Preparation and Chemistry of an Unexpectedly Stable α-Oxoketene−Pyridine Zwitterion, 2,2-Bis(*tert*-butylcarbonyl)-1-[4-(dimethylamino)pyridinio]ethen-1-olate

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Treatment of dipivaloylketene **1** and its dimers **2** and **3** with 4-(dimethylamino)pyridine (DMAP) in acetonitrile affords the α-oxoketene-pyridine zwitterion **4** as a pale yellow solid. This is the first example of a stable zwitterion obtained from a true α-oxoketene. In anhydrous solution at room temp., compound **4** largely cleaves into the reactants **1** and DMAP. At –60 °C the equilibrium is shifted entirely towards the zwitterion **4**, as shown by ^{13}C NMR measurements. Calculations using density functional theory (B3LYP/6–311+G**) are in excellent agreement with the formation and relative stability of **4**. ^{15}N labelling experiments demonstrate that the ring nitrogen atom of DMAP is involved in generating the new zwitterionic C–N bond. Reactions of **4** with NH and OH nucleophiles in solution afforded the corresponding dipivaloyl acetic acid derivatives **6** and **7**, whereas acetone or benzylidene aniline undergo cycloaddition reactions of the hetero-Diels–Alder type.

Introduction

Ketenes and ketene-nucleophile zwitterions are of continuing interest from preparative, mechanistic and theoretical points of view.[1] Zwitterionic species have been postulated as reactive intermediates in many reactions,[2] and in a few cases there is direct experimental evidence for their existence.[3] The synthesis of β-lactams by ketene−imine cycloaddition[2e,4] and the addition of N-nucleophiles to ketenes[5] have been investigated thoroughly in this context. It is interesting to note that, in the case of NH nucleophiles, the corresponding amide enols are formed rapidly, as shown by ^{1}H and ^{13}C NMR spectroscopy[6] and laser-flash photolysis with time-resolved infrared spectroscopy.[3i] Low-temperature matrix isolation has provided direct evidence for the existence and reactivity of ketene−pyridine zwitterions.[3g,3h] However, examples of stable ketene−nucleophile zwitterions under normal reaction conditions are extremely rare.

Gompper and Wolf[3a] were able to isolate and characterise spectroscopically a stable 1:2 zwitterionic adduct (a secondary product, not a ketene−pyridine zwitterion) from the addition of pyridine to bis(ethoxycarbonyl)ketene,[8] as well as a stable 1:1 adduct from the reaction of the same ketene with 4-(dimethylamino)pyridine (DMAP).

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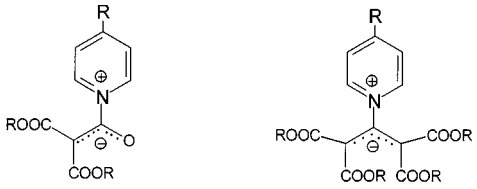
Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/eurjoc or from the author.



Dipivaloylketene (**1**) is generated in nearly quantitative yield by preparative flash vacuum thermolysis (FVT) of the corresponding furan-2,3-dione (Scheme 1).[9] Its chemistry has been well explored.[10] In particular, it slowly dimerizes at room temp. to afford the extraordinarily stable α-oxoketene **2**.[9b] However, when the dimerization is carried out in the presence of catalytic amounts of pyridine, DMSO, or phosphanes, among other substances, the dioxinone dimer **3** is obtained instantaneously instead. It was postulated that a zwitterionic intermediate of type **4** — with pyridine in place of 4-(dimethylamino)pyridine — was responsible for the changed mode of reaction.[9b] This proposal was confirmed by co-condensing dipivaloylketene (**1**) with pyridine vapour at 30 K. Subsequent warming to 100 K caused formation of the zwitterion, identified by its IR absorption bands (1677, 1605, 1596 and 1579 cm^{-1}). After further warming to room temperature, the dimer **3** was isolated (70% yield on a preparative scale).[3g] The electron-donating effect of the *p*-dimethylamino group enhances the basicity of the pyridine nitrogen from pK = 5.22 for pyridine to 9.61 for DMAP. Accordingly, the formation of a more stable zwitterion could be expected when using DMAP (see the Theory section).

Here we report the preparation of the stable α-oxoketene zwitterion **4**, obtained by addition of DMAP to the stable but nonetheless highly reactive dipivaloylketene (**1**). Altern-

