Kurzmitteilung / Short Communication

A New Synthetic Approach to Pyridinium *N*-Phenoxide Betaine Dyes

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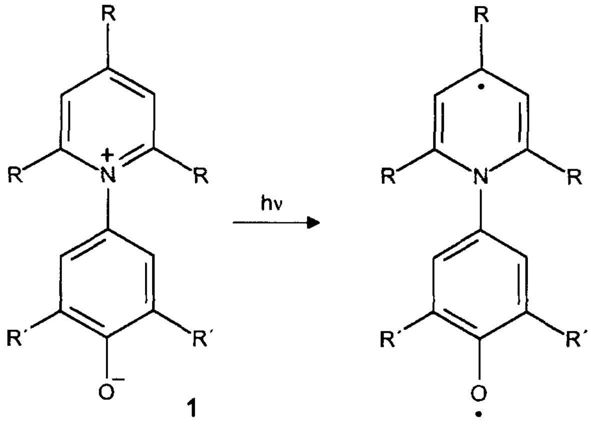
The reaction of 3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadienylidene (**3d**) with pyridine affords 2,6-di-*tert*-butyl-4-(2,4,6-tri-*tert*-butylpyridinio)phenolate (**1d**) – which is not accessible by the classical route via pyrylium salts – in reasonable yield. Carbene **3d** is generated by thermal decomposition of the corresponding quinone diazide **2d** in cyclohexane. Betaine **1d** shows the expected large solvatochromism.

Pyridinium *N*-phenolates **1** exhibit a very large negative solvatochromism and have been proposed by Dimroth and Reichardt as a basis for the characterization of solvent polarities[1]. The empirical $E_T(\mathbf{30})$ solvent polarity scale is defined as the molar electronic transition energy of dissolved 2,6-diphenyl-4-(2,4,6-triphenylpyridinio)phenolate (**1a**, R = R′ = Ph, Reichard's dye), measured in kcal/mol. Betaine **1a** exhibits a strong charge transfer absorption with a maximum in methanol at 515 nm, in acetonitrile at 622 nm, and in 1,4-dioxane at 795 nm[1]. The exact position of the charge transfer absorption not only depends on the solvent but also on the temperature (thermochromism)[2], added salts (halochromism)[3], and pressure (piezochromism)[4].



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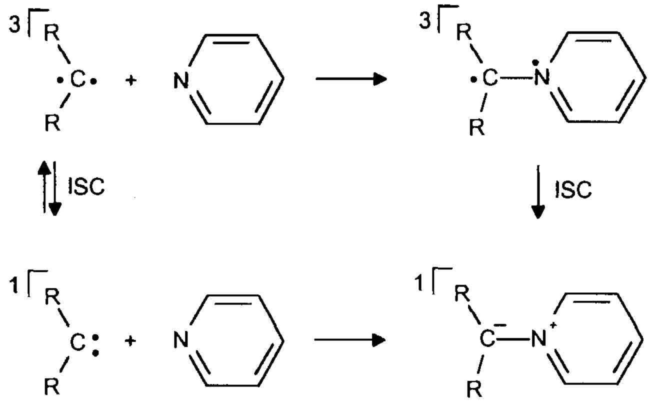
The classical synthesis of betaines **1**, developed by Dimroth et al.[1], is the reaction of pyrylium salts with primary arylamines. This method is limited to pyrylium salts with substituents in 2- and 6-position. In most cases, 2,4,6-triaryl-substituted pyridinium ylides have been synthesized by this route.

We have recently described the generation of **1b** and **c** by pyridine trapping of 4-oxo-2,5-cyclohexadienylidenes **3b** and **c** in a laser flash photolysis (LFP) study[5]. Pyridine trapping is a method developed by Platz et al.[6] to detect "invisible" carbenes in LFP studies. Pyridine ylides exhibit strong absorptions in the visible part of the spectrum and are thus easily observed by optical spectroscopy.



