Communication

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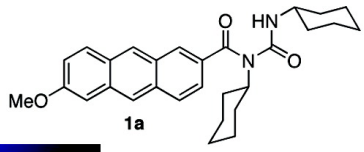
J. Am. Chem. Soc., **2005**, 127 (49), 17158-17159• DOI: 10.1021/ja052262c • Publication Date (Web): 15 November 2005



1a

A: C_6H_{12}, B: C_6H_6, C: 1,4-dioxane,
D: $CHCl_3$, E: DMSO, F: CH_3CN,
G: 2-propanol, H: EtOH, I: MeOH

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Published on Web 11/15/2005

N-Acylureido Functionality as Acceptor Substituent in Solvatochromic Fluorescence Probes: Detection of Carboxylic Acids, Alcohols, and Fluoride Ions

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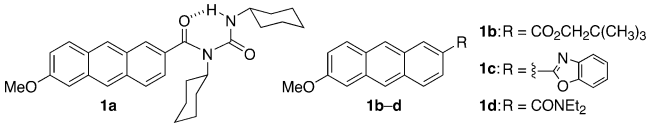
The design of organic fluorescence probes has provided important contributions to the development of sensitive tools which may be used for the detection of physiologically relevant analytes or for trace analysis in environmental chemistry.[1] Solvatochromic fluorophores are especially useful for these purposes since they usually cover a broad range of emission wavelengths which are dependent on external stimuli.[2] In contrast to PET-based fluorescence probes, which only show increasing or decreasing emission intensity at fixed wavelength, solvatochromic probes may indicate the presence of an analyte by a significant change of emission wavelength, which is unequivocally detectable. We observed that an anthracene fluorophore with an acylureido substituent exhibits solvatochromism, which can be modulated by the addition of analytes.



The *N*-acyl urea derivative **1a** was obtained in 70% yield by the reaction of 6-methoxyanthracene-2-carboxylic acid[3] with dicyclohexylcarbodiimide (DCC) in the presence of triethylamine. ^{1}H NMR and IR spectroscopic data are in agreement with the usual cyclic structure of the acylureido substituent.[4] Compound **1a** exhibits absorption properties characteristic of anthracene derivatives; i.e., the absorption spectrum in methanol shows an intense, broad β band at 267 nm (^1B_b) and a broad p band (^1L_a) with a maximum at $\lambda = 375$ nm. The absorption properties of **1a** are almost independent of the solvent (Table 1); however, with respect to the emission properties, **1a** exhibits an unexpected strong solvatochromism (Figure 1a, cf. Supporting Information (SI)). In the only previous reported example where the acylureido moiety was attached to a coumarin chromophore, the solvatochromic behavior was not discussed in detail.[5] Thus, the emission maximum for **1a** varies from 453 nm in cyclohexane to 534 nm in methanol. Attempts to correlate the fluorescence emission maxima in wavenumbers with the solvent properties gave an almost linear relationship ($r^2 = 0.96$) with the acceptor number (AN) (Figure 1b),[6] which reflects the ability of a solvent to stabilize negative charges. With solvent parameters such as the $E_T(30)$ data,[7] the Kosower parameter, Z,[6] or the Lippert−Mataga scale[8] (Δf), a correlation was also observed (Figure 1b, cf. SI), however, with less satisfying correlation factors ($r^2 = 0.84$, 0.78, and 0.82). With the donor number of the solvent, no linear correlation was observed. At 77 K the emission of **1a** in ethanol or toluene shifts to shorter wavelengths ($\lambda_{max} = 405-410$ nm, cf. SI). The spectra in both solvents are superimposable at 77 K. When the solid ethanol matrix is left to warm, the spectrum broadens and an intermediate maximum ($\lambda_{max} = 466$ nm, cf. SI) is observed for the emission maximum. During the warming process, a dual emission with two fixed wavelengths could not be observed. It is worth noting that the emission at 77 K does not correspond to a high-energy conformation that is only accessible in the solid matrix, because the excitation spectra at room temperature and at 77 K are