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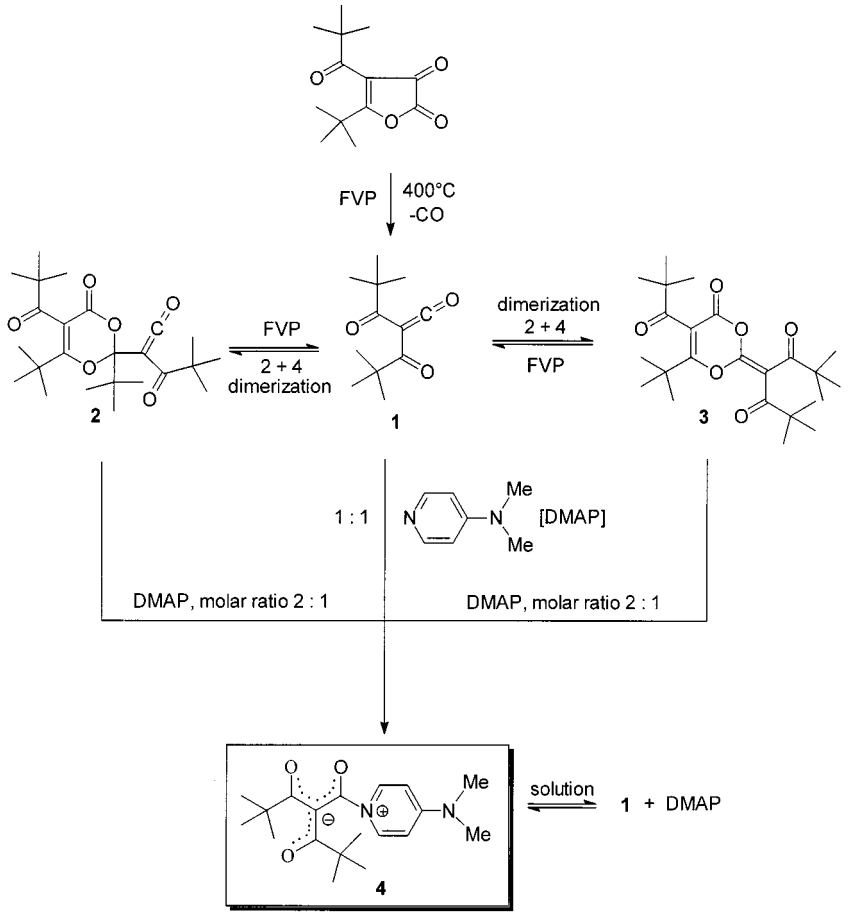


Scheme 1

atively, the ketene dimers **2** and **3** can both be used as precursors for **4** (Scheme 1).

Results and Discussion

When freshly prepared dipivaloylketene[9b] (**1**) was added dropwise to a solution of DMAP (molar ratio 1:1) in dry acetonitrile at room temperature, a pale yellow precipitate was formed immediately. After stirring for 20 min the precipitate (yield 86%) was separated by rapid suction filtration through a dry sintered glass filter. The adduct is highly sensitive to moisture, but can be stored in an evacuated desiccator over P_4O_{10} for several weeks without degradation. Starting from the ketene dimers **2** or **3** (molar ratio now 2:1), a similar experimental procedure can be employed. After addition of the corresponding dimer as a solid, the product precipitated from the clear yellow solutions after 2−5 min stirring at room temperature, in yields of 77−85%.

The formation of zwitterion **4** from **1** and DMAP is easily understood as a simple addition of the nucleophile to the ketene system. It is interesting to note that, when the primary amine 4-aminopyridine is employed instead of DMAP, the product obtained corresponds to addition of the NH_2 group to the ketene function (see below), but this product formation may well be preceded by a pre-equilibrium involving the zwitterion formed by attack of the pyridine N atom on the ketene. In the preparation of **4** from the dimers **2** or **3**, a [2+4] cycloreversion is required. This may be initiated by attack of DMAP on the dimers, thereby cleaving them to one molecule of ketene−DMAP zwitterion and one molecule of the monomeric dipivaloylketene.

The elemental analysis of **4** confirms the molecular formula of a 1:1 adduct of ketene **1** and DMAP. A FAB mass spectrum of **4** in a glycerine matrix did not yield a parent peak. Instead, peaks at m/z = 123 (100%) and 211 (30%) indicated the presence of the two fragments, DMAP and **1**. A FAB spectrum in a *p*-nitrobenzyl alcohol (NOBA) matrix yielded the same two fragments plus a signal at m/z = 486 (10%) corresponding to **4** + NOBA + H^+, thus providing indirect evidence for the presence of the intact molecules **4**.

The IR spectrum of **4** in KBr exhibits absorptions at 2980−2850m (*t*Bu), 1660s, 1635s, 1605vs, 1540m and 1520m cm^{-1}. The bands at 1660 and 1605 cm^{-1} are similar to those of the dipivaloylketene−pyridine zwitterion in a low temperature matrix (1677, 1605 cm^{-1}).[3h] The IR spectrum of an equimolar mixture of DMAP and dipivaloylmethane is very similar to that of the zwitterion, except that the bands at 1660−1635 cm^{-1} are missing, thus indicating that they are due to the zwitterion. The calculated values are 1678, 1633, 1611, 1585 and 1541 cm^{-1} (B3LYP/6−31G*, ε = 40; see Table S1 in the Supporting Information). In contrast, the IR spectrum of **4** in CH_2Cl_2 solution demon-

strates the presence of a ketene moiety (2115 cm^{-1}) as well as the C=O bands. Therefore, in solution, the zwitterion must exist in equilibrium with the starting components (vide infra). Further absorptions are at 1662, 1653, 1645 and 1601 (s) cm^{-1}.

