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Publication date
1993

Published in
Recueil des travaux chimiques des Pays-Bas = Journal of the Royal Netherlands Chemical Society

Recl. Trav. Chim. Pays-Bas 112, 535–548 (1993) 0165–0513/93/10535–14$6.00

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(Received March 19, 1993)

Abstract. We report a two-step synthesis for N-aryl- and N-alkyl-substituted 4-piperidones, in which the N substituent can easily be varied. A number of intramolecular donor–acceptor systems was synthesized from these piperidones by conversion of the carbonyl functionality. The influence of the *N*-aryl donor on the electronic absorption and fluorescence spectra was investigated systematically. It was concluded that some systems can be used as efficient fluorescent probes with a high sensitivity for solvent polarity.

1. Introduction

The synthesis of N-alkyl- and N-aryl-substituted 4-piperidones [a] is a subject of continuing research, because they are important building blocks in the preparation of alkaloids and analgesics. Some alkaloids, such as aristoserratine[1], elaekanidine A[2] and tropinone[3] contain the 4-piperidone unit in their structure, but the usefulness of the 4-piperidones as intermediates in pharmacological synthesis has been of more interest. Anaesthetics (such as α- and β-eucaine[4], 4-phenylpiperidines[5], morphans[6] and benzomorphan analogues[7]), neuromuscular blocking agents (such as fentanyl and clebopride derivatives[8,9]), cytostatic drugs (such as ellipticine analogues[10]) and several potential antihypertensive agents[11] can be prepared from 4-piperidones.

However, the synthesis of 4-piperidones is not only important from a pharmacological point of view. Our interest in the 4-piperidones is primarily based on the fact that these systems offer an attractive entry to preparation of conformationally well-defined bichromophoric and trichromophoric systems. The nitrogen function in N-substituted 4-piperidones can function as a strong one-electron donating moiety of which the strength can be varied by modification of the N substituent. Furthermore the carbonyl group can readily be converted into a variety of functional groups with powerful electron-accepting properties. In the D–A systems thus obtained, donating (D) and accepting (A) moieties are incorporated into the (semi)rigid structure of the interconnecting piperidine ring in such a way that there is no direct orbital overlap. Although D and A are separated by three or more σ bonds, intramolecular charge-transfer (CT) absorption[12], photoinduced electron transfer (ET) and exciplex-type emission are found in many cases[13,14]. These observations indicate that D and A are electronically coupled, despite their spatial separation, which has been ascribed to through-bond interaction (TBI)[15]. The degree of through-bond coupling between donor and acceptor sites depends in an interesting way on the conformation of the overall system[16]. Investigations on donor–bridge–acceptor systems containing various rigid bridges have shown that, under certain conditions, noticeable electronic coupling between D and A can still be inferred from the occurrence of intramolecular electron transfer across as many as twelve σ bonds[17].

Modification of the bridge and also systematic variation of D and/or A are important tools in determining the structure dependence of through-bond interaction in electron-donor–acceptor systems and its manifestation in photophysical properties. The N-substituted 4-piperidones and their derivatives are very suitable for such an approach.

In this paper, we describe a convenient synthesis of *N*-alkyl- and *N*-aryl-4-piperidones, which allows the introduction of various substituents on the nitrogen atom. Three series of donor–acceptor systems, synthesized by directly converting the carbonyl group into an effective electron acceptor, are discussed. Examples are given of other extensions of N-substituted 4-piperidones to construct more complex "electron-mediating" systems with the piperidine ring as a building block. Furthermore, we briefly discuss the interesting electronic-absorption and -emission properties of some of the intramolecular donor–acceptor systems synthesized.

2. Results and discussion

2.1. Synthesis of 4-piperidones

The long-standing interest in the synthesis of N-substituted 4-piperidones has yielded a rich variety of synthetic approaches[18]. Most of these approaches can be classified into four major categories according to the reaction type involved.

[a] Piperidone is a contraction of piperidinone.

The oldest approach is based on the Mannich reaction, which consists of the condensation of carbonyl compounds with ammonia or primary amines and an aromatic or aliphatic aldehyde. These reactions have been shown to be very successful for synthesis of 2,6-diaryl- or 2,6-dialkyl-substituted 4-piperidones[19] and other substituted 4-piperidones[20].

Perhaps the most extensively applied method to build the piperidone skeleton proceeds via the Dieckmann cyclization reaction[21]. In this approach, double N alkylation of a primary amine with an alkyl acrylate is followed by ring closure of the diester and subsequent decarboxylation. This procedure has also given various substituted 4-piperidones[22].

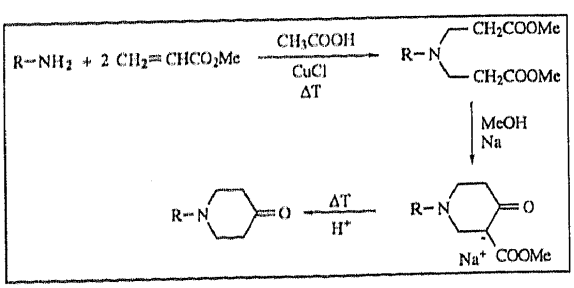
Another approach, which consists of four consecutive reaction steps, was described by *Nazarov*[20]. Condensation of vinylacetylenes (1-buten-3-ynes) with ketones followed by dehydration of the resulting vinylacetylenic alcohols yields the corresponding divinyl acetylenic hydrocarbons which are hydrated to divinyl ketones. By means of condensation with primary amines, a wide range of substituents can be introduced on the piperidine ring, depending on the structure of the ketones used in the condensation.

The fourth general route to 4-piperidones involves a hetero-Diels–Alder reaction between an imine and 1-methoxy-3-(trimethylsilyloxy)butadiene[23].

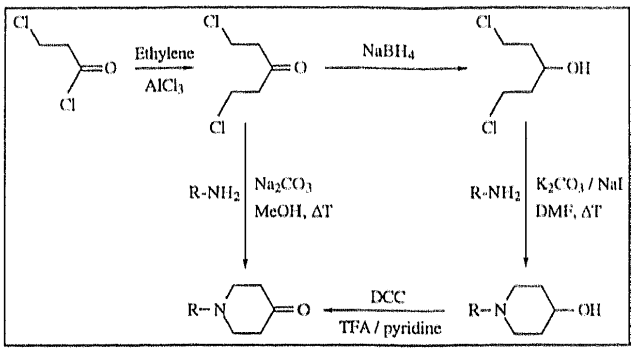
Other approaches to N-substituted 4-piperidones, *e.g.*, from 4-piperidinols or via the (partial) reduction of tetrahydropyridines or 4-methoxypyridines, are limited in their application[24].

Despite many efforts on the synthesis of alkyl- and aryl-substituted piperidones in general, remarkably little has been reported on the synthesis and properties of *N*-aryl-4-piperidones and their derivatives. Most examples found were prepared by Dieckmann cyclization according to Scheme 1. By this procedure, *Gallagher* and *Mann*[25] obtained *N*-phenyl-4-piperidone in 25% yield; by using *tert*-butyl acrylate instead of methyl acrylate, the total yield was improved to 40% by *Baty*, *Jones* and *Moore*[26]. We have also used this approach successfully for the synthesis of *N*-phenyl-4-piperidone and *N*-(4-methoxyphenyl)-4-piperidone[16b], although the yield of the latter was rather low (~ 14%).

Unfortunately, in the Dieckmann-cyclization-based synthesis, the N substituent is determined in the first step out of three, which obviously hampers simple variation of that substituent. This drawback was partly overcome by *Reese* and *Thompson*[27]. They described a four-step synthesis of some *N*-aryl-4-piperidones, which could be used as hydroxyl-protecting groups in polyribonucleotide synthesis. Their approach is outlined in Scheme 2. The first step consists of the synthesis of the intermediate, 1,5-dichloro-3-pentanone, from 3-chloropropionyl chloride and ethylene gas under the action of aluminum trichloride. The dichloropentanone compound was obtained in excellent yield and was subsequently reduced to 1,5-dichloro-3-pentanol. This was used for double N alkylation reaction with a primary (halogeno)aniline to give *N*-aryl-4-piperidols in good yields. After Moffatt oxidation, the corresponding *N*-aryl-4-piperidones were obtained.



Scheme 1. Dieckmann cyclization route to N-substituted 4-piperidones.



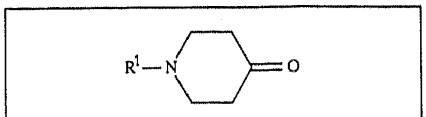
Scheme 2. Cyclization routes to N-substituted 4-piperidones.

This route can, in principle, be simplified considerably. *Bowden* and *Green*[28a] showed earlier that 1,5-dichloro-3-pentanone is also capable of reacting directly with methylamine to yield *N*-methyl-4-piperidone. However, a low yield (16%) was obtained with this alkylamine, which is probably due to cross-coupling reactions. To us, an attractive aspect of this latter method, nevertheless, seemed that the piperidone is made in a two-step synthesis in which the N substituent is introduced in the final step. In addition, *Hahn* et al.[28b] have shown, as early as 1943, that other 3-substituted (*e.g.*, NH_2 and NMe_2) 1,5-dichloropentanes can also be utilized in a similar way, although the reaction conditions used are much more vigorous.

Therefore, we decided to explore and optimize this straightforward approach. We were able to obtain a variety of N-substituted 4-piperidones (**1**–**13**), as shown in Chart 1, with a dramatically improved yield in the cyclization step. To avoid the problem of cross-coupling, the separate reactants were slowly added to a slurry of sodium carbonate in boiling methanol, thus maintaining low-concentration conditions that favour cyclization. In some cases, the reactants were added at room temperature, which gave a lower yield (see Experimental). Mostly anilines bearing various *para* or *meta* substituents were used as primary amine compounds. They reacted smoothly to give the corresponding arylpiperidones and even the sterically crowded 2,4,6-trimethylaniline could be converted to the corresponding piperidone, although in this case the reaction conditions are critical and the yield is rather low. For some primary alkylamines, the high-dilution conditions were also found to give good yields of the corresponding *N*-alkyl-4-piperidones (**10** and **13**) (see Chart 1).

2.2. Synthesis of donor–acceptor systems

The method outlined above allows convenient and rapid preparation of N-substituted 4-piperidones with a wide

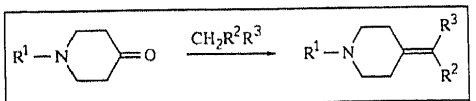


R^1		R^1	
C_6H_5	1	4-*n*-C_6H_{13}-C_6H_4	8
4-MeO-C_6H_4	2	4-*n*-$C_{14}H_{29}$-C_6H_4	9
4-Me-C_6H_4	3	c-C_6H_{11}	10
3,5-Me_2-C_6H_3	4	4-Br-C_6H_4	11
4-F-C_6H_4	5	4-Cl-C_6H_4	12
4-C_6H_5-C_6H_4	6	1-C_6H_5 - 4-piperidyl	13
2,4,6-Me_3-C_6H_2	7		

Chart 1. N-substituted 4-piperidones prepared via condensation of the corresponding amines with 1,5-dichloro-3-pentanone according to Scheme 2.

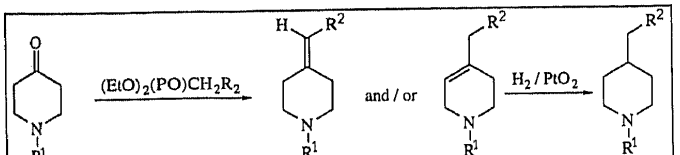
variety of substituents on the nitrogen atom. As already mentioned in the Introduction, these N-substituted 4-piperidones are crucial intermediates in the construction of intramolecular donor–bridge–acceptor systems through modification of the carbonyl function leading to various chromophores with electron-accepting properties. Charts 2A–D outline several routes followed for the preparation of the D–bridge–A systems **14–54**.

Knoevenagel condensation (Chart 2A) allows one-step conversion of the carbonyl group into a compact and powerful electron acceptor consisting of a double bond carrying two electron-withdrawing substituents (compounds **14–25**). In the majority of the donor–acceptor systems prepared, the acceptor contains an aromatic chromophore. These systems were mainly, but not exclusively, prepared via *Wadsworth–Emmons*[29] modification of Wittig condensation (Chart 2B). It was found that this modification usually lead to superior yields compared to the original Wittig reaction. This is especially true if electron-withdrawing substituents are present that reduce the reactivity of the Wittig ylide. The diethyl (arylmethyl)phosphonates required for condensation are readily prepared in high yield by Michaelis–Arbuzov reaction of triethyl phoshite with an aralkyl halide. In the condensation reactions with 4-piperidones however, it has frequently been observed[30], that the initially formed conjugated exocyclic double bond tends to isomerize to an endocyclic β,γ position. This isomerization is, in fact, dependent on the reaction conditions and the solvent



R^1	R^2	R^3	
C_6H_5	CN	CN	14
4-MeO-C_6H_4	CN	CN	15
4-Me-C_6H_4	CN	CN	16
4-F-C_6H_4	CN	CN	17
3,5-Me_2-C_6H_3	CN	CN	18
C_6H_5-C_6H_4	CN	CN	19
2,4,6-Me_3-C_6H_2	CN	CN	20
C_6H_5	COOMe	CN	21
4-MeO-C_6H_4	COOMe	CN	22
4-Me-C_6H_4	COOMe	CN	23
4-F-C_6H_4	COOMe	CN	24
3,5-Me_2-C_6H_3	COOMe	CN	25

Chart 2A. Donor-bridge-acceptor systems obtained via Knoevenagel condensation.



C_6H_5	1-(4-CN)-naphthyl	26	40	42
4-MeO-C_6H_4	1-(4-CN)-naphthyl	27		43
4-Me-C_6H_4	1-(4-CN)-naphthyl	28		44
4-*n*-C_6H_{13}-C_6H_4	1-(4-CN)-naphthyl	29		
4-*n*-$C_{14}H_{29}$-C_6H_4	1-(4-CN)-naphthyl	30		
4-C_6H_5-C_6H_4	1-(4-CN)-naphthyl	31		
2,4,6-Me_3-C_6H_2	1-(4-CN)-naphthyl	32		
C_6H_5	2-anthryl	33		
C_6H_5	1-pyrenyl	34		
C_6H_5	4-C_6H_5-C_6H_4	35	41	
C_6H_5	4-CN-C_6H_4	36		45
C_6H_5	2-naphthyl	37		46
c-C_6H_{11}	1-(4-CN)-naphthyl	38		47

Chart 2B. Donor-bridge-acceptor systems obtained via Wadsworth-Emmons reaction.

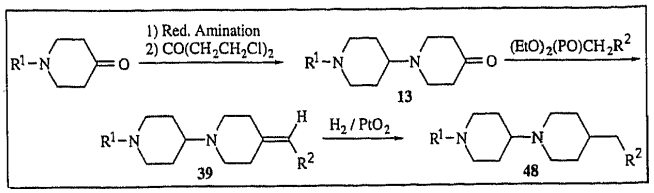
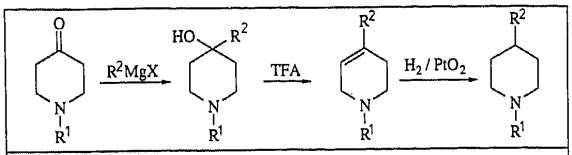


Chart 2C. Example of synthesis of extended donor-acceptor systems, $R^1 = C_6H_5$, R^2 = 1-(4-CN)-naphthyl.



R^1	R^2			
C_6H_5	1-naphthyl	49	50	51
4-MeO-C_6H_4	1-naphthyl	52	53	54

Chart 2D. Donor-bridge-acceptor systems obtained via Grignard reaction.

used. The exocyclic double-bond isomer could be obtained as a sole product by using DME or THF as solvent and no more base than required to deprotonate the phosphonate compound. When more base is used and DMF is the solvent, the isomerization leading to the endocyclic compound is strongly favoured.

Chart 2B compiles the donor–acceptor compounds prepared via Wadsworth–Emmons condensation of various piperidones (**26–38**), via consecutive isomerization of the double bond (**40, 41**) and via consecutive hydrogenation of the double bond (**42–47**). An example (see Chart 2C) is given of a piperidone which was first extended to a 1-(4-piperidyl)-4-piperidone via reductive amination followed by condensation with 1,5-dichloro-3-pentanone before an acceptor unit was introduced via Wadsworth–Emmons condensation (eventually followed by hydrogenation). This resulted in systems **39** and **48**, which contain two amino functions with electron-donating properties, separated from the acceptor site by one and two piperidine rings, respectively[31].

Finally, various aromatic electron-acceptor groups were connected directly to C-4 of the piperidine ring via Grignard reaction (see Chart 2D). While this primarily results in hydroxyl compounds (*i.e.*, **49, 52**), the acceptor chromophore can readily be extended with an endocyclic double bond via dehydration in trifluoroacetic acid (**50, 53**), which was then followed by hydrogenation (**51, 54**).

While a full discussion of the photophysical properties of all intramolecular donor–bridge–acceptor systems synthesized is outside the scope of this paper, we would like to note two remarkable features, displayed by many of these systems *viz.*, intramolecular charge-transfer absorption and strongly solvent-dependent fluorescence. These properties were investigated in three series of *N*-aryl-4-piperidone derivatives, in which the carbonyl group was converted to three different electron-accepting groups; dicyanoethylene, cyano(methoxycarbonyl)ethylene and 1-(4-cyanonaphthyl)ethylene moieties (see Chart 3).