It is generally accepted that singlet carbenes are rapidly trapped by pyridine, whereas the formally spin-forbidden reaction of triplet carbenes to produce singlet ylides is slow[6]. Platz et al. determined the activation parameters E_a and lg$A$ for two archetypical carbenes: singlet ground-state carbene phenylchlorocarbene (PCC)[6c] and triplet ground-state carbene diphenylcarbene (DPC)[6d]. The observed activation parameters were $E_a = 1.34 \pm 0.51$ and lg$A = 9.70 \pm 0.21$ for PCC in toluene and $E_a = 1.41 \pm 0.41$ and lg$A = 6.50 \pm 0.31$ for DPC in isooctane. Thus, the barriers of activation are almost identical for the reactions of the singlet and triplet carbene, and the major difference is the lower Arrhenius pre-exponential factor A for the DPC reaction. The conclusion of these observations is that ISC does not occur on the side of the carbenes or ylides, but rather somewhere along the reaction coordinate.

This is in accordance with our observations of the formation of pyridine ylides **1b** (λ_{max} = 560 nm, Freon-113) and **1c** (λ_{max} = 465 nm, Freon-113) from carbenes **3b** and **3c**[5]. Irradiation of quinone diazides **2** initially produces carbenes **3** in their singlet excited states, which can be trapped by suitable scavengers or undergo intersystem crossing to their triplet ground states. Ylides **1** are only

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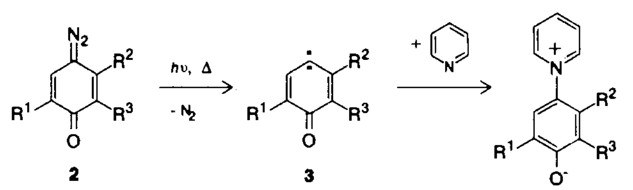
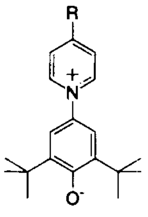


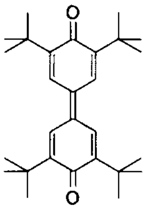
	R^1	R^2	R^3
b	H	H	H
c	CH_3	$-C_4H_4-$	
d	*t*Bu	H	*t*Bu

formed in diluted pyridine solutions, which indicates that carbenes **3** react with pyridine from their triplet ground states rather than from excited singlet states. This is confirmed by the observation of a rather long-lived (lifetime in the order of μs) intermediate with an absorption maximum around 620 nm[5]. The 620-nm transient then decays to the ylide. Presumably, the singlet excited carbenes undergo more rapidly C−H insertion into solvent molecules than ISC to the triplet ground states.

We have now found that the reaction of carbene **3d** with pyridine can be used for the preparative-scale synthesis of betaine **1d**. Dilute solutions of pyridine have to be used to allow ISC prior to the carbene reaction. Because of the intense color and the photolability of **1d**, thermal generation of carbene **3d** from 2,6-di-*tert*-butyl-4-diazo-2,5-cyclohexadien-1-one (**2d**) has proved to be more suitable than photochemical generation. Photolysis of dilute solutions of **2d** in the presence of pyridine produces small amounts of **1d**, which strongly absorbs in the visible region and thus inhibits further photolysis of the diazo precursor. Prolonged irradiation leads to decomposition of betaine **1d**.



1d



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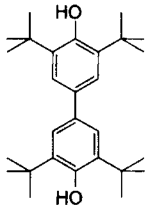

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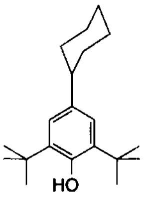

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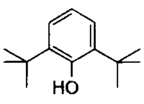

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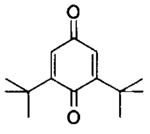

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Heating of a solution of quinone diazide **2d** in a mixture of 5−15% pyridine in cyclohexane at reflux rapidly yields a deeply colored precipitate. After 3 h **1d** is obtained in 20−30% yield as a crystalline powder. Ylide **1d** is almost insoluble in cyclohexane, benzene, and other unpolar solvents and only moderately soluble in DMSO, methanol, dichloromethane, and acetonitrile. The cyclohexane-soluble products formed in this reaction are identical to those described by Plekhanova et al.[7] for the thermal decomposition of **2d** in neat cyclohexane and are 3,3′,5,5′-tetra-*tert*-butyl-4,4′-diphenoquinone (**4**), 3,3′,5,5′-tetra-*tert*-butylbiphenyl-4,4-diol (**5**), 2,6-di-*tert*-butyl-4-cyclohexylphenol (**6**), and 2,6-di-*tert*-butylphenol (**7**). These compounds are the expected products of the C−H insertion, H abstraction, and dimerization of carbene **3d**. In addition, some 2,6-di-*tert*-butylquinone (**8**) is found, which is presumably formed by the oxidation of **3d** with molecular oxygen.