The ^1H NMR spectrum of compound **4** in dry $CDCl_3$ solution corroborates the dissociation of **4** to the components. A singlet at δ = 1.23 (18 H) is due to the *tert*-butyl groups of ketene **1**. Doublets at δ = 8.22 and 6.50 (2 H each) together with a singlet at δ = 3.03 (6 H) confirm the presence of free DMAP. For comparison, virtually identical chemical shift values of DMAP were recorded for a 1:1 mixture of dipivaloylmethane and DMAP.

Similar results were also obtained from numerous ^{13}C NMR spectra of **4** at significantly higher concentrations and with CD_2Cl_2 or $CDCl_3$ as solvents. Here it is extremely important to perform the whole procedure under thoroughly anhydrous conditions. The NMR measurements themselves must be carried out in sealed tubes in order to avoid any trace of moisture. Rapid measurements (30 min.) and long reaction times (overnight) at room temp. allowed observation of the most intense signals only. The DMAP carbon atoms C-3,5 (δ = 106.5), C-4 (δ = 156.5) and the CH_3 carbons (δ = 39.5) correlated well with those of several positively charged (protonated) DMAP species reported in the literature,[11] as well as unprotonated DMAP itself. In contrast, the signal for C-2 (C-6) of DMAP was shifted upfield by 4.7−5 ppm (!), thereby suggesting the presence of a fast equilibrium. Because of the rapid exchange, the chemical shift values found (δ = 144.1−144.8) represent signals originating from the mixture of starting materials and product, giving an approximately 50:50 distribution [C-2/C-6 in free DMAP: δ = 149.8; in protonated DMAP[11]: δ = 139.0−131.0, depending on the specific salt; in **4** at −60 °C: δ = 139.5, see also Figure 1]. The carbons vicinal to the positively charged pyridinium nitrogen usually exhibit significant upfield shifts.[11] Observation of the carbons of the ketene scaffold in **4** was difficult at room temp.: the pivaloyl C=O was detected at δ = 202.9−203.5 as a rather broad signal of low intensity, again representing an average value of the free dipivaloylketene (δ = 198.9 at −50 °C[9a]) and the zwitterionic species (δ = 211.5 at −60 °C, see below); signals for the carbon atoms of the ketene function (C=C=O at δ = 52.1 and 194.0) were not found at all. A priori, these are of low intensity and are probably further broadened due to the fast equilibrium, since these two carbons are most affected upon formation of the zwitterion.

In order to slow down the exchange rate and to shift the position of the equilibrium itself towards the adduct, low temperature experiments were performed. In fact, at −60 °C (CD_2Cl_2) a complete assignment of the signals resulting from the zwitterion was possible (Figure 1). No signals due to free DMAP itself were detectable, thus indicating that the equilibrium had shifted entirely towards the zwitterion. In addition, because of hindered rotations of the pivaloyl moieties, the signals of the pyridinium nucleus split into doublets at temperatures of −40 °C and below since, as easily deduced from models, either the carbonyl or the *tert*-butyl group must get close to the pyridine nucleus thus resulting in different shielding/deshielding of the carbons involved. These signals collapsed to singlets again upon warming and the complete signal pattern of the original spectrum of the equilibrium at room temp. reappeared.

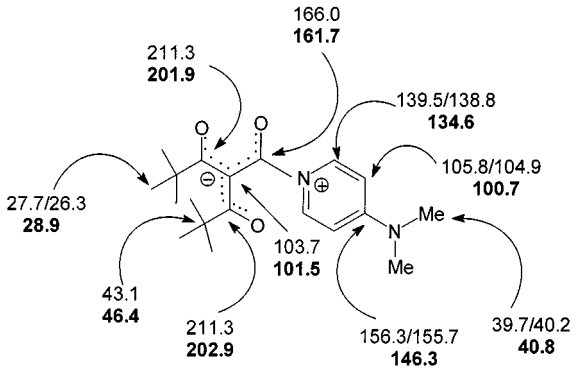
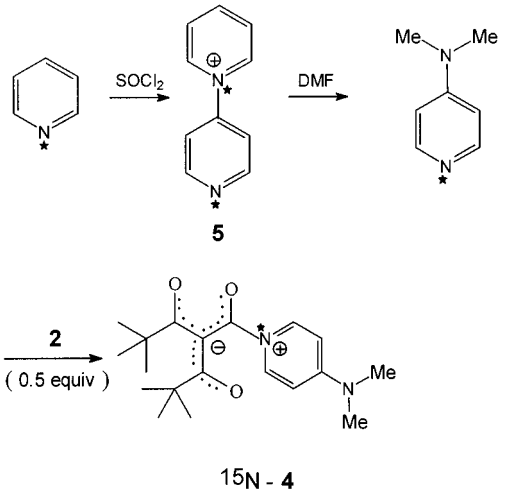


Figure 1. Calculated (GIAO-B3LYP/6−31G*) and observed (CH_2Cl_2, −60 °C) ^{13}C NMR chemical shifts for zwitterion **4**; calculated values are in bold

After addition of D_2O, further measurements indicated rapid hydrolysis to DMAP, as made evident by its most intense signals at δ = 149.1 and 106.6.