2.3. Intramolecular CT-absorption

The UV-absorption spectra of the systems in series **I** and **II** from Chart 3 show an additional absorption peak, which cannot be attributed to either of the absorptions of donor or acceptor chromophore (see Figure 1). Earlier studies[12] have shown that the appearance of such an additional long-wavelength-absorption peak in the UV-VIS region is a manifestation of through-bond interaction

Series I: R^1 =	phenyl	14
	4-methoxyphenyl	15
	4-methylphenyl	16
	4-fluorophenyl	17
	3,5-dimethylphenyl	18
	4-biphenylyl	19
	2,4,6-trimethylphenyl	20
Series II: R^1 =	phenyl	21
	4-methoxyphenyl	22
	4-methylphenyl	23
	4-fluorophenyl	24
	3,5-dimethylphenyl	25
Series III: R^1 =	phenyl	26
	4-methoxyphenyl	27
	4-methylphenyl	28
	4-n-hexylphenyl	29
	4-n-tetradecylphenyl	30
	4-biphenylyl	31
	2,4,6-trimethylphenyl	32

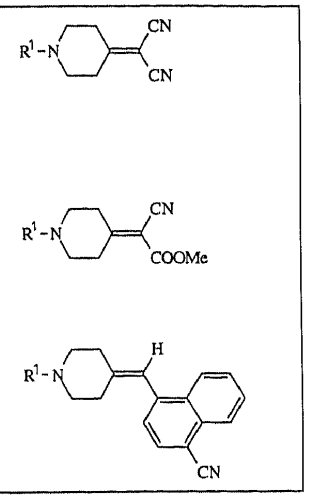


Chart 3. Intramolecular donor – acceptor systems for which photophysical data are presented.

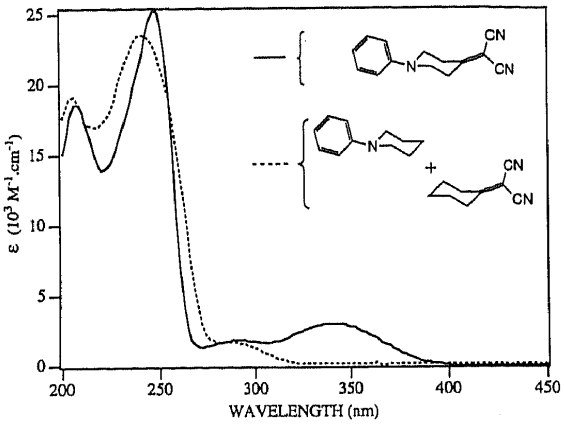


Fig. 1. UV-absorption spectrum of **14** *(–) and sum spectrum of 1-phenylpiperidine and cyclohexylidenepropanedinitrile (...) in n-hexane at 20°C.*

Table I CT-absorption maxima for series **I** *and* **II** *(see Chart 3) in n-hexane and dichlorometahene at 20°C* [a].

Compound	*n*-Hexane	Dichloromethane
14	342 {2970}	352 {3070}
15	356 {1520}	368 {2130}
16	350 {2440}	360 {2780}
17	336 {1930}	348 {2340}
18	350 {2780}	360 {3200}
19	352 {[b]}	362 {3590}
20	324 {2040}	340 {1970}
21	338 {2170}	
22	346 {1360}	
23	342 {1960}	
24	338 {1480} (sh)	
25	342 {2230}	

[a] Data presented as λ_{max} (nm) {ϵ ($M^{-1} \cdot cm^{-1}$)}. [b] Not determined.

between an electron donor and an acceptor over three or more σ bonds.

Thus, the long-wavelength-absorption peak at *ca.* 340 nm of **14** in Figure 1 is assigned to an intramolecular charge-transfer absorption, *i.e.*, an optical transition accompanied by electron transfer from D to A.

In Table I, the CT-absorption data for series **I** and **II** are compiled. (Note that in series **III**, the long-wavelength-absorption peak of the cyanonaphthalene chromophore obscures the CT absorption, if any.) As shown by the data in Table I, CT absorption undergoes a small, but consistent red shift upon transfer from a non-polar solvent (*n*-hexane) to a more polar one (dichloromethane). It is suprising that this shift is so small for a transition involving such a large increase in dipole moment. It should be realized, however, that CT absorption is a 'vertical' (Franck–Condon) process during which nuclear motions do not occur, including the solvent reorganization needed to stabilize the dipolar excited CT state, that typically occur on a picosecond time scale in liquid low-molecular-weight solvents. However, because the CT excited state typically decays on a nanosecond time scale, there is

Table II CT-fluorescence maxima ν_{ct} (10^3 cm^{-1}) and quantum yields (ϕ) for series I (see Chart 3) in various solvents (20°C) upon excitation in the CT-absorption band [a].

Solvent	Δf	**14**	**15**	**16**	**17**	**18**	**19**	**20**
n-hexane	0.092	22.3 (0.19)	19.7 (0.02)	21.1 (0.14)	21.9 (0.09)	21.4 (0.12)	21.3 (0.14)	22.1 (0.18)
c-hexane	0.100	22.2 (0.21)	19.6 (0.03)	21.0 (0.16)	21.7 (0.14)	21.2 (0.16)	21.2 (0.17)	21.9 (0.22)
di-*n*-butyl ether	0.194	19.5 (0.12)	17.3 (< 0.01)	18.6 (0.03)	19.3 (0.04)	19.2 (0.06)	19.4 (0.03)	19.9 (0.07)
diisopropyl ether	0.237	19.0 (0.05)	16.9 (< 0.01)	18.0 (0.01)	18.8 (0.02)	18.3 (0.02)	18.6 (0.01)	19.2 (0.02)
diethyl ether	0.251	18.5 (0.01)	16.4 (< 0.01)	17.3 (< 0.01)	17.9 (< 0.01)	17.5 (< 0.01)	18.5 (< 0.01)	18.4 (< 0.01)
ethyl acetate	0.292	16.9 (< 0.01)	[b]	16.0 (< 0.01)	16.4 (< 0.01)	16.2 (< 0.01)	[b]	17.3 (< 0.01)
intercept (10^3 cm^{-1})		24.7	21.6	23.4	24.4	23.8	23.0	24.3
slope (10^3 cm^{-1})		25.7	20.6	24.6	25.8	24.8	18.2	23.1
corr. coeff.		0.985	0.987	0.989	0.978	0.984	0.998	0.987

[a] Data presented as $\nu_{ct}(\phi)$. Δf (second column) refers to the polarity parameter defined in the text, whereas the lower three lines compile the results obtained by linear correlation of Δf and ν_{ct} via the Lippert–Mataga equation (see Figure 3). [b] No fluorescence observed.

Table III CT-fluorescence maxima ν_{ct} (10^3 cm^{-1}) and quantum yields (ϕ) for series II (see Chart 3) in various solvents (20°C) upon excitation in the CT-absorption band [a].

Solvent	Δf	**21**	**22**	**23**	**24**	**25**
n-hexane	0.092	21.8 (0.05)	19.7 (0.02)	21.0 (0.05)	21.8 (0.03)	21.3 (0.05)
c-hexane	0.100	21.7 (0.06)	19.5 (0.02)	20.9 (0.07)	21.6 (0.03)	21.1 (0.06)
di-*n*-butyl ether	0.194	19.5 (0.07)	17.7 (< 0.01)	18.7 (0.02)	19.5 (0.02)	19.0 (0.02)
diisopropyl ether	0.237	18.9 (0.02)	17.2 (< 0.01)	18.1 (< 0.01)	18.8 (< 0.01)	18.5 (0.01)
diethyl ether	0.251	18.1 (0.01)	[b]	17.6 (< 0.01)	18.0 (< 0.01)	17.7 (< 0.01)
ethyl acetate	0.292	[b]	[b]	16.3 (< 0.01)	16.7 (< 0.01)	16.4 (< 0.01)
intercept (10^3 cm^{-1})		23.9	21.3	23.1	24.1	23.5
slope (10^3 cm^{-1})		22.2	17.6	22.5	24.2	23.1
corr. coeff.		0.988	0.992	0.990	0.984	0.980

[a] Data presented as $\nu_{ct}(\phi)$. Δf (second column) refers to the polarity parameter defined in the text, whereas the lower three lines compile the results obtained by linear correlation of Δf and ν_{ct} via the Lippert–Mataga equation (see Figure 4). [b] No fluorescence observed.

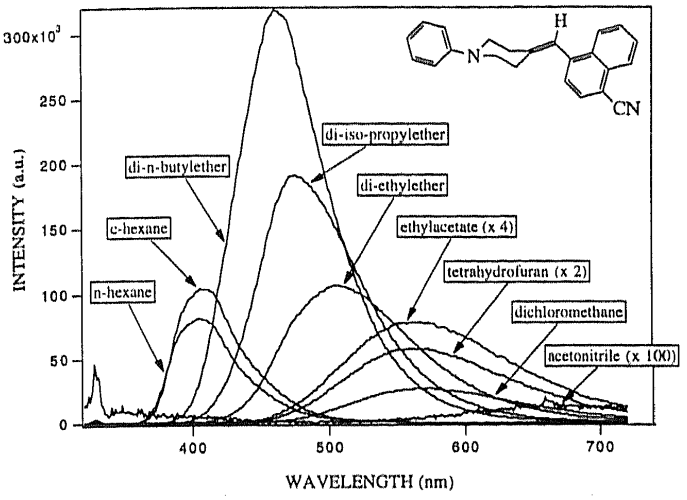


Fig. 2. Solvatochromic emission of compound **26** *("fluoroprobe") in a series of solvents.*

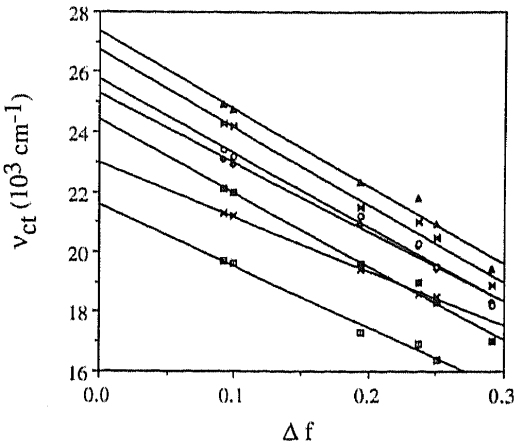


Fig. 3. Fluorescence maximum wavenumber ν_{ct} (10^3 cm^{-1}) of series I (see Chart 3) vs. the Δf values of various solvents. R = phenyl (∗) (offset + 2000 cm^{-1}), 4-methoxyphenyl (■), 4-methylphenyl (⊡) (offset + 1000 cm^{-1}), 4-fluorophenyl (▲) (offset + 3000 cm^{-1}), 3,5-dimethylphenyl (○) (offset + 2000 cm^{-1}), 4-biphenylyl (×), 2,4,6-trimethylphenyl (◆) (offset + 1000 cm^{-1}).

sufficient time to stabilize it by solvent relaxation before eventual fluorescence from it occurs. As will be demonstrated in the next section, this implies that the position of such CT fluorescence displays a very pronounced solvatochromism.

2.4. Solvent dependence of fluorescence

As we reported before[32] with a more limited set of compounds, the electronic coupling between the anilino group (as a one-electron donor) and electron acceptor groups at the 4-position, through the alicyclic framework provided by the piperidine ring, is sufficient to allow complete charge-transfer upon photoexcitation (if thermodynamically feasible). The dipolar charge-transfer (CT) excited state, thus populated, displays fluorescence which is highly solvatochromatic, making these systems of interest as a new class of fluorescent probes. By variation of the donor and acceptor, the fluorescence can be tuned for use as an optical polarity probe in solvents of widely different polarity and even as a probe for micropolarity and micromobility in polymers[33].

While in earlier studies[32] mainly the effect of acceptor variation was investigated, we are now in a position to study the effect of donor variation on solvatochromic CT fluorescence. In Tables II–IV, the position (in 10^3 cm^{-1}) and the quantum yields in various solvents are tabulated of the three series of *N*-aryl-4-piperidone derivatives compiled in Chart 3. The electronic emission spectra for all these compounds show a single, broad, structureless emission, which undergoes a large bathochromic shift with increasing solvent polarity (see Figure 2), indicative of the strongly dipolar character of the emissive CT state. The identification of the nature of the emissive state was confirmed by time-resolved microwave conductivity measurements, as performed by *Warman* and *de Haas*[32a], via electro-optical[34] measurements and by testing the applicability of the Lippert–Mataga relationship[35] (Eqn. 1a). This relationship should be applicable to describe the dependence of the wavenumber of the fluorescence maximum (ν_{ct}) on the solvent polarity parameter Δf (defined in Eqn. 2) if the dipole moment of the emissive state (μ) is solvent independent and much larger than that of the electronic ground state. In Eqn. 1a, $\nu_{ct}(0)$ is the emission maximum in the gas phase, the parameter ρ defines the effective radius of the cavity that the molecule occupies in the solvent medium, when the latter is being considered as a dielectric continuum with dielectric constant ε and refractive index n.

$$\nu_{ct} = \nu_{ct}(0) - \left[2\mu^2/(\rho^3 \cdot h \cdot c)\right] \cdot \Delta f \qquad (1a)$$

$$\nu_{ct} = \nu_{ct}(0) - 1.007 \cdot 10^4 \cdot (\mu^2/\rho^3) \cdot \Delta f \qquad (1b)$$

$$\Delta f = (\varepsilon - 1)/(2\varepsilon + 1) - (n^2 - 1)/(4n^2 + 2) \qquad (2)$$

Using Eqn. 1b, a plot of the observed maximum of the fluorescence ν_{ct} (in cm^{-1}) from a polar state versus the Δf value of the solvent should yield a straight line with an intercept $\nu_{ct}(0)$ (in cm^{-1}). The slope of this line is $1.007 \cdot 10^4 \cdot (\mu^2/\rho^3)$ if the dipole moment μ is expressed in Debye and the solvent cavity radius ρ in Å. Plotting the

Table IV CT-fluorescence maxima ν_{ct} (10^3 cm^{-1}) and quantum yields (ϕ) for series III (see Chart 3) in various solvents (20°C) upon excitation in the acceptor absorption band [a].

Solvent	Δf	**26**	**27**	**28**	**29**	**30**	**31**	**32**
n-hexane	0.092	24.6 (0.20)	22.6 (0.42)	24.0 (0.42)	24.0 (0.53)	24.0 (0.55)	24.1 (0.57)	24.8 (0.08)
c-hexane	0.100	24.4 (0.21)	22.4 (0.59)	23.9 (0.47)	23.7 (0.63)	23.7 (0.59)	24.0 (0.62)	24.6 (0.11)
di-*n*-butyl ether	0.194	21.5 (0.85)	19.2 (0.20)	21.0 (0.49)	21.0 (0.57)	21.1 (0.51)	21.1 (0.58)	21.9 (0.48)
diisopropyl ether	0.237	20.4 (0.78)	18.1 (0.06)	20.0 (0.33)	20.0 (0.41)	20.0 (0.38)	20.0 (0.50)	21.3 (0.38)
diethyl ether	0.251	19.5 (0.58)	17.5 (0.02)	19.2 (0.24)	19.2 (0.33)	19.4 (0.37)	19.5 (0.47)	20.7 (0.38)
ethyl acetate	0.292	17.5 (0.19)	15.8 (< 0.01)	16.9 (0.02)	17.0 (0.03)	17.0 (0.03)	17.3 (0.07)	18.2 (0.11)
tetrahydrofuran	0.308	17.5 (0.16)	15.1 (< 0.01)	16.7 (0.01)	16.8 (0.04)	16.8 (0.04)	17.2 (0.09)	18.0 (0.06)
dichloromethane	0.319	17.3 (0.21)	14.9 (< 0.01)	16.4 (0.01)	16.4 (0.02)	16.3 (0.02)	16.6 (0.05)	17.5 (0.05)
acetonitrile	0.393	14.4 (< 0.01)	[b]	14.7 (< 0.01)	14.6 (< 0.01)	14.6 (< 0.01)	14.5 (< 0.01)	[b]
intercept (10^3 cm^{-1})		27.9	25.8	27.2	27.1	27.2	27.3	28.0
slope (10^3 cm^{-1})		33.9	34.2	32.9	32.6	32.7	32.8	31.7
corr.coeff.		0.992	0.996	0.984	0.987	0.984	0.992	0.970

[a] Data presented as $\nu_{ct}(\phi)$. Δf (second column) refers to the polarity parameter defined in the text, whereas the lower three lines compile the results obtained by linear correlation of Δf and ν_{ct} via the Lippert–Mataga equation (see Figure 5). [b] No fluorescence observed.

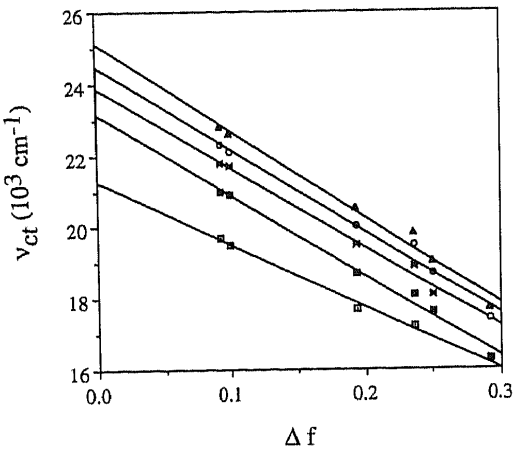


Fig. 4. Fluorescence maximum wavenumber ν_{ct} (10^3 cm^{-1}) of series II (see Chart 3) vs. the Δf values of various solvents. R = phenyl (*) (offset +2000 cm^{-1}), 4-methoxyphenyl (□), 4-methylphenyl (■), 4-fluorophenyl (▲) (offset +1000 cm^{-1}), 3,5-dimethylphenyl (○) (offset +1000 cm^{-1}).

observed emission maxima of the donor–acceptor series **I**, **II** and **III** against the Δf values results in all cases in a fairly good linear correlation (see Figures 3, 4 and 5). Values for the slope and intercept of the regression lines are given in Tables II–IV, together with the correlation coefficients of the linear fit.