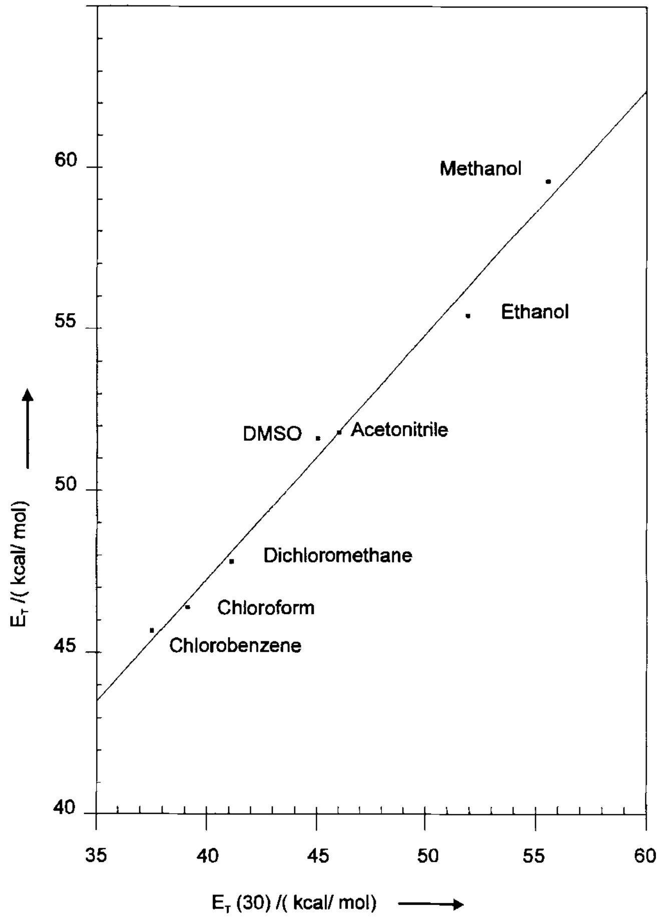

Figure 1. Diagram showing the linear correlation between E_T(**30**) values of standard dye **1a** and the molar transition energies E_T of betaine **1d**. Correlation equation: $E_T = 0.756 \cdot E_T(\mathbf{30}) + 17.026$ (7 data points, $R^2 = 0.9897$)

Ylide **1d** has proven to be labile in both acidic and basic media. The highest yields have been obtained in solvents such as cyclohexane, were **1d** is almost insoluble, whereas quinone diazide **2d** is easily soluble. In *para*-dichlorobenzene, tetrachloromethane, or pyridine, where **1d** shows a higher solubility, the yields are very poor. When **1d** is dissolved in pyridine rapid degradation is observed.

In solution the typical solvatochromism of betaine dyes **1** is observed. The long-wavelength absorption maximum (charge transfer transition) of **1d** is shifted from 318 nm (lg ε = 3.66) in DMSO and 324 nm (3.70) in CH_3OH to 552 nm (4.19) in CH_3CN and 599 nm (4.30) in CH_2Cl_2. In argon at 10 K the charge transfer transition is observed at 658 nm, close to the expected gas phase value. The correlation between the molar transition energies of the CT band of **1d** and Reichardt's E_T(**30**) values for several solvents is given in Figure 1. Betaine **1d** is somewhat less sensitive to solvent effects than the reference dye **1a** (R = R′ = Ph), and the absorption maxima are shifted to shorter wavelengths.