In order to demonstrate that it is the ring nitrogen atom of the DMAP that attacks the electrophilic carbon atom of the ketene, ^{15}N-labelling experiments were performed (Scheme 2). [^{15}N]DMAP, labelled at the ring nitrogen, was prepared from [^{15}N]pyridine (degree of labelling 20%) via the 4-pyridylpyridinium chloride (**5**) (Scheme 2).[12,13]



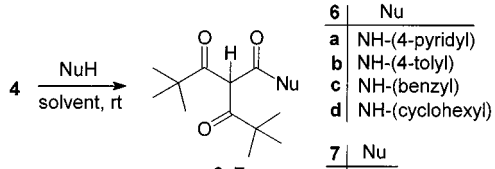
Scheme 2

In the ^{15}N NMR spectrum of [^{15}N]DMAP at room temp., the chemical shift of the ring nitrogen appears at δ = 112.5 (relative to nitromethane), while the corresponding signal for [^{15}N]**4** is shifted to δ = 121.0. Usually, ring nitrogens of pyridinium compounds exhibit signals some 50−100 ppm downfield from their neutral analogues.[14] For example, the ring nitrogens of closely related pyridinium dicyanomethylides appear in the range δ = 150−170.[15] The small downfield shift in [^{15}N]**4**, together with a broadening of the signal at δ = 121.0, again support the existence at room temp. of the equilibrium outlined in

Scheme 1. Because of a high rate of exchange, the signal represents an average value between that of free DMAP and the DMAP−ketene adduct, with the equilibrium strongly shifted toward the starting materials, DMAP and dipivaloylketene (perhaps by 80−90%). This experiment also confirms that DMAP attacks the ketene through the ring nitrogen atom. In a quite different area of investigation, it was concluded that the catalytic activity of DMAP in rearrangements of thionocarbonates is also due to ring nitrogen attack.[16]

Chemistry of 4

It is well documented that dipivaloylketene **1** adds primary amines to give the corresponding dipivaloylacetamides.[10b] In view of the equilibrium between zwitterion **4** and the starting materials, it is not surprising, therefore, that **4** reacted with primary amines to afford amides **6** in moderate to good yields. Nevertheless, ketene reactions are known to be catalysed by pyridines and other amines;[1b] hence it is not necessarily the monomeric ketene **1** itself that is reacting. Similarly, with alcohols, the corresponding dipivaloyl acetates **7** were obtained in yields of 60−80%. Remarkably, compounds **6** and **7** (Scheme 3) did not show any tendency to enolize in $CDCl_3$ solution, although enols should be stabilized by intramolecular hydrogen bonds. Earlier experimental and theoretical investigations into the keto-enol tautomerism of β-tricarbonyl compounds demonstrated influences arising from the physical condition of the sample as well as the kind of solvent employed.[17]

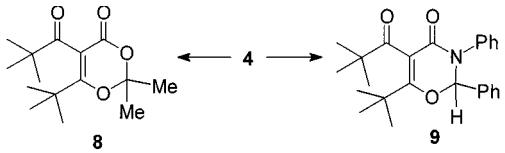


6	Nu
a	NH-(4-pyridyl)
b	NH-(4-tolyl)
c	NH-(benzyl)
d	NH-(cyclohexyl)

7	Nu
a	OMe
b	OEt
c	O*t*-Bu

Scheme 3

Dipivaloylketene **1** serves as an excellent oxadiene system in [4 + 2] cycloaddition reactions with C=O, C=N and C=S dienophiles.[18] In order to examine the ability of the zwitterion **4** to undergo similar reactions, dry acetone and benzylideneaniline were selected as dienophiles. The corresponding cycloadducts, 1,3-dioxin-4-one and 1,3-oxazin-4-one derivatives **8** and **9** (Scheme 4), were obtained in yields of 81% and 76%, respectively.



Scheme 4

Theory

To determine the structure and stability of the ketene-pyridine zwitterion **4**, density functional calculations were carried out using the Gaussian 98 series of programs.[19] Full geometry optimizations were performed with the B3LYP method,[20] using the split-valence polarized 6−31G* basis set. Higher-level relative energies were obtained through B3LYP/6−311+G** calculations, including a zero-point vibrational correction. The effect of a dielectric medium was examined using Onsager's self-consistent-reaction field theory.[21] NMR chemical shift calculations were performed using the gauge-independent atomic orbital (GIAO) method.[22] Infrared spectra were computed at the B3LYP/6−31G* level and the calculated frequencies were scaled by a factor of 0.9613.[23]