With the relatively compact acceptors used in series **I** and **II** (see Tables II and III), the slope of the regression line, which is a direct measure for the solvent-polarity sensitivity of the fluorescence frequency, varies between 17600 and 25800 cm^{-1}. In series **III**, incorporation of an acceptor with a more extended π system enhances the polarity sensitivity to 31700–34200 cm^{-1}. Clearly, the extension of the acceptor system in series **III** results in a larger effective charge-separation distance, corresponding to a larger μ_{ct} than in series **I**, and **II**, which more than compensates for the effect of the concomitant increase in the solvent cavity radius (ρ) that would tend to decrease the polarity sensitivity of ν_{ct} (see Eqn. 1).

It should be noted that, even for series **I** and **II**, the polarity sensitivity is quite high in comparison to that of other optical polarity probes[36]. Thus, for the well-known $E_T(30)$ probe[37], which displays strongly polarity-dependent CT absorption, the shift in wavenumber amounts to only 15900 cm^{-1} on a Δf scale (see Figure 6).

Thus, series **I** and **II**, but especially series **III** significantly outclass $E_T(30)$, with respect to spectral shift as a function of solvent polarity. In addition to spectral shift, the usefulness of a fluorescent polarity probe is, of course, related to its fluorescence quantum yield under a variety of solvent conditions. In this respect, series **III** also shows superior properties. Because of the polar nature of the emissive state and the resulting strong solvent dependence of the energy gap separating that state from the ground state, a rather strong solvent dependence of the fluorescence quantum yield is unavoidable. Nevertheless, systems from series **III** and, in particular, **26** maintain a high quantum yield over a wide solvent-polarity range, except in the range of very high polarity, where the energy gap between emissive and ground state apparently becomes so small that non-radiative decay processes prevail. We are presently engaged in efforts to increase that energy gap and, thereby, make available strongly solvatochromic fluorescent probes of the donor–bridge–acceptor type, that can be employed in highly polar media. It seems likely that this can only be achieved at the expense of the ability to show charge-transfer fluorescence in less polar media, in which, however, the systems described here can be used successfully.

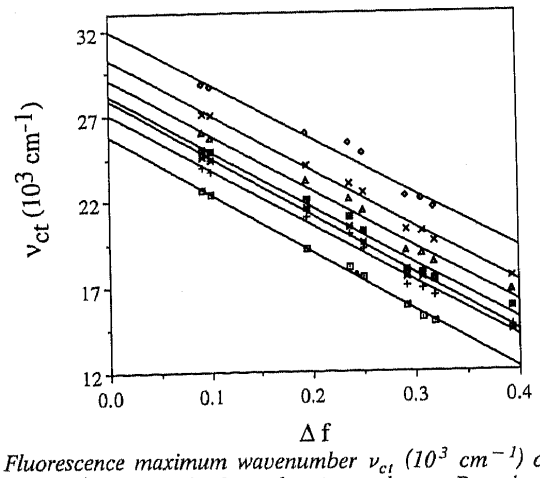


Fig. 5. Fluorescence maximum wavenumber ν_{ct} (10^3 cm^{-1}) of series III (see Chart 3) vs. the Δf values of various solvents. R = phenyl (*), 4-methoxyphenyl (□), 4-methylphenyl (■) (offset +1000 cm^{-1}), 4-hexylphenyl (+), 4-tetradecylphenyl (▲) (offset +2000 cm^{-1}), 4-biphenylyl (×) (offset +3000 cm^{-1}), 2,4,6-trimethylphenyl (◆) (offset +2000 cm^{-1}).

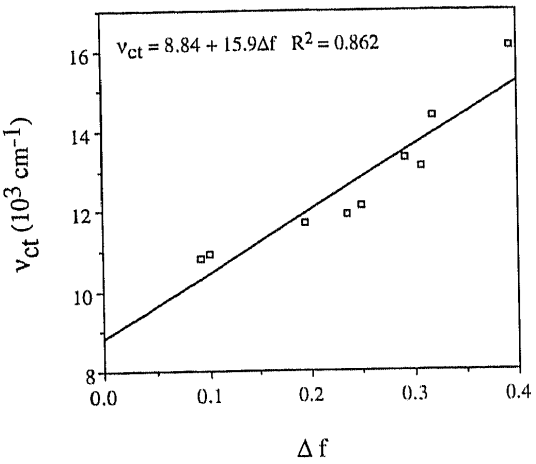


Fig. 6. CT-absorption wavenumber ν_{ct} (10^3 cm^{-1}) of $E_T(30)$ vs. the Δf values of various solvents.

3. Experimental

3.1. General information

Infrared (IR), nuclear magnetic resonance (NMR) and mass (MS) spectroscopy were used to identify the compounds synthesized. IR spectra were measured in $CHCl_3$ solution on a Perkin–Elmer 1310 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ solution (unless indicated otherwise) using Bruker AC 200 (200 MHz), Bruker WM 250 (250 MHz), Bruker AMX 300 (300 MHz) or Bruker ARX 400 (400 MHz) spectrometers. Chemical shifts are given in ppm downfield from tetramethylsilane. High-resolution mass measurements (MS) were carried out using a VG micromass ZAB-HFQ instrument.

In section 3.2, the proton and ^{13}C-NMR spectra of one of the studied compounds (**26**) are discussed in more detail, as these spectra are representative of the majority of the compounds studied. Experimental data on the piperidones **1–13** (Chart 1) and on the donor–bridge–acceptor systems **14–54** (Chart 2A–D) are reported in sections 3.3–3.7, according to their main reaction type. As in each section, most compounds are synthesized in a similar way with only minor variations in reaction conditions, general methods are given for these preparations. However, deviations and different purification methods are reported for each compound separately. No attempts were made to optimize the yields for each experiment.

Chromatograph purification refers to flash chromatography using Merck silica gel 60 (230–400 mesh) or Janssen Chimica silica gel (0.030–0.075 mm) with the indicated solvent. R_f values refer to thin-layer chromatography (TLC) on silica-gel-coated plastic sheets (Merck silica gel 60 $F254$) with the indicated solvent (mixture). Melting points were determined on a Reichert hot-stage microscope and are uncorrected.

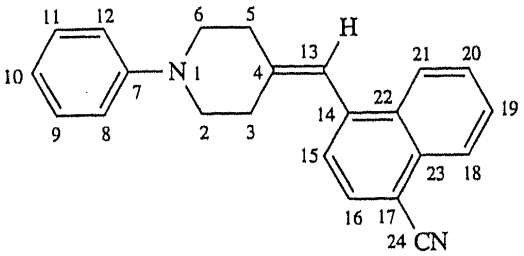


Fig. 7. Numbering of ring system of compound **26**.

Electronic-absorption spectra were recorded on a Hewlett Packard 8451 A diode array spectrophotometer and a Cary 17 D spectrophotometer. Electronic emission and excitation spectra were recorded on a Spex Fluorolog 2 spectrometer. Spectrograde solvents (Merck) were used throughout. The samples used for the fluorescence quantum-yield measurements were deoxygenated by purging with argon for 10–15 min, and were diluted to $0.1 < A(1\text{ cm}) < 0.2$ at the excitation wavelength used. The recorded emission spectra were all normalized to identical absorption at the excitation wavelength. The quantum yields (Φ) were obtained by determining the integrated fluorescence intensity of the sample fluorescence relative to the integrated fluorescence intensity of 9,10-diphenylanthracene (Φ 0.90[38]) determined at the same excitation wavelength in cyclohexane. Quantum yields determined in other solvents were corrected for changes in the refractive index of the solvent compared to cyclohexane.

3.2. ^1H- and ^{13}C-NMR spectra of **26**

These spectra have been fully assigned for compound **26**. Figure 7 shows the numbering used for the assignment of NMR resonances observed in **26**. Wherever appropriate, this system of numbering is maintained throughout the experimental section and assignments of proton and/or carbon resonances refer to Figure 7.

A strong resolution enhancement of the 400 MHz ^{1}H-NMR spectrum by means of Gaussian line transformation made it possible for us to determine proton–proton couplings as small as 0.7 ± 0.05 Hz. Combination of these results with the results of a two-dimensional homonuclear correlation experiment (COSY-45) and several NOE-difference experiments (irradiation at $H3_{a,e}$, $H5_{a,e}$ and H13) yielded an unambiguous assignment of all proton resonances as summarized in Table V.

The eight protons ($H2_{a,e}$ to $H6_{a,e}$) of the piperidine ring system are grouped into four apparent triplets due to fast ring inversion on NMR time scale, which interchanges axial and equatorial protons. This ring inversion is possibly due to the low inversion barrier in these systems. The observed pattern, however, is not a first-order pattern. It should be realized that the ring protons form an AA'BB'CC'DD'M system with H13. Using resolution enhancement, it is observed that the lines of the triplets of $H3_{a,e}$ and $H5_{a,e}$ are doubled due to the allylic coupling with H13 ($^4J \sim 1.24$ and 1.29 Hz, respectively). The coupling pattern of the protons of the phenyl ring is a high-order AA'BB'M pattern, although the main (^3J and ^4J) coupling constants could easily be estimated from the spectrum.

The assignment of H3 and H5 with respect to their orientation towards the naphthalene ring system was determined using NOE-difference techniques. Irradiation of the triplet at 2.43 ppm gives a strong NOE at 7.36 ppm (H15), while irradiation of the triplet at 2.68 ppm gives a NOE at 6.75 ppm (H13). In accordance, irradiation at 6.75 ppm (H13) gives NOEs at 2.68 ppm and 8.13 ppm. Based on these experiments, the triplet at 2.43 ppm is assigned to $H3_{a,e}$, while the triplet at 2.68 ppm is assigned to $H5_{a,e}$ and the complex pattern at 8.13 ppm to H21. Combination of these results with the results of a COSY-45 experiment leads to the assignments made in Table V.

The ^{13}C-NMR spectrum (recorded at 100 MHz) was assigned by means of two proton–carbon correlation experiments, optimized for $^1J_{H-C}$ and $^3J_{H-C-C-C}$ couplings, respectively. The assignments of the carbon atoms are tabulated in Table VI.

Table V ^1H-NMR data (400 MHz) of compound **26** *in $CDCl_3$.*

δ (ppm)	Multiplicity and coupling constants	Nucleus [a]
2.43	t, ^3J 5.75 Hz, d, ^4J 1.24 Hz	$H3_{a,e}$
2.68	t, ^3J 5.72 Hz, d, ^4J 1.29 Hz	$H5_{a,e}$
3.22	t, ^3J 5.75 Hz	$H2_{a,e}$
3.45	t, ^3J 5.72 Hz	$H6_{a,e}$
6.75	br. s	H13
6.87	t, ^3J 7.30 Hz, t, ^4J 1.06 Hz	H10
6.97	d, ^3J 8.82 Hz, d, ^4J 1.06 Hz	H8, H12
7.29	d, ^3J 8.82 Hz, d, ^3J 7.30 Hz	H9, H11
7.36	d, ^3J 7.38 Hz, d ^4J 0.99 Hz	H15
7.64	d, ^3J 8.39 Hz, d, ^3J 6.90 Hz, d, ^4J 1.35 Hz	H20
7.71	d, ^3J 8.29 Hz, d, ^3J 6.90 Hz, d, ^4J 1.33 Hz	H19
7.89	d, ^3J 7.38 Hz	H16
8.13	d, ^3J 8.39 Hz, d, ^4J 1.33 Hz, d, ^5J 0.72 Hz	H21
8.28	d, ^3J 8.29 Hz, d, ^4J 1.35 Hz, d, ^5J 0.72 Hz	H18

[a] For numbering, see Figure 7.

Table VI Data from the 100 MHz ^{13}C-NMR spectrum of compound **26** [a].

δ (ppm)	Nucleus	δ (ppm)	Nucleus	δ (ppm)	Nucleus
29.56	C3	119.54	C10	131.85	C22
35.88	C5	120.25	C13	132.01	C16
50.68	C2	125.56	C18	132.49	C23
51.50	C6	125.88	C15, C21	140.72	C14
108.71	C17	127.31	C20	143.23	C4
116.51	C8, C12	128.34	C19	150.82	C7
118.04	C24	129.14	C9, C11		

[a] For numbering, see Figure 7.

3.3. Synthesis of intermediate piperidones **1–13** (Method A)

1,5-Dichloro-3-pentanone was prepared according to published procedures[39]. Ethylene gas was bubbled through a stirred solution of 3-chloropropionyl chloride (150 g, 1.18 mol) (Janssen) in 1 l of CH_2Cl_2. The solution was cooled to -10°C (ice/salt mixture). In $4\frac{1}{2}$ h, small portions of $AlCl_3$ granulate (162.30 g, 1.22 mol) were added at such a rate that most of the ethylene gas was absorbed. The progress of the reaction was monitored by IR spectroscopy. The carbonyl band at 1790 cm^{-1} of 3-chloropropionyl chloride disappeared and a new absorption band appeared at 1720 cm^{-1} (1,5-dichloro-3-pentanone) and a weaker band at 1680 cm^{-1} probably due to an α,β-unsaturated ketone which was formed as a side-product. The yellow/brown reaction mixture was poured slowly into a stirred mixture of *ca.* 1 kg of ice, 240 ml of concentrated hydrochloric acid, and 600 ml of ether. The organic layer was separated from the residual water, dried over $MgSO_4$, filtered and evaporated to yield a dark brown oil. According to both IR and NMR spectroscopy, the isolated product contained one or more minor unsaturated impurities. However, further purification by distillation (b.p. lit.[39] 65–70.5°C at 0.2 mm Hg) strongly decreased the yield as the compound is not very stable at temperatures above room temperature. Therefore, the crude material was stored at -20°C and was advantageously used in subsequent reactions without further purification. Isolated yield 162.80 g (1.05 mol, 89%). IR, ν (cm^{-1}): 3020 (m), 2960 (m), 1720 (s), 650 (m). ^{1}H NMR (200 MHz), δ (ppm): 2.93, t, $J \approx 6.5$ Hz, 4H, CH_2CO; 3.76, t, $J \approx 6.5$ Hz, 4H, CH_2Cl.

1-Phenyl-4-piperidone (**1**) was synthesized by adding simultaneously a solution of 1,5-dichloro-3-pentanone (0.83 g, 5.37 mmol) and a solution of aniline (0.50 g, 5.37 mmol), both in 10 ml of methanol, to a refluxing slurry of sodium carbonate (0.68 g, 6.44 mmol) in 15 ml of methanol over a period of *ca.* $\frac{1}{2}$ h. After the addition of the two solutions, the reaction mixture was refluxed for $1-1\frac{1}{2}$ h. After cooling to room temperature, the reaction mixture was concentrated and poured into 30 ml of water. After extraction with dichloromethane (3×20 ml), the combined extracts were dried over $MgSO_4$, filtered over a glass filter, and evaporated to give a light yellow oil. Chromatography using petroleum ether (PE)-60–80/ether (1:2), yielded an almost colourless liquid, which solidified to give a white solid. Isolated yield 0.67 g (3.82 mmol, 71%). *M.p.* 32–37°C. *IR*, ν (cm^{-1}): 3000 (m), 2960 (m), 2905 (m), 1710 (vs), 1595 (vs), 1495 (vs), 685 (s). *^1H NMR* (200 MHz), δ (ppm): 2.55, t, $J \approx 6.0$ Hz, 4H, H3, H5; 3.62, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.89, t, $J \approx 7.3$ Hz, 1H, H10; 6.99 (d, $J \approx 7.8$ Hz, 2H, H8, H12; 7.30, t, $J \approx 7.4$ Hz, 2H, H9, H11. *^{13}C NMR* (75.5 MHz APT), δ (ppm): 40.6, C3, C5; 48.7, C2, C6; 115.8, C8, C12; 119.7, C10; 129.3, C9, C11; 149.0, C7; 208.1, C4.

1-(4-Methoxyphenyl)-4-piperidone (**2**). Method A with 4-methoxyaniline (2.00 g, 16.25 mmol), 1,5-dichloro-3-pentanone (2.50 g, 16.13 mmol) and sodium carbonate (2.06 g, 19.44 mmol). Chromatography using ether yielded an off-white solid.

Isolated yield 3.12 g (15.21 mmol, 94%). *M.p.* 64–65°C. *IR*, ν (cm^{-1}): 3010 (w), 2960 (w), 2830 (w), 1705 (s), 1580 (w), 1510 (w), 825 (m). *^1H NMR* (250 MHz), δ (ppm): 2.55, t, $J \approx 6.1$ Hz, 4H, H3, H5; 3.45, t, $J \approx 6.1$ Hz, 4H, H2, H6; 3.75, s, 3H, OCH_3; 6.85, 'd', $J \approx 9.1$

Hz, 2H, H8, H12; 6.95, 'd', $J \approx 9.1$ Hz, 2H, H9, H11. *High-resolution MS*: found m/z 205.1104; calcd. for $C_{12}H_{15}NO_2$ m/z 205.1103.

