: deposit@ccdc.cam.ac.uk).

Computational Procedures. Starting structures of the investigated compounds were created with the aid of the SYBYL molecular-modeling package [28]. Semiempirical molecular-orbital calculations were done by the MOPAC [5] program packages. Geometries for ground states were completely optimized (keyword PRECISE) by the semiempirical AM1 [5] *Hamiltonian* with the eigenvector following the routine in [29]. Based on the AM1-optimized structures, electronic transition energies were calculated by the ZINDO method [6]. Solvent effects (DMSO, $n = 1.479$, $D = 45.0$) were treated with the self-consistent reaction-field approximation [30].

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