The zwitterionic structure **4** is calculated to be a stable species in the gas phase. It is characterized by a rather short, ylide-type C−N bond length of 1.558 Å (Figure 2). For comparison, the parent ketene−pyridine (CH_2CO/C_5H_5N) analogue is predicted to be a weak van der Waals complex with a long C−N distance of 2.073 Å. This, together with other calculations we have performed, indicates that ketene-pyridine ylides are stabilized by electron-withdrawing substituents on the ketene and electron-donating substituents on the pyridine. The zwitterion **4** has a very large dipole moment of 14.4 Debyes. Based on natural bond orbital (NBO)[24] analysis at B3LYP/6−31G*, **4** is calculated to have a large degree of charge transfer (0.56 e) from DMAP to dipivaloylketene. Significant charge alternation is also seen in the charge distribution of **4** (Figure 3). In the presence of a polar medium (ε = 40), the zwitterion is significantly stabilized: the C−N bond length is shortened by 0.038 Å, while the charge transfer is increased by 0.07 e. Because of steric repulsion, the ketene and pyridine subunits of **4** are not coplanar (τCCNC = 40°). It is interesting to note that the CH···O interaction also plays an important role in stabilizing this complex. The distance between the ketene oxygen and the pyridine *ortho*-hydrogen is 2.373 Å, significantly shorter than the sum of their van der Waals radii (3.05 Å). Likewise, the distance between the carbonyl oxygen and the *ortho*-hydrogen is relatively short (2.889 Å). The *ortho*-C−H stretch is blue shifted to a higher wavenumber (by 85 cm^{-1}) on going from the monomer (DMAP) to the zwitterion **4**. A similar CH···O interaction has been observed for the C_3O_2···pyridine complex. [25]

How stable is the zwitterion? The calculated enthalpy of formation of **4** is endergonic in the gas phase (ΔG_{298} = 20 kJ mol^{-1}, Table 1), but a polar medium has a strong influence on the stability of this polar species. In a nonpolar environment (ε = 2), the formation of the zwitterion is slightly preferred (ΔG_{298} = −6 kJ mol^{-1}). This is in good accord with the experimental observation that **4** is in equilibrium with DMAP + **1** in CH_2Cl_2 solvent. In a polar medium of ε = 40, the equilibrium is strongly shifted towards the zwitterion (ΔG_{298} = −24 kJ mol^{-1}). Dissociation of **4** to dipivaloylketene (**1**) and DMAP is predicted to have a small activation barrier of 4 kJ mol^{-1}. However, this barrier increases substantially to 34 kJ mol^{-1} in a dielectric medium of ε = 40. As seen in Figure 1, the calculated ^{13}C NMR chemical shifts (B3LYP/6−31G*) are in excellent accord with the experimental data. Likewise, the calculated

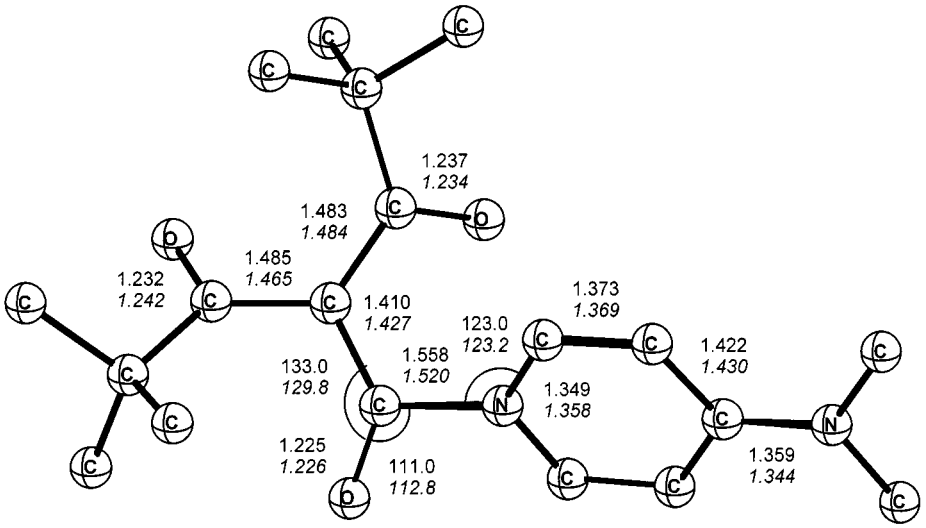


Figure 2. Optimized (B3LYP/6–31G*) structural parameters (bond lengths in Å and angles in degrees) of **4** in the gas phase (upright numbers) and in a polar medium of ε = 40 (numbers in italics)