1-(4-Methylphenyl)-4-piperidone (**3**). Method A with 4-methylaniline (0.76 g, 7.09 mmol), 1,5-dichloro-3-pentanone (1.00 g, 6.45 mmol) and sodium carbonate (1.40 g, 13.21 mmol). The solutions were added to a stirred slurry at room temperature in $\frac{3}{4}$ hr. and then the solution was refluxed for 1-1$\frac{1}{5}$ hrs. Chromatography using PE-40-60/ether (1:1) yielded an almost colourless liquid, which solidified to give a white solid. Isolated yield 0.63 g (3.33 mmol, 47%). *M.p.* 25–29°C. *IR*, ν (cm^{-1}): 3000 (w), 2960 (s), 2920 (s), 2810 (m), 1708 (s), 1610 (s), 1510 (s), 810 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.29, s, 3H, CH_3; 2.55, t, $J \approx 6.0$ Hz, 4H, H3, H5; 3.55, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.91, d, $J \approx 8.6$ Hz, 2H, H8, H12; 7.12, d, $J \approx 8.5$ Hz, 2H, H9, H11.

1-(3,5-Dimethylphenyl)-4-piperidone (**4**). Method A with 3,5-dimethylaniline (0.86 g, 7.10 mmol), 1,5-dichloro-3-pentanone (1.0 g, 6.45 mmol) and sodium carbonate (1.4 g, 13.2 mmol). The solutions were added to a stirred slurry at room temperature in $\frac{3}{4}$ h and then the solution was refluxed for 1–1$\frac{1}{2}$ h. Chromatography using PE-40–60/ether (1:1) yielded an almost colourless oil, which solidified to a white solid. Isolated yield 0.71 g (3.49 mmol, 54%). *M.p.* 40–44°C. *IR*, ν (cm^{-1}): 3000 (w), 2995 (s), 2960 (s), 2915 (s), 2815 (m), 1705 (s), 1590 (s), 1470 (s), 828 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.30, s, 6H, CH_3; 2.55, t, $J \approx 6.0$ Hz, 4H, H3, H5; 3.59, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.57, s, 1H, H10; 6.62, s, 2H, H8, H12.

1-(4-Fluorophenyl)-4-piperidone (**5**). Method A with 4-fluoroaniline (1.43 g, 12.9 mmol), 1,5-dichloro-3-pentanone (2.00 g, 12.9 mmol) and sodium carbonate (2.80 g, 26.42 mmol). The solutions were added to a stirred slurry at room temperature in $\frac{3}{4}$ h and then the solution was refluxed for 1–1$\frac{1}{2}$ h. Chromatography using PE-40–60/ether (1:1) yielded the product as an off-white solid. Recrystallization from PE-40–60/ether yielded a cream-coloured solid. Isolated yield 0.73 g (3.78 mmol, 29%). *M.p.* 77–79°C. *IR*, ν (cm^{-1}): 3000 (w), 2995 (m), 2980 (m), 2900 (m), 2800 (m), 1705 (s), 1500 (s), 822 (s), 809 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.57, t, $J \approx 6.1$ Hz, 4H, H3, H5; 3.50, *t*, $J \approx 6.1$ Hz, 4H, H2, H6; 6.85–7.10, m, 4H, H8, H9, H11, H12.

1-(4-Biphenylyl)-4-piperidone (**6**). Method A, using 4-aminobiphenyl (5.50 g, 32.50 mmol), 1,5-dichloro-3-pentanone (5.00 g, 32.26 mmol) and sodium carbonate (4.12 g, 38.87 mmol). The product was purified by chromatography using dichloromethane, recrystallization from ethanol with a few drops of CH_2Cl_2 yielded white needles. Isolated yield 3.81 g (15.17 mmol, 47%). *M.p.* 176–177°C. *IR*, ν (cm^{-1}): 3050 (m), 3000 m), 2950 (m), 2850 (m), 1705 (s), 1600 (s), 1530 (s), 840 (s), 690 (s). ^1H *NMR* (300 MHz), δ (ppm): 2.59, t, $J \approx 6.1$ Hz, 4H, H3, H5; 3.68, t, $J \approx 6.1$ Hz, 4H, H2, H6; 7.06, 'd', $J \approx 8.8$ Hz, 2H, H8, H12; 7.31, t, $J \approx 7.3$ Hz, t, $J \approx 1.2$ Hz, 1H; 7.43, t, $J \approx 7.5$ Hz, 2H; 7.55–7.59, m, 4H, H9, H11, H_{ar}. *High-resolution MS*: found m/z 251.1307; calcd. for $C_{17}H_{17}NO$ m/z 251.1310.

1-(2,4,6-Trimethylphenyl)-4-piperidone (**7**). Method A without refluxing, using 2,4,6-trimethylaniline (2.70 g, 20.0 mmol) in 750 ml of methanol, 1,5-dichloro-3-pentanone (3.1 g, 20.0 mmol) and sodium carbonate (4.34 g, 40.95 mmol). The reaction mixture was allowed to stand at room temperature for 6 days. The crude oil was first purified by chromatography using PE-40–60/ether (1:1) and then CH_2Cl_2/ether (20:1) to yield a white solid. This intermediate was not purified because from the spectroscopic data the purity appeared satisfactory. Isolated yield 0.64 g (2.95 mmol, 15%). *M.p.* 74–88°C. *IR*, ν (cm^{-1}): 3000 (w), 2960 (s), 2920 (s), 2820 (m), 1705 (s), 1480 (s), 850 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.25, s, 3H, C10-CH_3; 2.32 s, 6H; C8-CH_3, C12-CH_3; 2.56, t, $J \approx 5.9$ Hz, 4H, H3, H5; 3.37, t, $J \approx 5.9$ Hz, 4H, H2, H6; 6.85, s, 2H, H9, H11.

1-(4-Hexylphenyl)-4-piperidone (**8**). Method A with 4-hexylaniline (1.26 g, 7.10 mmol) (Aldrich), 1,5-dichloro-3-pentanone (1.01 g, 6.50 mmol) and sodium carbonate (1.41 g, 13.30 mmol). The product was purified by chromatography using ether/PE-60–80 (3:2), which yielded a colourless oil. Isolated yield 1.02 g (3.93 mmol, 60%). *IR*, ν (cm^{-1}): 3000 (m), 2960 (s), 2930 (vs), 2850 (s), 1705 (vs), 1605 (s), 1505 (s), 810 (m). ^1H *NMR* (200 MHz), δ (ppm): 0.89, t, $J \approx 6.4$ Hz, 3H, CH_3; 1.20–1.45, m, 6H, $(CH_2)_3CH_3$; 1.50–1.70, m, 2H, C10-CH_2CH_2; 2.40–2.70, m, 6H, C10-CH_2, H3, H5; 3.56, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.92, d, $J \approx 8.5$ Hz, 2H, H8, H12; 7.12, d, $J \approx 8.5$ Hz, 2H, H9, H11. *High-resolution MS*: found m/z 259.1978; calcd. for $C_{17}H_{25}NO$ m/z 259.1936.

1-(4-Tetradecylphenyl)-4-piperidone (**9**). Method A, using 4-tetradecylaniline (3.09 g, 11.05 mmol), 1,5-dichloro-3-pentanone (1.57 g, 10.12 mmol) and sodium carbonate (2.20 g, 20.71 mmol). The product was purified by chromatography using ether/PE-60–80 (3:2), which yielded an off-white solid. Isolated yield 1.84 g (4.96 mmol, 49%). *M.p.* 42–46°C. *IR*, ν (cm^{-1}): 3000 (w), 2920 (vs), 2850 (s), 1705 (vs), 1600 (s), 1505 (s), 820 (w). ^1H *NMR* (200 MHz), δ (ppm): 0.89, t, $J \approx 6.3$ Hz, 3H, CH_3; 1.26 (br.s, 22H, $(CH_2)_{11}CH_3$), 1.45–1.65, m, 2H, C10-CH_2CH_2; 2.45–2.65, m, 6H, C10-CH_2, H3, H5; 3.56, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.92, d, $J \approx 8.5$ Hz, 2H, H8, H12; 7.12, d, $J \approx 8.5$ Hz, 2H, H9, H11. *High-resolution MS*: found m/z 371.3158; calcd. for $C_{25}H_{41}NO$ m/z 371.3188.

1-Cyclohexyl-4-piperidone (**10**). Method A, using freshly distilled cyclohexylamine (0.50 g, 5.04 mmol) (Merck), 1,5-dichloro-3-pentanone (0.78 g, 5.04 mmol) and sodium carbonate (0.64 g, 6.04 mmol). The crude oil was purified by chromatography using ethyl acetate (R_f 0.12) and was isolated as a colourless oil. Isolated yield 0.66 g (3.64 mmol, 72%). *IR*, ν (cm^{-1}): 2930 (vs), 2850 (s), 2700 (s), 1710 (vs), 1460 (m), 1450 (s). ^1H *NMR* (200 MHz), δ (ppm): 1.00–1.35, m, 5H, $H8_a$, $H9_a$, $H10_a$, $H11_a$, $H12_a$; 1.62, br. d, $J \approx 10.3$ Hz, 1H, $H10_e$; 1.70–1.90, m, 4H, $H8_e$, $H9_e$, $H11_e$, $H12_e$; 2.41, t, $J \approx 6.0$ Hz, 5H, H3, H5, H7; 2.83, t, $J \approx 6.0$ Hz, 4H, H2, H6. *High-resolution MS*: found m/z 181.1483; calcd. for $C_{11}H_{19}NO$ m/z 181.1467.

1-(4-Bromophenyl)-4-piperidone (**11**). Method A with 4-bromoaniline (5.16 g, 30.00 mmol), 1,5-dichloro-3-pentanone (4.55 g, 29.35 mmol) and sodium (4.25 g, 40.10 mmol). The solutions were added to a stirred slurry at room temperature in $\frac{3}{4}$ h and then the solution was refluxed for 1–1$\frac{1}{2}$ h. The product was purified by chromatography using dichloromethane (R_f 0.19), which yielded a light yellow solid. Isolated yield 2.87 g (11.25 mmol, 37%). *M.p.* 81–84°C. *IR*, ν (cm^{-1}): 3000 (s), 2960 (s), 2900 (m), 2810 (s), 1710 (vs), 1580 (vs), 810 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.55, t, $J \approx 6.0$ Hz, 4H, H3, H5; 3.58, t, $J \approx 6.0$ Hz, 4H; H2, H6; 6.84, d, $J \approx 9.0$ Hz, 2H, H8, H12, 7.34, d, $J \approx 9.0$ Hz, 2H, H9, H11. *High-resolution MS*: found m/z 253.0135; calcd. for $C_{11}H_{12}NBrO$ m/z 253.0102.

1-(4-Chlorophenyl)-4-piperidone (**12**). Method A, using 4-chloroaniline (2.01 g, 15.76 mmol), 1,5-dichloro-3-pentanone (2.45 g, 15.81 mmol) and sodium carbonate (1.99 g, 18.81 mmol). The product was purified by chromatography using dichloromethane (R_f 0.17), which yielded a light yellow solid. Isolated yield 2.62 g (12.49 mmol, 79%). *M.p.* 50–53°C. *IR*, ν (cm^{-1}): 3000 (m), 2960 (m), 2900 (m), 2810 (m), 1710 (vs), 1590 (s), 810 (s). ^1H *NMR* (200 MHz), δ (ppm): 2.55, t, $J \approx 6.1$ Hz, 4H, H3, H5; 3.57, t, $J \approx 6.1$ Hz, 4H, H2, H6; 6.89, d, $J \approx 9.0$ Hz, 2H, H8, H12; 7.24, d, $J \approx 9.0$ Hz, 2H, H9, H11. *High-resolution MS*: found m/z 209.0614; calcd. for $C_{11}H_{12}NClO$ m/z 209.0607.

1-(1-Phenyl-4-piperidyl)-4-piperidone (**13**). 1-Phenyl-4-piperidone (**1**) was converted to the corresponding oxime in quantitative yield by refluxing **1** (1.75 g, 10.0 mmol), potassium carbonate (2.4 g, 18 mmol) and the HCl salt of hydroxylamine (1.04 g, 15.0 mmol) according to published procedures[40]. Reduction of the oxime with an excess RED-Al[41] gave 1-phenyl-4-aminopiperidine (1.26 g, 7.10 mmol) in 71% yield. This amine (1.26 g, 7.10 mmol), 1,5-dichloro-3-pentanone (1.00 g, 6.25 mmol) and sodium carbonate (1.40 g, 13.21 mmol) were reacted as described in method A. The product was purified by chromatography using ether/PE-60–80 (1:1) (R_f 0.42). Isolated yield 1.53 g (5.90 mmol, 84%). *IR*, ν (cm^{-1}): 3000 (m), 2920 (s), 2800 (s), 1710 (vs), 1595 (vs), 1570 (s), 1495 (s), 755 (s), 690 (s). ^1H *NMR* (250 MHz), δ (ppm): 1.72, q, $J \approx 11.8$ Hz, d, $J \approx 3.4$ Hz, 2H, $H3'_a$, $H5'_a$; 1.90, br. d, $J \approx 12.7$ Hz, 2H, $H3'_e$, $H5'_e$; 2.42, t, $J \approx 6.1$ Hz, 4H, H3, H5; 2.50, m, 1H, H4'; 2.75, t, $J \approx 10.3$ Hz, d, $J \approx 1.9$ Hz, 2H, $H2'_a$, $H6'_a$; 2.87, t, $J \approx 6.0$ Hz, 4H, H2, H6; 3.75 br. d, $J \approx 12.4$ Hz, 2H, $H2'_e$, $H6'_e$; 6.82, t, $J \approx 7.2$ Hz, 1H, H10; 6.93, d, $J \approx 8.0$ Hz, 2H, H8, H12; 7.23, t, $J \approx 7.9$ Hz, 2H, H9, H11.

3.4. Knoevenagel synthesis of donor–bridge–acceptor systems **14–25** *(Method B)*

1-Phenyl-4-(dicyanomethylene)piperidine (**14**) was synthesized by stirring and refluxing under nitrogen a mixture of **1** (1.60 g, 9.13 mmol), propanedinitrile (0.59 g, 8.93 mmol), 0.67 g of ammonium acetate, and 1.5 ml of acetic acid in *ca.* 50 ml of benzene for 1$\frac{1}{2}$ h in a Dean–Stark apparatus[16b]. After cooling, the clear light-orange solution was washed with water, saturated sodium bicarbonate and water. The combined organic solutions were dried over $MgSO_4$, filtered, and evaporated to dryness. The yellow solid was recrystallized from ethyl acetate. Isolated yield 1.18 g (5.29 mmol, 58%). M.p.

ca. 139°C (dec.) (suitable crystals for X-ray analysis were obtained by slow evaporation of an ether/CH_2Cl_2 solution). *IR*, ν (cm^{-1}): 3050 (w), 3020 (m), 2970 (w), 2830 (m), 2230 (s), 1600 (s), 1500 (s). *^1H NMR* (250 MHz), δ (ppm): 2.84, t, $J \approx 6.0$ Hz, 4H, H3, H5; 3.48, t, $J \approx 6.0$ Hz, 4H, H2, H6; 6.91, m, 3H, H8, H10, H12; 7.28, m, 2H, H9, H11. *^{13}C NMR* (50.3 MHz, APT), δ (ppm): 33.5, C3, C5; 49.9, C2, C6; 83.7, C13; 111.3, CN; 116.3, C8, C12; 120.7, C10; 129.6, C9, C11; 148.5, C7; 180.4, C4. *UV* (n-hexane), nm (ε): 208 (18580), 248 (25180), 392 (1770), 342 (2970). *High-resolution MS*: found m/z 223.1092; calcd. for $C_{14}H_{13}N_3$ m/z 223.1109. The structure was further confirmed by X-ray analysis[16b].

1-(4-Methoxyphenyl)-4-(dicyanomethylene)piperidine (**15**). Method B with **2** (146.9 mg, 0.72 mmol), propanedinitrile (73.1 mg, 1.11 mmol), 150 mg of ammonium acetate, and 0.11 ml of acetic acid in 3 ml of toluene[16b]. Recrystallization from ether/CH_2Cl_2 (1:1) yielded a red solid. Further chromatography using PE(−)40–60/ether (1:3) yielded a yellow crystalline compound. Isolated yield 106 mg (0.42 mmol, 59%). *M.p.* 129–130°C (suitable crystals for the X-ray analysis were obtained by slow evaporation of an ether/CH_2Cl_2 solution). *IR*, ν (cm^{-1}): 3000 (m), 2960 (m), 2930 (m), 2905 (m), 2830 (m), 2230 (m), 1595 (m), 1510 (s), 825 (m). *^1H NMR* (250 MHz), δ (ppm): 2.86, t, $J \approx 5.6$ Hz, 4H, H3, H5; 3.34, t, $J \approx 5.6$ Hz, 4H, H2, H6; 3.77, s, 3H, OCH_3; 6.80–6.95, m, 4H, H8, H9, H11, H12. *^{13}C NMR* (62.9 MHz, APT), δ (ppm): 33.9, C3, C5; 51.4, C2, C6; 55.6, OCH_3; 83.6, C13; 111.3, CN; 114.8, C9, C11; 118.8, C8, C12; 143.0, C7; 154.7, C10; 180.4, C4. *UV* (n-hexane), nm (ε): 200 (20000), 246 (22810), 300 (2000), 356 (1520). *High-resolution MS*: found m/z 253.1219; calcd. for $C_{15}H_{15}N_3O$ m/z 253.1215. The structure was further confirmed by X-ray analysis[16b].