Our results clearly show that betaine **1d** can be synthesized by pyridine trapping of cyclohexadienylidene **3d** in reasonable yields, and LFP studies can be used to optimize reaction conditions. The advantage of this synthesis – compared to the synthesis via pyrylium salts[1] – is that betaines without substituents in the pyridinium moiety are accessible. Quinone diazides **2** are readily available and by variation of substituents in both **2** and the pyridines a large variety of new betaines **1** should be accessible. We are presently exploring the scope of this reaction.

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Experimental

2,6-Di-*tert*-butyl-4-diazo-2,5-cyclohexadien-1-one (**2d**) was prepared according to a procedure by Ried and Dietrich[8]. – ^{1}H and ^{13}C NMR: 400.1 and 100.6 MHz, respectively (Bruker AM 400), CD_3OD as solvent, $(CH_3)_4Si$ internal standard. – MS (EI, 70 eV): Varian MAT CH7 or MAT 8222. – IR: Bruker IFS 66 FT-IR spectrometer, range 4000–400 cm^{-1}, resolution 1 cm^{-1}. – UV-Vis spectra: Hewlett-Packard 8452A diode array spectrophotometer with 2-nm resolution. – Elemental analyses: Institut für Pharmazeutische Chemie, Technische Universität Braunschweig.

2,6-Di-tert-butyl-4-pyridiniophenolate (**1d**): A solution of 144 mg of **2d** (0.62 mmol) in 50 ml of cyclohexane and 2.5 ml of pyridine was heated at reflux for 3 h under nitrogen. The deep-red betaine **1d** was filtered off, dried in vacuo to remove traces of pyridine, and washed with hexane. Byproducts were removed by Soxhlet extraction with hexane, and finally the betaine was extracted with methanol. After removal of the solvent in vacuo, 52 mg (0.18 mmol, 29%) of **1d** was obtained as dark red crystals; m.p. 251–258°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3438.2 cm^{-1} (s), 3426.8 (s), 3106.5 (m), 3071.6 (m), 2992.2 (m), 2951 (s), 2918.6 (m), 2871.2 (m), 1575.0 (m), 1490.5 (m), 1471.3 (vs), 1467.6 (vs), 1435.8 (vs), 1377.8 (m), 1338.0 (vs), 1250.7 (m), 1225.3 (m), 1198.8 (m), 1077.2 (m), 879.2 (m), 786.2 (m), 692.1 (w), 591.9 (w), 533.4 (w) (rel. intensity). – UV (CH_3OH): λ_{max} (lg ε) = 204 nm (4.45), 212 (4.22), 238 (3.70), 260 (3.69), 324 (3.70). – UV (CH_3CN): λ_{max} (lg ε) = 200 nm (4.49), 260 (3.98), 268 (3.88), 314 (3.75), 552 (4.19). – UV (CH_2Cl_2): λ_{max} (lg ε) = 228 nm (6.61), 262 (3.94), 272 (3.84), 316 (3.74), 404 (2.82), 598 (4.30). – ^{1}H NMR (CD_3OD): δ = 1.45 (s, 18H, *t*Bu), 7.23 (s, 2H, phenol), 8.02 (t, J = 6.98 Hz, 2H, *m*-pyridine), 8.39 (t, J = 7.75 Hz, *p*-pyridine), 8.97 (d, J = 7.75 Hz, 2H, *o*-pyridine). – ^{13}C NMR (CD_3OD): δ = 30.6 (*t*Bu), 36.3 (*t*Bu), 120.3 (*m*-phenol), 127.8 (*o*-phenol), 128.9 (*m*-pyridine), 141.9 (*p*-phenol), 142.9 (*o*-pyridine), 143.9 (*p*-pyridine), 172.8 (phenol C–O). – MS (EI, 160°C), *m/z* (%): 284 (22), 283 (50) [M$^+$], 282 (28), 268 (100) [M$^+$ – CH_3], 252 (50), 241 (50) 226 (25) [M$^+$ – *t*Bu], 212 (18), 199 (72). – $C_{19}H_{25}NO$: calcd. 283.19361; found 283.1936 ± 2 ppm. – $C_{19}H_{25}NO \cdot 0.5\,H_2O$ (283.2): calcd. C 78.03, H 8.98, N 4.79; found C 78.27, H 9.41, N 4.47.

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