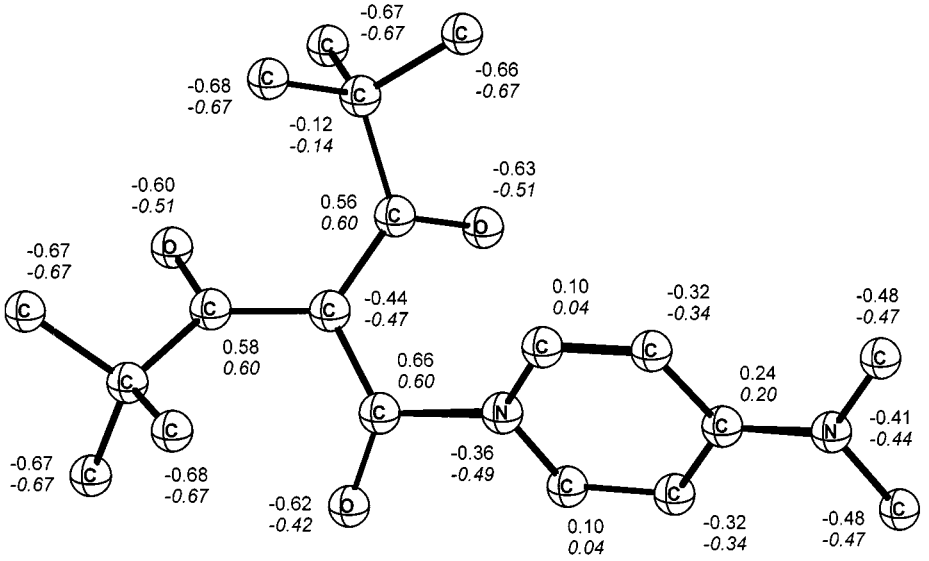


Figure 3. Calculated NBO atomic charges of **4** in the gas phase; the corresponding values in the precursors **1** and DMAP are given in italics

infrared frequencies agree well with the observed values (Table S1). In summary, calculation strongly supports the characterization of zwitterion **4**.

Table 1. Calculated energies of **4** (kJ mol^{-1})

	Enthalpy/free energy of formation[a][b]			Barrier		
	ε = 1	ε = 2	ε = 40	ε = 1	ε = 2	ε = 40
ΔH_0	6.9	−18.5	−37.1	3.5	15.9	37.4
ΔH_{298}	4.9	−20.6	−39.3	4.8	15.1	36.7
ΔG_{298}	20.0	−5.7	−24.1	3.7	14.0	35.7

[a] B3LYP/6–311+G**//B3LYP/6–31G* + ZPVE level. Calculated total energies (ε = 1) for **1**, DMAP, **4** and T.S. are −693.76630, −382.25730, −1076.03291 and −1076.02659 Hartrees, respectively. Calculated zero-point vibrational energies (ε = 1) for **1**, DMAP, **4** and T.S. are 724.6, 420.4, 1156.7 and 1150.9 kJ mol^{-1}, respectively. – [b] The free energies were calculated using the formula $\Delta G = \Delta H - T\Delta S$. Calculated entropies ($S$) for **1**, DMAP, **4** and T.S. were 134.5, 89.9, 173.0 and 176.7 J mol^{-1}K^{-1}, respectively.

Conclusion

Zwitterion **4**, obtained from treatment of dipivaloylketene (**1**) or its dimers **2** or **3** with 4-(dimethylamino)pyridine, is remarkably stable in the solid state (m.p. >170 °C!). It represents the first example of a stable zwitterion of this kind derived from a true α-oxoketene. In completely anhydrous solution (such as CD_2Cl_2, $CDCl_3$) the adduct dissociates into the reactants, thus creating a fast equilibrium at room temp. At low temperature (−60 °C), the equilibrium is shifted nearly completely towards the zwitterionic adduct, as evidenced by ^{13}C NMR measurements. This can be attributed to a negative $\Delta S°$ for zwitterion formation. The adduct **4** is highly sensitive to moisture, immediately hydrolysing into 4-(dimethylamino)pyridine and dipivaloylmethane. The stability and properties of **4** are in excellent accord with density functional quantum chemical calculations. Reactions between **4** and nucleophiles, as well as its

cycloaddition reactions, reveal chemical behaviour identical with that of dipivaloylketene **1** itself.

Experimental Section

General: 5-*tert*-Butyl-4-pivaloyl-2,3-dihydrofuran-2,3-dione and dipivaloylketene **1** and its dimers **2** and **3** were prepared according to the literature.[9b] [^{15}N]pyridine (95% ^{15}N) was purchased from Chemotrade (Germany). All commercial materials were used without further purification. Liquids and solvents, including NMR solvents (CD_2Cl_2, $CDCl_3$), were dried over molecular sieves (Merck, 0.4 nm); *n*-hexane was freshly distilled before use; solid materials were stored over P_4O_{10}. All reactions were performed under dry N_2, and the reaction vessels were equipped with $CaCl_2$ tubes. − ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded on a Varian X-200 (Gemini Version) and/or a Bruker 360 MHz instrument (selected ^{13}C NMR spectra are available as Supporting Information). − IR spectra were recorded on a Perkin−Elmer 298 spectrometer and UNICAM Galaxy Series 7000 (FTIR). − Mass spectral data (FAB mode) were obtained on a VG ZAB-2SEQ, MS-902 spectrometer.