1-(4-Methylphenyl)-4-(dicyanomethylene)piperidine (**16**). Method B, using **3** (0.21 g, 1.11 mmol), propanedinitrile (83 mg, 1.26 mmol), 120 mg of ammonium acetate, and 0.20 ml of acetic acid in 10 ml of toluene. Chromatography using PE-40–60/ether (3:2) yielded 0.15 g of a yellow solid. Recrystallization from cyclohexane/ether (with a few drops of CH_2Cl_2) yielded large yellow crystals, suitable for X-ray analysis. Isolated yield 0.15 g (0.63 mmol, 57%). *M.p. ca* 111°C (dec.). *IR*, ν (cm^{-1}): 3020 (m), 2995 (m), 2955 (m), 2910 (m), 2805 (m), 2210 (s), 1590 (s), 1505 (s), 804 (s). *^1H NMR* (200 MHz), δ (ppm): 2.29, s, 3H, CH_3; 2.86, t, $J \approx 5.6$ Hz, 4H, H3, H5; 3.45, t, $J \approx 5.6$ Hz, 4H, H2, H6; 6.87, d, $J \approx 8.6$ Hz, 2H, H8, H12; 7.12, d, $J \approx 8.3$ Hz, 2H, H9, H11. *^{13}C NMR* (50.3 MHz, APT), δ (ppm): 20.3, CH_3; 33.5, C3, C5; 50.3, C2, C6; 83.4, C13; 111.3, CN; 116.5, C8, C12; 130.0, C9, C11; 130.3, C10; 146.3, C7; 180.6, C4. *UV* (*n*-hexane), nm (ε): 206 (21200), 248 (23870), 298 (1530), 350 (2440). *High-resolution MS*: found m/z 237.1280; calcd. for $C_{15}H_{15}N_3$ m/z 237.1266. The structure was further confirmed by X-ray analysis[12c].

1-(4-Fluorophenyl)-4-(dicyanomethylene)piperidine (**17**). Method B with **5** (193 mg, 1.00 mmol), propanedinitrile (86 mg, 1.30 mmol), and 89 mg of ammonium acetate in 5 ml of toluene. The product was purified by chromatography using PE 40-60/ether (1:1). Recrystallization from ether/CH_2Cl_2 (1:1) yielded the product as pale yellow crystals. Isolated yield 133 mg (0.55 mmol, 55%). *M.p.* 134–138°C. *IR*, ν (cm^{-1}): 3020 (m), 2960 (m), 2900 (w), 2810 (m), 2225 (s), 1595 (s), 1505 (s), 825 (s), 810 (s). *^1H NMR* (250 MHz), δ (ppm): 2.86, t, $J \approx 5.6$ Hz, 4H, H3, H5; 3.37, t, $J \approx 5.7$ Hz, 4H, H2, H6; 6.85–7.05, m, 4H, H8, H9, H11, H12. *^{13}C NMR* (50.3 MHz, APT), δ (ppm): 33.7, C3, C5; 50.9, C2, C6; 83.9, C13; 111.2, CN; 116.0, d, $^2J_{CF} \approx 22.4$ Hz, C9, C11; 118.5, d, $^3J_{CF} \approx 7.7$ Hz, C8, C12; 145.5, d, $^4J_{CF} \approx 2.5$ Hz, C7; 157.5, d, $^1J_{CF} \approx 240.7$ Hz, C10; 180.0, C4. *UV* (n-hexane), nm (ε): 204 (20580), 242 (22680), 298 (2170), 336 (1930). *High-resolution MS*: found m/z 241.1002; calcd. for $C_{14}H_{12}FN_3$ m/z 241.1015. The structure was further confirmed by X-ray analysis[12c].

1-(3,5-Dimethylphenyl)-4-(dicyanomethylene)piperidine (**18**). Method B with **4** (0.25 g, 1.23 mmol), propanedinitrile (95 mg, 1.44 mmol), 95 mg of ammonium acetate, and 0.22 ml of acetic acid in 10 ml of toluene. The product was purified by chromatography using PE-40–60/ether (1:1) and subsequent recrystallization from ether/CH_2Cl_2 (1:1) yielded light yellow crystals. Isolated yield 0.20 g (0.80 mmol, 65%). *M.p. ca.* 150°C. (dec.) *IR*, ν (cm^{-1}): 3030 (w), 3000 (m), 2960 (m), 2920 (m), 2820 (m), 2225 (s), 1590 (s), 825 (m). *^1H NMR* (200 MHz), δ (ppm): 2.30, s, 6H, CH_3; 2.84, t, $J \approx 5.6$ Hz, 4H, H3, H5; 3.48, t, $J \approx 5.6$ Hz, 4H, H2, H6; 6.59, s, 3H, H8, H10, H12. *^{13}C NMR* (62.9 MHz, APT), δ (ppm): 21.6, CH_3; 33.6, C3, C5; 50.0, C2, C6; 83.4, C13; 111.4, CN; 114.1, C8, C12; 122.6, C10; 139.2, C9, C11; 148.5, C7; 180.7, C4. *UV* (n-hexane), nm (ε): 218 (24060), 250 (20140), 294 (1480), 350 (2780). *High-resolution MS*: found m/z 251.1383; calcd. for $C_{16}H_{17}N_3$ m/z 251.1422. The structure was further confirmed by X-ray analysis[12c].

1-(4-biphenylyl)-4-(dicyanomethylene)piperidine (**19**). Method B with **6** (1.00 g, 4.15 mmol), propanedinitrile (0.30 g, 4.15 mmol), 0.42 g of ammonium acetate and 0.20 ml of acetic acid in 25 ml of toluene. Purification by recrystallization from ether/dichloromethane (1:1) yielded a yellow powder. Isolated yield 0.71 g (2.35 mmol, 57%). *M.p.* 171–172°C. *IR*, ν (cm^{-1}): 3050 (m), 3000 (m), 2950 (m), 2820 (m), 2225 (s), 1600 (s), 1530 (s), 840 (s). *^1H NMR* (300 MHz), δ (ppm): 2.89, t, $J \approx 5.6$ Hz, 4H, H3, H5; 3.55, t, $J \approx 5.6$ Hz, 4H, H2, H6; 7.03, 'd', $J \approx 8.8$ Hz, 2H, H8, H12; 7.32, t, $J \approx 7.3$ Hz, t, $J \approx 1.6$ Hz, 1H; 7.43, t, $J \approx 7.5$ Hz, 2H; 7.56, m, 4H, H9, H11, H_{ar}. *UV* (dichloromethane), nm (ε): 232 (16620), 288 (21840), 362 (3590). *High-resolution MS*: found m/z 299.1419; calcd. for $C_{20}H_{17}N_3$ m/z 299.1422.

1-(2,4,6-Trimethylphenyl)-4-(dicyanomethylene)piperidine (**20**). Method B, using **7** (209 mg, 0.96 mmol), propanedinitrile (94 mg, 1.42 mmol) and 217 mg of ammonium acetate in 5 ml of toluene. The product was purified by chromatography (CH_2Cl_2) and recrystallization from PE-40–60/ether (1:1) (with a few drops of CH_2Cl_2) yielded pale yellow crystals. Isolated yield 146.6 mg (0.55 mmol, 57%). *M.p.* 147.3–148.3°C. *IR*, ν (cm^{-1}): 3000 (m), 2960 (m), 2920 (m), 2820 (m), 2230 (s), 1590 (s), 1480 (s), 855 (s). *^1H NMR* (200 MHz), δ (ppm): 2.27, s, 9H, CH_3; 2.88, t, $J \approx 5.4$ Hz, 4H, H3, H5; 3.27, t, $J \approx 5.4$ Hz, 4H, H2, H6; 6.85, s, 2H, H9, H11. *^{13}C NMR* (62.9 MHz, APT), δ (ppm): 19.3, C8-$\underline{C}H_3$, C12-$\underline{C}H_3$; 20.6 C10-$\underline{C}H_3$, 36.2, C3, C5; 50.7, C2, C6; 83.6, C13; 111.5, CN; 129.7, C9, C11; 135.5, C10; 136.3, C8, C12; 144.2, C7; 181.8, C4. *UV* (n-hexane), nm (ε): 220 (22710), 324 (2040). *High-resolution MS*: found m/z 265.1586; calcd. for $C_{17}H_{19}N_3$ m/z 265.1579.

1-Phenyl-4-[[cyano(methoxycarbonyl)]methylene]piperidine (**21**). Method B, using **1** (1.74 g, 9.92 mmol), methyl cyanoacetate (1.14 g, 11.5 mmol), 0.7 g of ammonium acetate, and 2 ml of acetic acid in 50 ml toluene. The product was purified by recrystallization from ethanol to yield yellow crystals. Isolated yield 1.22 g (4.76 mmol, 48%). *M.p.* 94–95°C. *IR*, ν (cm^{-1}): 2220 (m), 1725 (s), 1592 (vs), 1490 (s). *^1H NMR* (300 MHz), δ (ppm): 2.91, t, $J \approx 5.7$ Hz, 2H, H5; 3.28, t, $J \approx 5.6$ Hz, 2H, H3; 3.42, t, $J \approx 5.6$ Hz, 2H, H2; 3.49, t, $J \approx 5.7$ Hz, 2H, H6; 3.85, s, 3H, OCH_3; 6.85–7.00, m, 3H, H8, H10, H12; 7.30, t, $J \approx 8.0$ Hz, 2H, H9, H11. *^{13}C NMR* (75.5 MHz APT), δ (ppm): 30.6, 35.1, C3, C5; 49.2, 49.6, C2, C6; 52.6, OCH_3; 102.9, C13; 115.1, CN; 115.8, C8, C12; 119.9, C10; 129.3, C9, C11; 149.2, C7; 162.1, CO; 175.9, C4. *UV* (n-hexane), nm (ε): 250 (22840), 292 (1990), 338 (2170). *High-resolution MS*: found m/z 256.1216; calcd. for $C_{15}H_{16}N_2O_2$ m/z 256.1212. The structure was further confirmed by X-ray analysis[12c].

1-(4-Methoxyphenyl)4-[[cyano(methoxycarbonyl)]methylene]piperidine (**22**). Method B, using **2** (150 mg, 0.73 mmol), methyl cyanoacetate (89 mg, 0.90 mmol), ca. 90 mg of ammonium acetate, and 0.15 ml of acetic acid in 5 ml of toluene. Recrystallization from ether/CH_2Cl_2 and subsequent chromatography using *n*-hexane/ether (1:3) yielded a yellow crystalline solid. Isolated yield 78 mg (0.27 mmol, 37%). *M.p.* 108–109.5°C. *IR*, ν (cm^{-1}): 3005 (m), 2960 (m), 2930 (m), 2910 (m), 2830 (m), 2810 (m), 2220 (m), 1730 (s), 1605 (m), 1510 (s), 820 (m). *^1H NMR* (250 MHz, C_6D_6), δ (ppm): 2.39, t, $J \approx 5.7$ Hz, 2H, H5; 2.70, m, 4H, H2, H3; 2.92, t, $J \approx 5.6$ Hz, 2H, H6; 3.28, s, 3H; C10-OCH_3, 3.38 (s, 3H; CO-OCH_3, 6.55, 'd', $J \approx 9.0$ Hz, 2H, H8, H12; 6.78, 'd', $J \approx 9.0$ Hz, 2H, H9, H11. *^{13}C NMR* (62.9 MHz, APT), δ (ppm): 31.1, 35.6, C3, C5; 51.3, 51.6, C2, C6; 52.6, CO-$\underline{O}CH_3$; 55.6, C10-$\underline{O}CH_3$; 102.9, C13; 114.8, C9, C11; 115.1, CN; 118.5, C8, C12; 144.0, C7; 154.3, C10; 162.2, CO; 175.7, C4. *UV* (n-hexane), nm (ε): 204 (20420), 248 (23220), 302 (2300), 346 (1360). *High-resolution MS*: found m/z 286.1317; calcd. for $C_{16}H_{18}N_2O_3$ m/z 286.1317.

1-(4-Methylphenyl)-4-[[cyano(methoxycarbonyl)]methylene]piperidine (**23**). Method B with **3** (0.61 g, 3.22 mmol), methyl cyanoacetate (358 mg, 3.61 mmol), 328 mg of ammonium acetate, and 0.57 ml of acetic acid. The product was purified by chromatography using PE-40–60/ether (1:1) yielding a yellow solid. Recrystallization from PE-40–60/ether (1:1) yielded crystals suitable for X-ray analysis. Isolated yield 0.44 g (1.63 mmol, 51%). *M.p.* 85.5–86.5°C. *IR*, ν (cm^{-1}): 3030 (m), 3000 (m), 2950 (m), 2920 (m), 2810 (m), 2220 (m), 1725 (s), 1605 (s), 1508 (s), 808 (m). *^1H NMR* (200 MHz), δ (ppm): 2.29, s, 3H, C10-CH_3; 2.90, t, $J \approx 5.7$ Hz, 2H, H5; 3.27, m, 2H, H3; 3.35, m, 2H, H2; 3.44, t, $J \approx 5.8$ Hz, 2H, H6; 3.85, s, 3H, OCH_3; 6.87, d, $J \approx 8.6$ Hz, 2H, H8, H12; 7.12, d, $J \approx 8.3$ Hz, 2H, H9, H11. *^{13}C NMR* (50.3 MHz, APT), δ (ppm): 20.3, C10-$\underline{C}H_3$, 30.6, 35.2, C3, C5; 50.0, 50.3, C2, C6; 52.5, OCH_3; 102/7, C13; 115.0, CN; 116.3, C8, C12; 129.6, C10; 129.8, C9, C11; 147.0, C7; 162.0, CO; 175.9, C4. *UV* (n-hexane), nm (ε): 206 (21390), 250 (23200), 298 (1880), 342 (1960). *High-resolution MS*: found m/z 270.1350; calcd. for $C_{16}H_{18}N_2O_2$ m/z 270.1368. The structure was further confirmed by X-ray analysis[12c].

1-(4-Fluorophenyl)-4-[[cyano(methoxycarbonyl)]methylene]piperidine (**24**). Method B, using **5** (103 mg, 0.53 mmol), methyl cyanoacetate (59 mg, 0.60 mmol) and 119 mg of ammonium acetate in 5 ml of toluene. The product was purified by chromatography (CH_2Cl_2). Recrystallization from ether/CH_2Cl_2 (1:1) yielded white/yellow crystals. Isolated yield 99.6 mg (0.36 mmol, 68%). *M.p.* 125.5–127.5°C. *IR*, ν (cm^{-1}): 3030 (m), 2995 (m), 2950 (m), 2900 (m), 2810 (m), 2220 (m), 1725 (s), 1600 (m), 1505 (s), 825 (m), 810 (m). ^1H *NMR* (200 MHz), δ (ppm): 2.91, t, $J \approx 5.7$ Hz, 2H, H5; 3.30, m, 4H, H2, H3; 3.38, t, $J \approx 5.7$ Hz, 2H, H6, 3.85, s, 3H, OCH_3; 6.80–7.05, m, 4H, H8, H9, H11, H12. ^{13}C *NMR* (50.3 MHz, APT), δ (ppm): 30.8, 35.4, C3, C5; 50.6, 50.9, C2, C6; 52.6, OCH_3; 103.2, C13; 115.0, CN; 115.8, d, $^2J_{CF} \approx 22.2$ Hz, C9, C11; 118.1, d, $^3J_{CF} \approx 7.7$, Hz, C8, C12; 146.2, d, $^4J_{CF} \approx 2.0$ Hz, C7; 157.4, d, $^1J_{CF} \approx 239.8$, Hz, C10; 162.1, CO; 175.3, C4. *UV* (n-hexane), nm (ε): 202 (17460), 244 (21030), 302 (2290), 338 (sh, 1480). *High-resolution MS*: found m/z 274.1120; calcd. for $C_{15}H_{15}FN_2O_2$ m/z 274.1117.

1-(3,5-Dimethylphenyl)-4-[[cyano(methoxycarbonyl)]methylene]-piperidine (**25**). Method B with **4** (0.25 g, 1.23 mmol), methyl cyanoacetate (140 mg, 1.41 mmol), 122 mg of ammonium acetate, and 0.22 ml of acetic acid in 10 ml of toluene. The product was purified by chromatography using PE-40–60/ether (1:2) and subsequent recrystallization from PE-40–60/ether (1:1) yielded 91 mg of small yellow needle-like crystals. Evaporation of the filtrate after isolating the crystals and recrystallization of the isolated solid from PE-40–60/CH_2Cl_2 (1:1) yielded another 78 mg of yellow crystals. Total yield 169 mg (0.59 mmol, 48%). *M.p.* 89–91°C (both fractions). *IR*, ν (cm^{-1}): 3025 (m), 3000 (m), 2955 (m), 2915 (m), 2805 (m), 2220 (m), 1725 (s), 1590 (s), 825 (m). ^1H *NMR* (200 MHz), δ (ppm): 2.30, s, 6H, CH_3; 2.89, t, $J \approx 5.7$ Hz, 2H, H5; 3.26, t, $J \approx 6.0$ Hz, 2H, H3; 3.39, m, 2H, H2; 3.47, t, $J \approx 5.8$ Hz, 2H, H6; 3.85, s, 3H, OCH_3; 6.57, s, 3H, H8, H10, H12. ^{13}C *NMR* (50.3 MHz, APT), δ (ppm): 21.6 CH_3, 30.8, 35.3, C3, C5; 49.5, 49.9, C2, C6; 52.6, OCH_3; 102.8, C13; 113.9, C8, C12; 115.2, CN; 122.0, C10; 139.0, C9, C11; 149.4, C7; 162.2, CO; 176.2, C4. *UV* (n-hexane), nm (ε): 218 (27190), 252 (20650), 296 (1830), 342 (2230). *High-resolution MS*: found m/z 284.1505; calcd. for $C_{17}H_{20}N_2O_2$ m/z 284.1525.