Table 1. Absorption and Fluorescence Maxima, λ_{abs} and λ_{fl} (in nm), and Relative Fluorescence Quantum Yields, ϕ_{em}, of **1a**

solvent[a]	λ_{abs}(**1a**)[b]	λ_{fl}(**1a**)[c]	ϕ_{em}(**1a**)[d]
methanol	393	534	0.44
ethanol	393	526	0.48
2-propanol	393	517	0.58
acetonitrile	393	487	0.64
DMSO	396	470	0.67
$CHCl_3$	397	488	0.63
1,4-dioxane	396	456	0.68
benzene	397	464	0.50
cyclohexane	395	453 (433)	0.54

[a] Solvents arranged in order of decreasing $E_T(30)$ value. [b] Absorption maximum with lowest energy, c(**1a**) = 10^{-4} M. [c] Emission maximum, c(**1a**) = 10^{-5} M, $\lambda_{ex} = 370$ nm. [d] Relative to quinine sulfate 10^{-5} M in 1 N H_2SO_4; estimated error, ±5% of the given values.

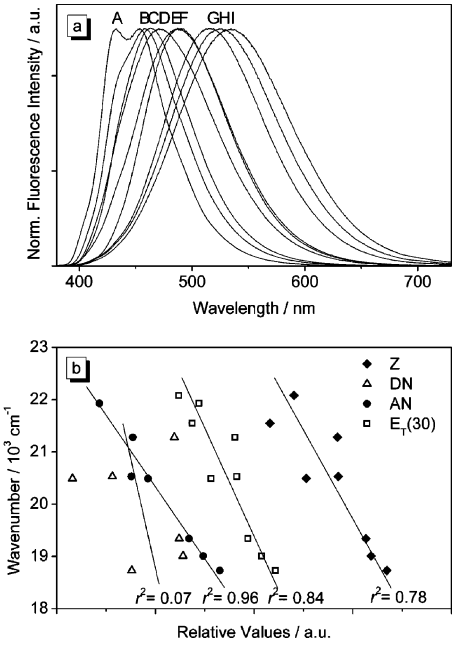


Figure 1. (a) Normalized emission spectra of **1a** ($c = 10^{-5}$ M, $\lambda_{ex} = 370$ nm) in different solvents (A, cyclohexane; B, 1,4-dioxane; C, benzene; D, DMSO; E, CH_3CN; F, $CHCl_3$; G, 2-propanol; H, ethanol; I, methanol). (b) Correlation of the emission maxima (in cm^{-1}) of **1a** (acetonitrile, c(**1a**) = 10^{-5} M, $\lambda_{ex} = 370$ nm) with selected solvent parameters such as Z, DN (donor number), AN (acceptor number), and $E_T(30)$.

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10.1021/ja052262c CCC: $30.25

very similar (cf. SI). The fluorescence properties of **1a** are also viscosity dependent, as demonstrated by experiments in glycerol at different temperatures. In this medium the emission maxima shift from 474 nm at 5 °C ($\eta = 5959$ cP) to 543 nm at 95 °C ($\eta = 27.3$ cP) (cf. SI). Notably, at intermediate temperature (40 °C), the emission bands are significantly broader as compared to the ones at higher or lower temperature, which usually indicates two emissive species, i.e., the Franck−Condon state and the relaxed state.[2c]

The absorption properties of **1a** are almost independent of the solvent properties, which indicates that neither S_0 nor the Franck−Condon excited state experiences a particular stabilization by the employed solvent. Thus, the shift in the emission maxima is consistent with an adiabatic process after excitation, which leads to an excited state where its energy is decreased in solvents with high AN.[6] Similar observations have been made with moderately solvatochromic anthracene derivatives **1b** or **1c**,[9] but in these cases the solvatochromic shifts are significantly smaller (ca. 30 nm) and the emission maxima correlate well with the $E_T(30)$ parameter only when protic solvents are omitted.[9] Notably, the amide **1d** is not solvatochromic. Further evidence for an adiabatic process is the fact that the fluorescence quantum yield did not decrease when the excited-state energy was decreased in solvents with high AN.