Synthesis of 2,2-Bis(*tert*-butylcarbonyl)-1-[4-(dimethylamino)pyridinio]ethen-1-olate (4). − (a) From Dipivaloylketene (1): Dipivaloylketene (**1**) (300 mg, 1.43 mmol), freshly prepared by flash vacuum thermolysis of the corresponding furandione,[9b] was rapidly added dropwise with stirring to a solution of 4-(dimethylamino)pyridine ("Steglich" base, 180 mg, 1.48 mmol) in dry acetonitrile (2.5 mL). During this procedure a yellow solid started to precipitate, and the resulting reaction mixture was stirred for 20 min. at 20 °C. The yellow precipitate was separated by rapid suction filtration and immediately stored in an evacuated desiccator over P_4O_{10} (yield 407 mg, 86%), m.p. >170 °C (closed capillary). − ^{1}H NMR (200 MHz, $CDCl_3$; the spectrum is the result of dissociation into **1** and DMAP): δ = 1.23 (s, 18 H, *t*Bu), 3.03 (s, 6 H, CH_3), 6.50 (d, *J* = 8.5 Hz, 2 H), 8.22 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (90.5 MHz, CD_2Cl_2, −60 °C): see Figure 1. − IR (KBr): $\tilde{\nu}$ = 3020−2860, 1650, 1605 cm^{-1}. − FT-IR (CD_2Cl_2): $\tilde{\nu}$ = 2969, 2115, 1662, 1653, 1645, 1638, 1601 cm^{-1}. − FAB-MS: (a) glycerine matrix *m*/*z* (%) = 57 (90) [*t*Bu], 123 (100) [M + 1, DMAP], 211 (30) [M + 1, **1**]; (b) *p*-nitrobenzyl alcohol matrix *m*/*z* (%) = 57 (40) [*t*Bu], 123 (100) [M + 1, DMAP], 211 (10) [M + 1, **1**], 486 (10) [**4** + NOBA + 1]. − $C_{19}H_{28}N_2O_3$ (332.44): calcd. C 68.64, H 8.49, N 8.34; found C 68.88, H 8.89, N 8.49.

(b) From Dimer 2: Solid **2** (300 mg, 0.71 mmol) was added to a solution of 4-(dimethylamino)pyridine (180 mg, 1.48 mmol) in dry acetonitrile (2.5 mL). The solution turned yellow, and after 2−3 min. the yellow product (365 mg, 77%) precipitated. The reaction mixture was stirred for another 30 min at 20 °C. The final workup was performed as described under (a).

(c) From Dimer 3: Compound **4** (140 mg, 89%) was obtained by exactly following the procedure given under (b), from 4-(dimethylamino)pyridine (60 mg, 0.49 mmol) and dimer **3** (100 mg, 0.24 mmol) in dry acetonitrile (1.0 mL).

Synthesis of [^{15}N]4. (a) 4-[^{15}N]Pyridyl-[^{15}N]pyridinium Chloride (5):[12,13] Thionyl chloride (2.0 mL, 27.5 mmol) was added dropwise to a mixture of [^{15}N]pyridine (200 mg, degree of labelling 95%) and dry pyridine (0.8 mL, 12.7 mmol, degree of labelling now 19.3%). The solution was allowed to stand at 20 °C for 6 days, forming a deep brownish, viscous liquid. The excess of thionyl chloride was removed at the vacuum line (10^{-3} mbar) by lyophilization and the brownish residue was triturated with dry ethanol (1 mL) to afford a suspension, which was centrifuged (3000 rpm) for 3 min. The liquid layer was removed and the residue was transferred into a round bottomed flask with the aid of 2 mL of dry ethanol. The ethanol was evaporated to afford brownish crude **5** (900 mg).

(b) 4-(Dimethylamino)[^{15}N]pyridine:[12,13] Crude **5** (900 mg) was refluxed in freshly distilled dimethylformamide (1.5 mL) for 2 h (bath temperature 180 °C). After cooling, aqueous sodium hydroxide (3.6 mL, 1% solution) was added to the dark suspension, which was stirred for 1 h at 20 °C. The reaction mixture was subsequently extracted five times, each with 6.0 mL of dichloromethane, and checked by TLC. The combined organic layers were dried over Na_2SO_4, decolourised by short boiling with charcoal, and evaporated. The pale yellow residue was recrystallized from diisopropyl ether and dried by lyophilization to afford pure 4-(dimethylamino)[^{15}N]pyridine (90 mg, 6% based on pyridine). ^{15}N NMR ($CDCl_3$): δ = 112.5 (referenced to nitromethane).

(c) [^{15}N]4: Dimer **3** (100 mg, 0.23 mmol) was added to 4-(dimethylamino)[^{15}N]pyridine (70 mg, 0.45 mmol, degree of labelling 19%) dissolved in dry acetonitrile (0.5 mL). After 3 min. stirring at 20 °C, a yellow solid started to precipitate. After 30 min. this was separated by suction filtration and immediately stored over P_4O_{10} in an evacuated desiccator. Yield 90 mg (52%). − ^{15}N NMR ($CDCl_3$): δ = 121 (reference to nitromethane).