3.5. Wadsworth–Emmons and Wittig synthesis of donor–bridge–acceptor systems **26–47** *(Method C)*

1-Phenyl-4-[(4-cyano-1-naphthyl)methylene]piperidine (**26**) ("fluoroprobe") was synthesized in two steps. Refluxing a mixture of 4-bromomethyl-1-naphthonitrile[42] (5.45 g, 22.14 mmol) and triethyl phosphite (4.00 g, 24.07 mmol) for 4 h[29] and removal of the excess triethyl phosphite *in vacuo* gave the corresponding phosphonate in quantitative yield, which was used without further purification.

A solution of **1** (0.53 g, 3.0 mmol) and the phosphonate (0.91 g, 3.0 mmol) in 10 ml of dimethoxyethane (dried on 3 Å mol sieves) under a nitrogen atmosphere, was coolded in ice[32]. During 10 min, NaH (0.14 g, 3.2 mmol) (55–60% suspension in paraffin oil) was added. After removal of the ice-waterbath, the reaction mixture was stirred for an additional period of at least 4 h. The reaction mixture was poured into water and extracted with chloroform. The organic layers were dried over $MgSO_4$ and the solvent evaporated. The crude product was purified by chromatography (dichloromethane) and recrystallized from ethanol to give off-white needles. Isolated yield 0.468 g (1.44 mmol, 48%). *M.p.* 121–122°C. *IR*, ν (cm^{-1}): 2220 (m), 1600 (s), 1580 (m), 1490 (s). ^1H *NMR and* ^{13}C *NMR*: see section 3.2, Tables V and VI and Figure 7. *UV* (n-hexane), nm (ε): 234 (48100), 248 (19700), 308 (11700). *High-resolution MS*: found m/z 324.1627; calcd. for $C_{23}H_{20}N_2$ m/z 324.1626.

1-(4-Methoxyphenyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**27**). Method C, using **2** (0.42 g, 2.05 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (0.60 g, 1.98 mmol) and sodium dried THF instead of DME. The product was purified by chromatography using dichloromethane, recrystallization from methanol yielded yellow needles. Isolated yield 0.33 g (0.93 mmol, 46%). *M.p.* 141–142°C. *IR*, ν (cm^{-1}): 3000 (m), 2950 (m), 2900 (m), 2820 (m), 2800 (m), 2220 (s), 1570 (m), 1505 (s), 820 (m). ^1H *NMR* (250 MHz), δ (ppm): 2.42, t, $J \approx 5.6$ Hz, 2H, H3; 2.67, t, $J \approx 5.7$ Hz, 2H, H5; 3.05, t, $J \approx 5.3$ Hz, 2H, H2; 3.28, t, $J \approx 5.4$ Hz, 2H, H6; 3.76, s, 3H, OCH_3; 6.72, s, 1H, H13; 6.90, m, 4H, H8, H9, H11, H12; 7.33, d, $J \approx 7.4$ Hz, 1H, H15; 7.61, m, 1H, H20; 7.69, m, 1H, H19; 7.87, d, $J \approx 7.4$ Hz, 1H, H16; 8.11, 'd', $J \approx 7.8$ Hz, 1H, H21; 8.26, 'd', $J \approx 7.8$ Hz, 1H, H18. *UV* (n-hexane), nm (ε): 236 (sh 48710), 310 (14470). *High-resolution MS*: found m/z 354.1703; calcd. for $C_{24}H_{22}N_2O$ m/z 354.1732.

1-(4-Methylphenyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**28**). Method C, using **3** (3.29 g, 17.4 mmol) and diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (5.00 g, 16.5 mmol) and sodium dried THF instead of DME. The product was purified by chromatography using dichloromethane; recrystallization from ethanol yielded yellow needles. Isolated yield 1.45 g (4.28 mmol, 26%). *M.p.* 101–102°C. *IR*, ν (cm^{-1}): 3000 (m), 2950 (m), 2800 (m), 2220 (s), 1600 (m), 1570 (m), 1505 (s), 810 (m). ^1H *NMR* (250 MHz), δ (ppm): 2.28, s, 3H, CH_3; 2.43, t, $J \approx 5.5$ Hz, 2H, H3; 2.68, t, $J \approx 5.4$ Hz, 2H, H5; 3.15, t, $J \approx 5.7$ Hz, 2H, H2; 3.38, t, $J \approx 5.6$ Hz, 2H, H6; 6.74, s, 1H, H13; 6.88, d, $J \approx 8.6$ Hz, 2H, H8, H12; 7.09, d, $J \approx 8.4$ Hz, 2H, H9, H11; 7.36, d, $J \approx 7.4$ Hz, 1H, H15; 7.62, m, 1H, H20; 7.72, m, 1H, H19; 7.84, d, $J \approx 7.4$ Hz, 1H, H16; 8.12, 'd', $J \approx 8.4$ Hz, 1H, H21; 8.28, 'd', $J \approx 7.8$ Hz, 1H, H18. *High-resolution MS*: found m/z 338.1769; calcd. for $C_{24}H_{22}N_2$ m/z 338.1783.

1-(4-Hexylphenyl)-4-[(cyano-1-naphthyl)methylene]piperidine (**29**). Methyl C with **8** (0.26 g, 1.01 mmol), diethyl [(4-cyano-1-naphthyl) methyl]phosphonate (0.31 g, 1.01 mmol) and using sodium-dried THF instead of DME. The product was purified by crystallization from ethanol, which yielded yellow crystals. Isolated yield 0.26 g (0.63 mmol, 62%). *M.p.* 64–65°C. *IR*, ν (cm^{-1}): 3000 (w), 2950 (m), 2920 (m), 2850 (m), 2220 (s), 1600 (m), 1505 (s), 860 (w). ^1H *NMR* (200 MHz), δ (ppm): 0.88, t, $J \approx 6.3$ Hz, 3H, CH_3; 1.20–1.40, m, 6H, $(CH_2)_3CH_3$; 1.45–1.65, m, 2H, C10-CH_2CH_2; 2.43, t, $J \approx 5.3$ Hz, 2H, H3; 2.53, t, $J \approx 7.6$ Hz, 2H, C10-CH_2; 2.68, t, $J \approx 5.2$ Hz, 2H, H5; 3.16, t, $J \approx 5.7$ Hz, 2H, H2; 3.39, t, $J \approx 5.6$ Hz, 2H, H6; 6.74, s, 1H, H13; 6.89, d, $J \approx 8.4$ Hz, 2H, H8, H12; 7.08, d, $J \approx 8.5$ Hz, 2H, H9, H11; 7.36, d, $J \approx 7.4$ Hz, 1H, H15; 7.62, m, 1H, H20; 7.72, m, 1H, H19; 7.89, d, $J \approx 7.4$ Hz, 1H, H16; 8.12 'd', $J \approx 8.4$ Hz, 1H, H21; 8.27 'd', $J \approx 8.4$ Hz, 1H, H18. *High-resolution MS*: found m/z 408.2597; calcd. for $C_{29}H_{32}N_2$ m/z 408.2565.

1-(4-Tetradecylphenyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**30**). Method C, using **9** (0.37 g, 1.01 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (0.32 g, 1.04 mmol) and sodium-dried THF instead of DME. The product was purified by crystallization from ethanol, which yielded yellow crystals. Isolated yield 0.44 g (0.86 mmol, 82%). *M.p.* 62–63°C. *IR*, ν (cm^{-1}): 3000 (w), 2920 (s), 2850 (m), 2220 (s), 1600 (w), 1505 (m), 860 (w). ^1H *NMR* (200 MHz), δ (ppm): 0.88, t, $J \approx 6.4$ Hz, 3H, CH_3; 1.26, br. s, 22H, $(CH_2)_{11}CH_3$; 1.59, br. s, 2H, C10-CH_2CH_2, 2.43, t, $J \approx 5.3$ Hz, 2H, H3; 2.53, t, $J \approx 7.6$ Hz, 2H, C10-CH_2; 2.68, t, $J \approx 5.2$ Hz, 2H, H5; 3.16, t, $J \approx 5.6$ Hz, 2H, H2; 3.39, t, $J \approx 5.6$ Hz, 2H, H6; 6.74, s, 1H, H13; 6.89, d, $J \approx 8.3$ Hz, 2H, H8, H12; 7.08, d, $J \approx 8.5$ Hz, 2H, H9, H11; 7.35, d, $J \approx 7.4$ Hz, 1H, H15; 7.64, m, 1H, H20; 7.71, m, 1H, H19; 7.89, d, $J \approx 7.4$ Hz, 1H, H16; 8.12 'd', $J \approx 7.7$ Hz, 1H, H21; 8.27, 'd', $J \approx 7.3$ Hz, 1H, H18. *High-resolution MS*: found m/z 520.3889; calcd. for $C_{37}H_{48}N_2$ m/z 520.3817.

1-(4-Biphenylyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**31**). Method C, using **6** (0.75 g, 3.0 mmol), diethyl [(4-cyano-1-naphthyl) methyl]phosphonate (0.91 g, 3.0 mmol) and sodium-dried THF instead of DME. The product was purified by chromatography using dichloromethane, recrystallization from ethanol yielded yellow needles. Isolated yield 0.82 g (1.93 mmol, 64%). *M.p.* 167–168°C. *IR*, ν (cm^{-1}): 3060 (m), 3000 (m), 2950 (m), 2810 (m), 2220 (s), 1600 (s), 1560 (s), 1540 (s), 1460 (s), 840 (m), 690 (s). ^1H *NMR* (300 MHz), δ (ppm): 2.45, t, $J \approx 5.4$ Hz, 2H, H3; 2.70, t, $J \approx 5.3$ Hz, 2H, H5; 3.28, t, $J \approx 5.7$ Hz, 2H, H2; 3.51, t, $J \approx 5.7$ Hz, 2H, H6; 6.77, s, 1H, H13; 7.02 'd', $J \approx 8.8$ Hz, 2H, H8, H12; 7.29–7.60, m, 8H, H9, H11, H15, H_{ar}; 7.64, m, 1H, H20; 7.72 m, 1H, H19; 7.90, d, $J \approx 7.3$ Hz, 1H, H16; 8.14, 'd', $J \approx 7.9$ Hz, 1H, H21; 8.29 'd', $J \approx 8.1$ Hz, 1H, H18. *High-resolution MS*: found m/z 400.1942; calcd. for $C_{29}H_{24}N_2$ m/z 400.1939.

1-(2,4,6-Trimethylphenyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**32**). Method C with **7** (394 mg, 1.81 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (556 mg, 1.83 mmol) and DMF (dried on 3 Å mol sieves) instead of DME. The product was purified by chromatography using dichloromethane, recrystallization from ethanol yielded yellow needles. Isolated yield 324 mg (0.89 mmol, 49%). *M.p.* 143.2–144.3°C. *IR*, ν (cm^{-1}): 2995 (m), 2945 (s), 2900 (s), 2805 (s), 2215 (s), 1640 (m), 1570 (m), 1480 (s), 850 (s). ^1H *NMR* (300 MHz), δ (ppm): 2.25, s, 3H, C10-CH_3; 2.31, s, 6H, C8-CH_3, C12-CH_3; 2.40, t, $J \approx 5.3$ Hz, 2H, H3; 2.63, t, $J \approx 5.0$ Hz, 2H, H5; 3.03, t, $J \approx 5.5$ Hz, 2H, H2; 3.25, t, $J \approx 5.4$ Hz, 2H, H6; 6.74, s, 1H, H13; 6.84, s, 2H, H9, H11; 7.39, d, $J \approx 7.4$ Hz, 1H, H15; 7.6–7.8, m, 2H, H19, H20; 7.90, d, $J \approx 7.4$ Hz, 1H, H16; 8.18 'd', $J \approx 7$ Hz, 1H, H21; 8.28, 'd', $J \approx 7$ Hz, 1H, H18. ^{13}C*-APT* (75.5 MHz), δ (ppm): 19.4, C8-CH_3, C12-CH_3; 20.6 C10-CH_3; 31.7, C3; 38.2, C5; 51.4, C2; 52.2, C6; 108.5, C17; 118.1, C24; 120.1, C13; 125.5, C18; 126.0, C15, C21; 127.2, C20; 128.3, C19; 129.5, C9, C11; 131.96, C22; 132.02, C16;

132.5, C23; 134.5, C8, C12; 136.6, C10; 141.1, C14; 144.6, C4; 146.1, C7. *High-resolution MS*: found m/z 366.2084; calcd. for $C_{26}H_{26}N_2$ m/z 366.2096.

1-Phenyl-4-[(2-anthryl)methylene]piperidine (**33**). Method C with **1** (0.54 g, 3.1 mmol) and diethyl [(2-anthryl)methyl]phosphonate (0.98 g, 3.0 mmol), which was prepared from 2-(bromomethyl)anthracene (0.81 g, 3.0 mmol) and triethyl phosphite (0.55 g, 23.3 mmol). 2-(Bromomethyl)anthracene was prepared from 2-(hydroxymethyl) anthracene (2.4 g, 11.6 mmol) and phosphorus tribromide (1.80 g, 7.0 mmol) via published procedures[40]. Isolated yield 2.09 g (7.7 mmol, 66%). 2-(Hydroxymethyl)anthracene was prepared by the reduction of 2-(hydroxymethyl)-9,10-anthraquinone (5.0 g, 21.0 mmol) (Merck) via published procedures[43]. Isolated yield 4.00 g (16.8 mmol, 80%). The product **33** was purified by chromatography using dichloromethane; recrystallization from acetonitrile yielded pale yellow plates. Isolated yield 72 mg (0.21 mmol, 7%). *M.p.* 189–190°C. *^{1}H NMR* (250 MHz), δ (ppm): 2.61, t, 2H, H3; 2.80, t, 2H, H5; 3.30, t, 2H, H2; 3.41, t, 2H, H6; 6.55, s, 1H, H13; 6.86, t, 1H, H10; 6.99, d, 2H, H8, H12; 7.25–7.51 m, 5H, H9, H11, H_{ar}; 7.83, s, 1H, 7.95–8.03, m, 3H, 8.39; s, 1H. *UV* (n-hexane), nm (ε): 228 (24000), 258 (82000), 272 (78000), 328 (sh. 4100), 348 (5400), 364 (6400), 384 (4500). *High-resolution MS*: found m/z 349.1838; calcd. for $C_{26}H_{23}N$ m/z 349.1830.

1-Phenyl-4-[(1-pyrenyl)methylene]piperidine (**34**). Method C with **1** (0.70 g, 4.0 mmol) and diethyl [(1-pyrenyl)methyl]phosphonate (1.41 g, 4.0 mmol), which was prepared from 1-(chloromethyl)pyrene (1.28 g, 5.1 mmol) and triethyl phosphite (0.93 g, 5.6 mmol). Isolated yield 1.37 g (3.9 mmol, 76%). 1-Chloromethyl)pyrene was prepared from 1-(hydroxymethyl)pyrene (1.00 g, 4.32 mmol) and phosphorus trichloride (0.34 g, 2.48 mmol) via published procedures[44]. Isolated yield 0.92 g (3.67 mmol, 85%). 1-(Hydroxymethyl)pyrene was prepared in quantitative yield from 1-pyrenecarboxyaldehyde (10.0 g, 43.4 mmol) (Aldrich) and sodium borohydride (1.80 g, 47.6 mmol) via published procedures[40]. The product **34** was purified by chromatography using dichloromethane (R_f 0.80); recrystallization from acetonitrile yielded yellow plates. Isolated yield of **34** 80 mg (0.21 mmol, 5%). *M.p.* 164–167°C. *IR*, ν (cm^{-1}): 3000 (m), 1595 (s), 1495 (s), 840 (s). *^{1}H NMR* (250 MHz), δ (ppm): 2.50, t, $J \approx 5.3$ Hz, 2H, H3; 2.74, t, $J \approx 5.4$ Hz, 2H, H5; 3.23, t, $J \approx 5.6$ Hz, 2H, H2; 3.49, t, $J \approx 5.6$ Hz, 2H, H6; 6.86, t, $J \approx 7.2$ Hz, 1H, H10; 6.97, s, 1H, H13; 7.02, d, $J \approx 7.1$ Hz, 2H, H8, H12; 7.28, t, $J \approx 7.9$ Hz, 2H, H9, H11; 7.86, d, $J \approx 7.7$ Hz, 1H; 7.90–8.30, m, 8H. *UV* (n-hexane, nm (ε): 246 (11200), 268 (6300), 278 (8100), 321 (sh 2800), 331 (sh 4900), 344 (7400). *High-resolution MS*: found m/z 373.1825; calcd. for $C_{28}H_{23}N$ m/z 373.1830. The structure was further confirmed by X-ray analysis[45].