As in other solvatochromic systems,[2] an internal charge transfer (ICT) due to a strong donor−acceptor interplay between the methoxyanthryl- and the *N*-acylureido moieties may take place in the excited state of **1a**. Although the acylurea substituent is only a weak electron acceptor in the ground state, it may be a strong acceptor in the excited state. As in carboxylic amides and imides,[10] the acyl carbonyl in **1a** is likely to exhibit increased hydrogen-bond-acceptor properties upon excitation, and the strength of the intramolecular hydrogen bond between the carbonyl and the amido proton increases significantly in the excited state. This leads to an increased acceptor strength of the carbonyl group by the positive polarization of the carbonyl carbon atom. The subsequent adiabatic ICT leads to an intermediate that most likely develops a negative charge that is, after solvent relaxation,[2b,c,6] stabilized by polar solvents, especially those with high AN. This ICT−solvent relaxation sequence explains the significant red shift of the emission spectra in polar solvents as well as the temperature and viscosity dependence of the emission properties.[2c,6]

Although the actual excited-state behavior of **1a** cannot be unambiguously deduced from the observed data, it is clear that a transient is formed which is highly sensitive toward the anion-stabilizing properties of external molecules. This feature may be used to apply **1a** as a fluorescence sensor for analytes with high AN. To test this proposal we added selected carboxylic acids and alcohols with relatively high AN to a solution of **1a** in acetonitrile (Figure 2). The addition of acetic acid, propionic acid, 1-hexanoic acid, lactic acid, and ethylene glycol resulted in significant red shifts of the emission maxima. Moreover, the effect of ethylene glycol addition ($\Delta\lambda = 14$) was not as pronounced as the one obtained upon addition of acid ($\Delta\lambda = 40$), which is consistent with the larger AN of carboxylic acids relative to the ones of alcohols.[11] In contrast, the addition of fluoride to **1a** in acetonitrile resulted in a blue shift ($\Delta\lambda = 50$) of the fluorescence maximum. Presumably, the fluoride ion forms a strong hydrogen bond with the amido proton,[12] so that the hydrogen is not available for intramolecular hydrogen bonding and the solvent-sensitive transient cannot be formed. This result demonstrates the importance of the amide hydrogen for the solvatochromic properties of **1a**.

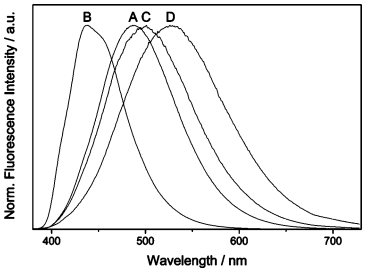

Figure 2. Normalized fluorescence spectra of **1a** ($c = 10^{-5}$ M) in CH_3CN (A), and in the presence of $Bu_4N^+F^-$ (1.5×10^{-3} M, B), ethylene glycol (1.0 M, C), and lactic acid (1.0 M, D), $\lambda_{ex} = 370$ nm.

In summary, we have shown that the *N*-acylureido substituent is a useful substituent in solvatochromic fluorescence probes, which may be used to detect analytes with high acceptor number, such as alcohols and carboxylic acids, and analytes such as fluoride which form strong hydrogen bonds with the amido hydrogen atom. The significant shifts observed, which can occur in opposite directions with different types of analytes, open up the possibility for detection using ratiometric techniques.

Acknowledgment. This paper is dedicated to Professor Harald Günther, University of Siegen, on the occasion of his 70th birthday. This work was generously financed by the Deutsche Forschungsgemeinschaft. C.B. thanks NSERC for the partial support of this research.

Supporting Information Available: Synthesis, characterization, and pictures of fluorescent **1a**; correlation of emission maxima of **1a** with the Lippert−Mataga scale; emission and excitation spectra of **1a** at varying temperature and viscosity. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA052262C