1-Phenyl-4-[(4-biphenylyl)methylene]piperidine (**35**). Method C with **1** (4.66 g, 26.6 mmol) and diethyl [(4-biphenylyl)methyl]phosphonate (8.02 g, 26.6 mmol) and sodium dried THF instead of DME. Diethyl [(4-biphenylyl)methyl]phosphonate was prepared from 4-(bromomethyl)biphenyl (7.35 g, 29.7 mmol) and triethyl phosphite (6.31 g, 37.9 mmol) by refluxing for 17 h. Isolated yield 8.14 g (26.7 mmol, 90%). 4-(Bromomethyl)biphenyl was prepared from 4-biphenylmethanol (6.12 g, 33.2 mmol) (Aldrich) and phosphorus tribromide (8.99 g, 33.2 mmol) via published procedures[40]. Isolated yield 7.35 g (29.7 mmol, 90%). The product was purified by chromatography using dichloromethane (R_f 0.58). Recrystallization from ethanol yielded off-white crystals. Isolated yield of **35** 4.32 g (13.28 mmol, 50%). *M.p.* 107–109°C. *IR*, ν (cm^{-1}): 3000 (m), 2960 (m), 2890 (m), 2810 (m), 1590 (vs), 1490 (s), 1460 (m), 860 (m), 690 (s). *^{1}H NMR* (300 MHz), δ (ppm): 2.55, t, $J \approx 5.3$ Hz, 2H, H3; 2.72, t, $J \approx 5.3$ Hz, 2H; H5; 3.27, t, $J \approx 5.7$ Hz, 2H, H2; 3.37, t, $J \approx 5.7$ Hz, 2H, H6; 6.41, s, 1H, H13; 6.86, t, $J \approx 7.3$ Hz, 1H, H10; 6.98, d, $J \approx 7.9$ Hz, 2H, H8, H12; 7.24–7.64, m, 11H, H9, H11, H_{ar}. *High-resolution MS*: found m/z 325.1821; calcd. for $C_{24}H_{23}N$ m/z 325.1830.

1-Phenyl-4-[(4-cyanophenyl)methylene]piperidine (**36**). This compound was synthesized as described [32b] earlier.

1-Phenyl-4-[(2-naphthyl)methylene]piperidine (**37**). This compound was synthesized by a Wittig-type condensation as described earlier[32a].

1-Cyclohexyl-4-[(4-cyano-1-naphthyl)methylene]piperidine (**38**). Method C with 1-cyclohexyl-4-piperidine (**10**) (1.81 g, 10.0 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (3.04 g, 10.0 mmol) and sodium-dried THF instead of DME. The product was purified by chromatography using dichloromethane and methanol; recrystallization from methanol yielded white crystals. Isolated yield 3.11 g (9.42 mmol, 94%). *M.p.* 126–127°C. *IR*, ν (cm^{-1}): 2930 (vs), 2850 (vs), 2800 (s), 2220 (vs), 1570 (s), 1505 (m), 860 (m), 850 (s). *^{1}H NMR* (200 MHz), δ (ppm): 1.00–1.35, m, 5H, $H8_a$, $H9_a$, $H10_a$, $H11_a$, $H12_a$; 1.62, br.d, $J \approx 11.4$ Hz, 1H, $H10_e$; 1.70–1.90, m, 4H, $H8_e$, $H9_e$, $H11_e$, $H12_e$, 2.20–2.40 m, 3H, H3, H7; 2.45–2.60, m, 4H, H2, H5; 2.73, t, $J \approx 5.6$ Hz, 2H, H6; 6.61, s, 1H, H13; 7.31, d, $J \approx 7.4$ Hz, 1H, H15; 7.55–7.75, m, 2H, H19, H20; 7.85, d, $J \approx 7.4$ Hz, 1H, H16; 8.09, 'd', $J \approx 8.2$ Hz, 1H, H21; 8.23, 'd', $J \approx 8.0$ Hz, 1H, H18. *^{13}C NMR* (50.3 MHz APT), δ (ppm): 26.0, C9, C11; 26.3, C10; 28.9, C8, C12; 30.4, C3; 36.9, C5; 50.2, C2; 50.8, C6; 63.7, C7; 108.5, C17; 118.1, C24; 119.3, C13; 125.5, C18; 125.9, C15; 126.0, C21; 127.2, C20; 128.2, C19; 131.9, C22; 132.0, C16; 132.5, C23; 141.1, C14; 144.6, C4. *UV* (n-hexane), nm (ε): 236 (sh 41310), 318 (12665). *High-resolution MS*: found m/z 330.2099; calcd. for $C_{23}H_{26}N_2$ m/z 330.2096.

1-(1-Phenyl-4-piperidyl)-4-[(4-cyano-1-naphthyl)methylene]piperidine (**39**). Method C with **13** (1.02 g, 3.96 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (1.20 g, 3.96 mmol) and sodium-dried THF instead of DME. The product was purified by chromatography using chloroform; recrystallization from methanol yielded yellow crystals. Isolated yield 1.22 g (2.99 mmol, 76%). *M.p.* 148°C. *IR*, ν (cm^{-1}): 3000 (w), 2950 (vs), 2800 (s), 2220 (vs), 1595 (vs), 1575 (s), 1490 (s), 880 (m), 860 (m), 690 (s). *^{1}H NMR* (250 MHz), δ (ppm): 1.74, q, $J \approx 11.9$ Hz, d, $J \approx 3.8$ Hz, 2H, $H3'_a$, $H5'_a$; 1.90, br.d, $J \approx 13.0$ Hz, 2H, $H3'_e$, $H5'_e$; 2.32, t, $J \approx 5.3$ Hz, 2H, H3; 2.55, m, 5H, H2, H5, H4'; 2.70, t, $J \approx 12.2$ Hz, d, $J \approx 2.5$ Hz, 2H, $H2'_a$, $H6'_a$; 2.77, t, $J \approx 5.5$ Hz, 2H, H6; 3.73, br.d, $J \approx 12.1$ Hz, 2H, $H2'_e$, $H6'_e$; 6.64, s, 1H, H13; 6.82, t, $J \approx 7.3$ Hz, 1H, H10; 6.91, d, $J \approx 7.8$ Hz, 2H, H8, H12; 7.23, t, $J \approx 7.9$ Hz, 2H, H9, H11; 7.31, d, $J \approx 7.4$ Hz, 1H, H15; 7.57–7.71, m, 2H, H19, H20; 7.85, d, $J \approx 7.4$ Hz, 1H, H16; 8.09, d, $J \approx 8.6$ Hz, 'd', $J \approx 0.8$ Hz, 1H, H21; 8.24, d, $J \approx 8.3$ Hz, 'd', $J \approx 0.7$ Hz, 1H, H18. *^{13}C NMR* (62.9 MHz APT), δ (ppm): 28.1 C3', C5'; 30.3, C3; 36.8, C5; 49.6, C2', C6'; 50.5, C2; 51.0, C6; 62.0, C4'; 116.5, C7, C12; 118.1, C24; 119.4, C10; 119.6, C13; 125.6, C18; 125.9, C15, C21; 127.2, C20; 128.3, C19; 129.0, C9, C11; 131.9, C22; 132.0, C16; 132.6, C23; 140.9, C14; 144.2, C4; 151.4, C7. *UV* (acetonitrile), nm (ε): 236 (sh 45790), 314 (13410). *High-resolution MS*: found m/z 407.2358; calcd. for $C_{28}H_{29}N_3$ m/z 407.2361.

1-Phenyl-4-[(4-cyano-1-naphthyl)methyl]-1,2,3,6-tetrahydropyridine (**40**). Method C, using **1** (2.93 g, 18.0 mmol), diethyl [(4-cyano-1-naphthyl)methyl]phosphonate (5.45 g, 18.0 mmol) and sodium hydride (0.86 g, 35.9 mmol) (55–60% suspension in paraffin oil) in DMF instead of DME or THF[46]. The crude reaction mixture contained the endocyclic- as well as the exocyclic compound **26** (dichloromethane, R_f 0.31) (20%). The endocyclic product was isolated by chromatography using dichloromethane (R_f 0.25); recrystallization from ethanol yielded white crystals. Isolated yield 1.39 g (4.28 mmol, 24%). *M.p.* 165–166°C. *IR*, ν (cm^{-1}): 3000 (m), 2900 (vs), 2820 (m), 2220 (vs), 1590 (s), 845 (m), 690 (m). *^{1}H NMR* (300 MHz), δ (ppm): 2.27 br.s, 2H, H5; 3.38, t, $J \approx 5.7$ Hz, 2H, H6; 3.65, d, $J \approx 2.4$ Hz, 2H, H2; 3.85, s, 2H, H13; 5.38, t, $J \approx 1.4$ Hz, 1H, H3; 6.82, t, $J \approx 7.2$ Hz, 1H, H10; 6.89, d, $J \approx 8.2$ Hz, 2H, H8, H12; 7.25, t, $J \approx 7.3$ Hz, 2H, H9, H11; 7.39, d, $J \approx 7.4$ Hz, 1H, H15; 7.62, m, 1H, H20; 7.69, m, 1H, H9; 7.85, d, $J \approx 7.4$ Hz, 1H, H16; 8.10, 'd', $J \approx 8.1$ Hz, 1H, H21; 8.27, 'd', $J \approx 7.7$ Hz, 1H, H18. *^{13}C-NMR* (62.9 MHz APT), δ (ppm): 29.4, C5; 40.5, C13; 45.6, C6; 48.1, C2; 109.0, C17; 115.2, C8, C12; 117.9, C24; 118.8, C10; 121.7, C3; 124.9, C21; 125.8, C18; 126.3, C15; 127.4, C20; 128.1, C19; 129.0, C9, C11; 132.0, C22; 132.2, C16; 132.5, C23; 134.6, C4; 141.8, C14; 150.6, C7. *UV* (ethanol), nm (ε): 230 (64250), 250 (sh. 15500), 300 (12740), 310 (9550), 325 (4430). *High-resolution MS*: found m/z 324.1633; calcd. for $C_{23}H_{20}N_2$ m/z 324.1626.

1-Phenyl-4-[(4-biphenylyl)methyl]-1,2,3,6-tetrahydropyridine (**41**). Method C, using **1** (3.10 g, 17.7 mmol), diethyl [(4-biphenylyl)methyl]-phosphonate (5.45 g, 18.0 mmol) (see **35**) and sodium hydride (0.85 g, 35.4 mmol) in DMF instead of DME or THF. The crude reaction mixture contained the endocyclic as well as the exocyclic compound **35** (20%). The endocyclic product was purified by chromatography using dichloromethane (R_f 0.58); recrystallization three times from ethanol yielded off-white crystals. Isolated yield 1.37 g (4.21 mmol, 24%). *M.p.* 118–119°C. *IR*, ν (cm^{-1}): 3000 (m), 2900 (m), 2820 (m), 1590 (s), 850 (m), 690 (m). *^{1}H NMR* (200 MHz), δ (ppm): 2.22, br.s, 2H, H5; 3.36, t, $J \approx 5.6$ Hz, 2H, H6; 3.41, br.s, 2H, H2; 3.74, s, 2H, H13; 5.58, br.s, 1H, H3; 6.81, t, $J \approx 7.2$ Hz, 1H, H10; 6.92, d, $J \approx 8.3$ Hz, 2H, H8, H12; 7.26–7.61, m, 11H, H9, H11, H_{ar}. *High-resolution MS*: found m/z 325.1862; calcd. for $C_{24}H_{23}N$ m/z 325.1830.

3.6. Hydrogenation reactions leading to donor-bridge-acceptor systems **42–48** *(Method D)*

1-Phenyl-4-[(4-cyano-1-naphthyl)methyl]piperidine (**42**) was synthesized by catalytic hydrogenation. A mixture of **26** (250 mg, 0.77

mmol) in ethanol (20 ml), acetic acid (0.2 ml) and PtO_2 (10 mg) was hydrogenated at 50 psi in a Parr apparatus for *ca.* 7 h.[14a]. It was found that the time required to achieve complete conversion showed erratic variation, probably dependent on the quality of the catalyst used. The catalyst was filtered off after addition of water (100 ml) and extraction with chloroform. The organic layers were collected and the solvent was evaporated. The crude product was purified by chromatography using dichloromethane, which yielded a white solid. Isolated yield 214 mg (0.66 mmol, 85%). *M.p.* 134–135°C. *IR*, ν (cm^{-1}): 2820 (m), 2225 (m), 1600 (s), 1580 (m), 1495 (m). *^{1}H NMR* (250 MHz), δ (ppm): 1.55, q, $J \approx 13.0$ Hz, d, $J \approx 4.0$ Hz, 2H, $H3_a$, $H5_a$; 1.75, br.d, $J \approx 12.7$ Hz, 2H, $H3_e$, $H5_e$; 1.85, m, 1H, H4; 2.61, t, $J \approx 12.1$ Hz, d, $J \approx 2.0$ Hz, 2H, $H2_a$, $H6_a$; 3.07, d, $J \approx 7.0$ Hz, 2H, H13; 3.65, br.d, $J \approx 12.6$ Hz, 2H, $H2_e$, $H6_e$; 6.81, t, $J \approx 7.2$ Hz, 1H, H10; 6.90, d, $J \approx 8.2$ Hz, 2H, H8, H12; 7.24, t, $J \approx 7.9$ Hz, 2H, H9, H11; 7.34, d, $J \approx 7.4$ Hz, 1H, H15; 7.67, m, 2H, H19, H20; 7.83, d, $J \approx 7.3$ Hz, 1H, H16; 8.11, 'd', $J \approx 8.5$ Hz, 1H, H21; 8.29, 'd', $J \approx 8.4$ Hz, 1H, H18. *UV* (cyclohexane), nm (ϵ): 253 (16100), 288 (11300), 300 (13500), 310 (8600), 314 (8800), 324 (2600). *High-resolution MS*: found m/z 326.1759; calcd. for $C_{23}H_{22}N_2$ m/z 326.1783.

1-(4-Methoxyphenyl)-4-[(4-cyano-1-naphthyl)methyl]piperidine (**43**). Method D, using **27** (1.06 g, 3.1 mmol) and ethyl acetate instead of ethanol[14c]. The product was purified by chromatography using dichloromethane recrystallization from ethyl acetate yielded yellow needles. Isolated yield 0.29 g (0.85 mmol, 27%). *M.p.* 167–168°C. *IR*, ν (cm^{-1}): 3000 (m), 2930 (s), 2825 (m), 2800 (m), 2220 (s), 1600 (w), 1580 (m), 1505 (s), 820 (m). *^{1}H NMR* (200 MHz), δ (ppm): 1.58, q, $J \approx 12.0$ Hz, d, $J \approx 3.0$ Hz, 2H, $H3_a$, $H5_a$; 1.75, br.d, $J \approx 12.0$ Hz, 2H, $H3_e$, $H5_e$; 1.80, m, 1H, H4; 2.58, t, $J \approx 12.0$ Hz, d, $J \approx 2.0$ Hz, 2H, $H2_a$, $H6_a$; 3.09, d, $J \approx 7.0$ Hz, 2H, H13, 3.60 br.d, $J \approx 12.0$ Hz, 2H, $H2_e$, $H6_e$; 3.80, s, 3H, OCH_3; 6.75–6.95, m, 4H, H8, H9, H11, H12; 7.36, d, $J \approx 7.4$ Hz, 1H, H15; 7.60–7.75, m, 2H, H19, H20; 7.87, d, $J \approx 6.2$ Hz, 1H, H16; 8.10, m, 1H, H21; 8.30, m, 1H, H18. *UV* (ethanol), nm (ϵ): 289 (9400), 300 (11700), 310 (8800), 324 (4200). *High-resolution MS*: found m/z 356.1858; calcd. for $C_{24}H_{24}N_2O$ m/z 356.1888.

1-(4-Methylphenyl)-4-[(4-cyano-1-naphthyl)methyl]piperidine (**44**). Method D with **28** (0.94 g, 2.8 mmol)[14c]. Chromatography using dichloromethane and recrystallization from methanol yielded white needles. Isolated yield 0.24 g (0.69 mmol, 25%). *M.p.* 111–112°C. *IR*, ν (cm^{-1}): 3000 (m), 2930 (s), 2800 (m), 2220 (s), 1605 (m), 1575 (m), 1505 (s), 810 (m). *^{1}H NMR* (300 MHz), δ (ppm): 1.58, q, $J \approx 13.0$ Hz, d, $J \approx 4.0$ Hz, 2H, $H3_a$, $H5_a$; 1.75, br.d, $J \approx 13.0$ Hz, 2H, $H3_e$, $H5_e$; 1.80, m, 1H, H4; 2.26 s, 3H, CH_3; 2.58, t, $J \approx 12.0$ Hz, d, $J \approx 2.0$ Hz, 2H, $H2_a$, $H6_a$; 3.09, d, $J \approx 7.0$ Hz, 2H, H13; 3.60, br.d, $J \approx 12.0$ Hz, 2H, $H2_e$, $H6_e$; 6.84, d, $J \approx 8.5$ Hz, 2H, H8, H12; 7.06, d, $J \approx 8.4$ Hz, 2H, H9, H11; 7.36, d, $J \approx 7.4$ Hz, 1H, H15; 7.60–7.75, m, 2H, H19, H20; 7.84, d, $J \approx 7.3$ Hz, 1H, H16; 8.13 'd', $J \approx 6.7$ Hz, 1H, H21; 8.29, 'd', $J \approx 6.8$ Hz, 1H, H18. *UV* (cyclohexane), nm (ϵ): 289 (10700), 300 (13400), 310 (9700), 324 (4000). *High-resolution MS*: found m/z 340.1981; calcd. for $C_{24}H_{24}N_2$ m/z 340.1939.

1-Phenyl-4-[(4-cyanophenyl)methyl]piperidine (**45**). Method D with **36** (0.20 g, 0.72 mmol). The crude product was purified by chromatography using dichloromethane; recrystallization from ethanol yielded white needles. Isolated yield 36 mg (0.13 mmol, 18%). *M.p.* 176–177°C. *IR*, ν (cm^{-1}): 3000 (w), 2930 (m), 2810 (w), 2225 (s), 1595 (s), 1490 (s), 850 (m), 690 (m). *^{1}H NMR* (200 MHz), δ (ppm): 1.30–1.90, m, 5H, H3, H4, H5; 2.55–2.80, m, 4H, $H2_a$, $H6_a$, H13; 3.66, br.d, $J \approx 12.2$ Hz, 2H, $H2_e$, $H6_e$; 6.84, t, $J \approx 7.1$ Hz, 1H, H10; 6.94, d, $J \approx 8.1$ Hz, 2H, H8, H12; 7.25, m, 4H, H9, H11, H_{ar}; 7.60, d, $J \approx 8.1$ Hz, 2H. *High-resolution MS*: found m/z 276.1654; calcd. for $C_{19}H_{20}N_2$ m/z 276.1626.

1-Phenyl-4-[(2-naphthyl)methyl]piperidine (**46**). Method D with the HCl salt of **37** (400 mg, 1.46 mmol)[14d]. The product was purified by recrystallization from ethanol, which yielded the HCl salt. The free base was obtained by addition of potassium hydroxide and extraction with ether. The free base was purified by recrystallization from methanol. Isolated yield 110 mg (0.37 mmol, 25%). *M.p.* 144°C. *IR*, ν (cm^{-1}): 3000 (m), 2920 (s), 2840 (m), 2800 (m), 1590 (s), 1490 (s), 850 (s), 690 (s). *^{1}H NMR* (200 MHz), δ (ppm): 1.45, q, $J \approx 11.8$ Hz, d, $J \approx 2.5$ Hz, 2H, $H3_a$, $H5_a$; 1.65–1.95, m, 3H, $H3_e$, $H5_e$, H4; 2.60–2.80, m, 4H, $H2_a$, $H6_a$, H13; 3.68, br.d, $J \approx 12.3$ Hz, 2H, $H2_e$, $H6_e$; 6.84, t, $J \approx 7.2$ Hz, 1H, H10; 6.94, d, $J \approx 8.0$ Hz, 2H, H8, H12; 7.20–7.55, m, 6H, H9, H11, H_{ar}; 7.62 s, 1H, 7.75–7.90, m, 2H. *UV* (acetonitrile), nm (ϵ): 255 (17500), 286 (4980). *High-resolution MS*: found m/z 301.1830; calcd. for $C_{22}H_{23}N$ m/z 301.1830.

1-Cyclohexyl-4-[(4-cyano-1-naphthyl)methyl]piperidine (**47**). Method D, using **38** (49 mg, 0.15 mmol) and ethyl acetate instead of ethanol. The product was purified by chromatography using ether/methanol (3:1) (R_f 0.22), which yielded an off-white solid. Isolated yield 33.6 mg (0.10 mmol, 70%). *M.p.* 114–115°C. *IR*, ν (cm^{-1}): 3000 (w), 2930 (m), 2810 (w), 2225 (s), 1595 (s), 1490 (s), 850 (m), 690 (m). *^{1}H-NMR* (250 MHz), δ (ppm): 0.95–1.30, m, 6H, H4, $H8_a$, $H9_a$, $H10_a$, $H11_a$, $H12_a$; 1.42, 'q', $J \approx 11.3$ Hz, 2H, $H3_a$, $H5_a$; 1.55–1.90, m, 7H, $H3_e$, $H5_e$, $H8_e$, $H9_e$, $H10_e$, $H11_e$, $H12_e$; 2.08, 't', $J \approx 11.3$ Hz, 2H, $H2_a$, $H6_a$; 2.15–2.30, m, 1H, H7; 2.87, br.d, $J \approx 11.5$ Hz, 2H, $H2_e$, $H6_e$; 3.02, d, $J \approx 6.7$ Hz, 2H, H13; 7.31, d, $J \approx 7.4$ Hz, 1H, H15; 7.55–7.75, m, 2H, H19, H20; 7.81, d, $J \approx 7.4$ Hz, 1H, H16; 8.08, 'd', $J \approx 7.5$ Hz, 1H, H21; 8.25, 'd', $J \approx 7.7$ Hz, 1H, H18. *^{13}C NMR* (62.9 MHz APT), δ (ppm): 26.0, C9, C11; 26.4, C10; 28.8, C8, C12; 33.0, C3, C5; 37.6, C4; 40.6, C13; 49.2, C2, C6; 64.0, C7; 108.6, C17; 118.1, C24; 124.8, C21; 126.0, C18; 126.3, C15; 127.2, C20; 128.0, C19; 131.9, C22; 132.0, C16; 132.8, C23; 143.6, C14. *High-resolution MS*: found m/z 332.2287; calcd. for $C_{23}H_{28}N_2$ m/z 332.2252.

1-(1-Phenyl-4-piperidyl)-4-[(4-cyano-1-naphthyl)methyl]piperidine (**48**). Method D, using **39** (0.32 g, 0.78 mmol) and ethyl acetate instead of ethanol. The product was purified by chromatography using ether/methanol (3:1), which yielded a light yellow solid. Isolated yield 57.0 mg (0.14 mmol, 18%). *M.p.* 163–164°C. *IR*, ν (cm^{-1}): 3000 (w), 2940 (m), 2810 (m), 2220 (s), 1595 (s), 1495 (s), 850 (m), 690 (m). *^{1}H NMR* (250 MHz), δ (ppm): 1.30–1.50, 'q', $J \approx 11.6$ Hz, 2H, $H3_a$ $H5_a$; 1.55–1.80, m, 5H, H4, $H3'_a$, $H5'_a$, $H3_e$, $H5_e$; 1.86, br.d, $J \approx 12.0$ Hz, 2H, $H3'_e$, $H5'_e$; 2.10, t, $J \approx 10.0$ Hz, 2H, $H2_a$, $H6_a$; 2.30–2.45, m, 1H, H4'; 2.66, t, $J \approx 12.1$ Hz, d, $J \approx 1.8$ Hz, 2H, $H2'_a$, $H6'_a$; 2.92, br.d, $J \approx 11.3$ Hz, 2H, $H2_e$, $H6_e$; 3.03, d, $J \approx 6.6$ Hz, 2H, H13; 3.71, d, $J \approx 12.4$ Hz, 2H, $H2'_e$, $H6'_e$; 6.81, t, $J \approx 7.3$ Hz, 1H, H10; 6.91, d, $J \approx 7.9$ Hz, 2H, H8, H12; 7.22, t, $J \approx 7.9$ Hz, 2H, H9, H11; 7.32, d, $J \approx 7.4$ Hz, 1H, H15; 7.60–7.75, m, 2H, H19, H20; 7.82, d, $J \approx 7.4$ Hz, 1H, H16; 8.09, 'd', $J \approx 7.5$ Hz, 1H, H21; 8.26, 'd', $J \approx 6.8$ Hz, 1H, H18. *High-resolution MS*: found m/z 409.2406; calcd. for $C_{28}H_{31}N_3$ m/z 409.2418.

3.7. Grignard synthesis leading to donor–bridge–acceptor systems **49–54** *(Method E and F)*

1-Phenyl-4-(1-naphthyl)-4-piperidinol (**49**) was prepared by slowly adding **1** (4.23 g, 24.1 mmol) in 30 ml dry THF to a Grignard reagent, which was prepared from magnesium granulates (1.22 g, 50.1 mmol) and 1-bromonaphthalene (5.02 g, 24.2 mmol) (Aldrich) in sodium-dried THF[47]. The mixture was stirred for 1 h and the yellow/orange suspension was poured into satd. NH_4Cl and extracted with dichloromethane. The organic layer was washed with brine and dried over Na_2SO_4. After decanting and evaporation, the crude product was purified by precipitation from an ethyl acetate/PE-60-80 (1:3) mixture. This yielded a yellow powder. Isolated yield 1.64 g (5.41 mmol, 22%). *M.p.* 144–146°C. *IR*, ν (cm^{-1}): 3590 (m), 3050 (m), 3000 (m), 2950 (m), 2830 (m), 1595 (s), 1495 (s), 1460 (m), 685 (m). *^{1}H NMR* (300 MHz), δ (ppm): 1.87, s, 1H, OH; 2.35, d, $J \approx 14.4$ Hz, d, $J \approx 2.3$ Hz, 2H, $H3_e$, $H5_e$; 2.47, t, $J \approx 12.6$ Hz, d, $J \approx 4.3$ Hz, 2H, $H3_a$, $H5_a$; 3.42, t, $J \approx 12.0$ Hz, d, $J \approx 2.7$ Hz, 2H, $H2_a$, $H6_a$; 3.65, br.d, $J \approx 12.2$ Hz, 2H, $H2_e$, $H6_e$; 6.88, t, $J \approx 7.3$ Hz, 1H, H10; 7.05, d, $J \approx 8.0$ Hz, 2H, H8, H12; 7.31, t, $J \approx 7.9$ Hz, 2H, H9, H11; 7.41–7.54, m, 3H; 7.58, d, $J \approx 7.3$ Hz, 1H; 7.81, d, $J \approx 8.1$ Hz, 1H; 7.88, m, 1H; 8.91, m, 1H.

Method F: 1-Phenyl-4-(1-naphthyl)-1,2,3,6-tetrahydropyridine (**50**) was prepared by slowly adding trifluoracetic acid (10 ml) to **49** (1.64 g, 5.41 mmol). After 30 min stirring, the solution was poured into 200 ml satd. $NaHCO_3$. The mixture was extracted with dichloromethane. The organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. The crude product was purified by chromatography using dichloromethane (R_f 0.63) and recrystallized from ethanol to yield white needles. This compound was used as intermediate and was not purified further because from the spectroscopic data the purity appeared satisfactory. Isolated yield 0.77 g (2.70 mmol, 50%). *M.p.* 166–171°C. *IR*, ν (cm^{-1}): 3050 (m), 3000 (m), 2920 (m), 2810 (m), 1595 (s), 1495 (s), 1460 (s), 1440 (m), 685 (m). *^{1}H NMR* (250 MHz), δ (ppm): 2.70, m, 2H, H5; 3.60, t, $J \approx 5.6$ Hz, 2H, H6; 3.95, d, $J \approx 5.7$ Hz, d, $J \approx 2.7$ Hz, 2H, H2; 5.65, quin., $J \approx 1.7$ Hz, 1H, H3; 6.86, t, $J \approx 7.2$ Hz, 1H, H10; 7.03, d, $J \approx 8.0$ Hz, 2H, H8, H12; 7.29–7.51, m, 6H, H9, H11, H_{ar}, 7.75, d, $J \approx 8.2$ Hz, 1H, 7.85, m, 1H; 8.00, m, 1H.

1-Phenyl-4-(1-naphthyl)piperidine (**51**). Method D (see section 3.6), using **50** (0.68 g, 2.37 mmol) and a reaction time of approximately 24 h. The crude product was purified by chromatography using dichloromethane (R_f 0.55) and recrystallized from ethanol to yield fine white needles. Isolated yield 0.37 g (1.29 mmol, 54%). *M.p.* 131–133°C. *IR*, ν (cm^{-1}): 3050 (m), 3000 (m), 2940 (m), 2800 (m), 1595 (s), 1495 (s), 1460 (m), 1440 (m), 785 (m). *^{1}H NMR* (300 MHz), δ (ppm): 2.00, q, $J \approx 12.3$ Hz, d, $J \approx 3.4$ Hz, 2H, $H3_a$, $H5_a$; 2.10, br.d, $J \approx 11.5$ Hz, 2H, $H3_e$, $H5_e$; 2.98, t, $J \approx 12.0$ Hz, d, $J \approx 2.8$ Hz, 2H,

$H2_a$, $H6_a$; 3.50, t, $J \approx 11.6$ Hz, t, $J \approx 3.7$ Hz, 1H, H4; 3.85, br.d, $J \approx 12.2$ Hz, 2H, $H2_e$, $H6_e$; 6.83, t, $J \approx 7.3$ Hz, 1H, H10; 7.01 d, $J \approx 8.3$ Hz, 2H, H8, H12; 7.26, t, $J \approx 8.0$ Hz, 2H, H9, H11; 7.44–7.57, m, 4H; 7.74, m, 1H; 7.88, br.d, $J \approx 8.5$ Hz, 1H; 8.17, br.d, $J \approx 8.5$ Hz, 1H. *UV* (cyclohexane), nm (ϵ): 226 (73840), 256 (15950), 284 (10290). *High-resolution MS*: found m/z 287.1669; calcd. for $C_{21}H_{21}N$ m/z 287.1674.

1-(4-Methoxyphenyl)-4-(1-naphthyl)-4-piperidinol (**52**). Method E, using **2** (2.82 g, 13.7 mmol), 1-bromonaphthalene (2.84 g, 13.7 mmol) and magnesium granulates (1.46 g, 60 mmol)[49]. The same purification yielded a yellow powder, which was not purified further because from the spectroscopic data the purity appeared satisfactory. Isolated yield 0.28 g (0.84 mmol, 6%). *M.p.* 150–157°C. *IR*, ν (cm^{-1}): 3590 (m), 3040 (m), 3000 (m), 2950 (m), 2830 (m), 1505 (s), 1460 (s), 620 (s). *^1H NMR* (250 MHz), δ (ppm): 1.93, s, 1H, OH, 2.35, br.d, $J \approx 13.2$ Hz, 2H, $H3_e$, $H5_e$; 2.52, t, $J \approx 12.3$ Hz, d, $J \approx 4.7$ Hz, 2H, $H3_a$, $H5_a$; 3.36, t, $J \approx 12.1$ Hz, d, $J \approx 3.2$ Hz, 2H, $H2_a$, $H6_a$; 3.48, br.d, $J \approx 8.3$ Hz, 2H, $H2_e$, $H6_e$; 3.79, s, 3H, OCH_3; 6.85–6.90, m, 2H, H9, H11; 7.03–7.08, m, 2H, H8, H12; 7.39–7.61, m, 4H; 7.80, d, $J \approx 8.0$ Hz, 1H; 7.85, m, 1H; 8.91, m, 1H.

1-(4-Methoxyphenyl)-4-(1-naphthyl)-1,2,3,6-tetrahydropyridine (**53**). Method F with **52** (0.28 g, 0.84 mmol). Chromatography using dichloromethane (R_f 0.29) yielded white needles. This compound was used as intermediate and was not purified further because from the spectroscopic data the purity appeared satisfactory. Isolated yield 0.09 g (0.29 mmol, 34%). *M.p.* 123–132°C *IR*, ν (cm^{-1}): 3050 (m), 2990 (m), 2940 (m), 2810 (m), 1585 (m), 1505 (s), 1455 (m), 1440 (m), 820 (m). *^1H NMR* (250 MHz), δ (ppm): 2.71, m, 2H, H5; 3.51, t, $J \approx 5.6$ Hz, 2H, H6; 3.81, s, 3H, OCH_3; 3.88, d, $J \approx 5.8$ Hz, d, $J \approx 2.8$ Hz, 2H, H2; 5.91, quin., $J \approx 1.7$ Hz, 1H, H3; 6.87–7.07, m, 4H, H8, H9, H11, H12; 7.32–7.53, m, 4H; 7.78, d, $J \approx 8.1$ Hz, 1H; 7.87, m, 1H; 8.04, m, 1H.

1-(4-Methoxyphenyl)-4-(1-naphthyl)piperidine (**54**). Method D (see section 3.6) with **53** (0.09 g, 0.28 mmol) and a reaction time of approximately 24 h. Chromatography using dichloromethane (R_f 0.23) yielded white needles. Isolated yield 79 mg (0.25 mmol, 89%). *M.p.* 114–115°C. *IR*, ν (cm^{-1}): 3050 (w), 3000 (w), 2940 (s), 2830 (w), 2800 (m), 1590 (w), 1500 (s), 1460 (s), 1440 (m), 840 (s). *^1H NMR* (250 MHz), δ (ppm): 2.04, q, $J \approx 11.2$ Hz, d, $J \approx 3.5$ Hz, 2H, $H3_a$, $H5_a$; 2.13, m, 2H, $H3_e$, $H5_e$; 2.91, t, $J \approx 11.2$ Hz, d, $J \approx 3.7$ Hz, 2H, $H2_a$, $H6_a$; 3.44, t, $J \approx 10.2$ Hz, t, $J \approx 5.0$ Hz, 1H, H4; 3.71, br.d, $J \approx 12.0$ Hz, 2H, $H2_e$, $H6_e$; 3.78, s, 3H, OCH_3; 6.84–7.02, m, 4H, H8, H9, H11, H12; 7.43–7.56, m, 4H; 7.73, m, 1H; 7.87, br.d, $J \approx 8.3$ Hz, 1H; 8.13, br.d, $J \approx 8.1$ Hz, 1H. *UV* (cyclohexane), nm (ϵ): 226 (79870), 252 (14870), 284 (9970). *High-resolution MS*: found m/z 317.1785; calcd. for $C_{22}H_{23}NO$ m/z 317.1780.

Acknowledgements

The investigations were supported in part by The Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Research (NWO). The authors gratefully acknowledge the synthetic efforts and photophysical measurements made by *Bas Wegewijs, Nathalie Zenden, Michiel Bouwman, Herman Verhey, Robert Willemse* and *Demi Theodory* and the NMR measurements performed by *Jan Geenevasen* and *Hana van der Laan-Ctorteckova*.

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