Reactions between Zwitterion 4 and Primary Amines. − *N*-(4-Pyridyl)dipivaloylacetamide (6a). − (a) From 4: Solid 4-aminopyridine (30 mg, 0.3 mmol) was added to a solution of **4** (100 mg, 0.45 mmol) in DMF (1.5 mL). The solution decolourised and was stirred at 20 °C for 20 min. After addition of diethyl ether (3 mL), it was washed with 0.35 mL of aqueous HCl (1 N). The organic layer was dried over sodium sulfate and evaporated. The crude amide was recrystallized from *n*-hexane to afford 60 mg of **6a** (55%). − **b) From 1:** Dipivaloylketene (**1**) (210 mg, 1.0 mmol) was added dropwise to a solution of 4-aminopyridine (94 mg, 1.0 mmol) with stirring. After 1 h at 20 °C, the solvent was evaporated and the remaining crude product was recrystallized from *n*-hexane to give 235 mg (78%) of colourless crystals, m.p. 165−166 °C. − IR (KBr): $\tilde{\nu}$ = 3140, 3000−2860, 1715, 1690, 1600 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 18 H, *t*Bu), 5.81 (s, 1 H, CH), 7.44 (d, *J* = 9.0 Hz, 2 H), 8.48 (d, *J* = 9.0 Hz, 2 H), 8.90 (br s, 1 H, NH). − $C_{17}H_{24}N_2O_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 67.02, H 8.01, N 9.27.

***N*-(4-Tolyldipivaloyl)acetamide (6b):** *p*-Toluidine (60 mg, 0.56 mmol) dissolved in dry acetonitrile (1.5 mL) was added dropwise to a solution of **4** (150 mg, 0.45 mmol) in dry acetonitrile (5 mL). After 20 min. stirring at 20 °C, the yellow solution decolourised, and the acetonitrile was removed in vacuo. Trituration with 3 mL of *n*-hexane dissolved the 4-(dimethylamino)pyridine and the remaining colourless residue was recrystallized from *n*-hexane to yield 90 mg (63%) of **6b**; m.p. 126 °C. − IR(KBr): $\tilde{\nu}$ = 3300, 2970, 1725, 1700, 1605 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.27 (s, 18 H, *t*Bu), 2.32 (s, 3 H, CH_3), 5.79 (s, 1 H, CH), 7.12 (d, *J* = 9.5 Hz, 2 H), 7.39 (d, *J* = 9.5 Hz, 2 H), 8.61 (br s, 1 H, NH). − $C_{19}H_{27}NO_3$ (317.43): calcd. C 71.89, H 8.57, N 4.41; found C 71.36, H 8.72, N 4.28.

***N*-(Benzyldipivaloyl)acetamide (6c):** Freshly distilled benzylamine (50 mg, 0.46 mmol), dissolved in dry acetonitrile (2.0 mL), was rapidly added dropwise to a solution of **4** (150 mg, 0.45 mmol) in dry acetonitrile (4 mL). After stirring for 1 h at 20 °C and evaporation of the solvent, the residue was dissolved in 200μL of ethyl acetate. This solution was filtered through a short column (3.5 g of

Merck 60 H silica gel) using 30 mL of ethyl acetate/petroleum ether (3:5) as eluent. The combined filtrates were again filtered through a fine-pore sintered glass filter and evaporated. The crude product was recrystallized from *n*-hexane to obtain 117 mg (82%) of colourless crystals, m.p. 130−132 °C. − IR(KBr): $\tilde{\nu}$ = 3350, 3000−2860, 1720, 1705, 1655 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.22 (s, 18 H, *t*Bu), 4.40 (d, *J* = 5.0 Hz, 2 H), 5.75 (s,1 H, CH), 7.12 (br s, 1 H, NH), 7.20−7.33 (m, 5 H). − $C_{19}H_{27}NO_3$ (317.43): calcd. C 71.89, H 8.57, N 4.41; found C 71.80, H 8.49, N 4.53.

***N*-Cyclohexyl-dipivaloylacetamide (6d):** Freshly distilled cyclohexylamine (20 mg, 0.30 mmol), dissolved in dichloromethane (100 µL), was mixed with **4** (60 mg, 0.30 mmol), dissolved in dichloromethane (1.5 mL), and stirred at 20 °C for 1 h. The decolourised solution was evaporated, and the residue was treated with diethyl ether (3 mL) and washed with aqueous 1 N HCl (0.3 mL) to remove the 4-(dimethylamino)pyridine. The organic layer was evaporated and the crude residue recrystallized from *n*-hexane to afford 90 mg (54%) of pure **6d**, m.p. 116−118 °C. − IR (KBr): $\tilde{\nu}$ = 3380−3300, 3000−2860, 1720, 1640 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.1−2.0 (m, 28 H, CH_2 and *t*Bu), 3.65 (m, 1 H), 5.64 (s, 1 H, CH), 7.27 (br s., 1 H, NH). − $C_{18}H_{31}NO_3$ (309.45): calcd. C 69.87, H 10.10, N 4.53; found C 69.99, H 10.17, N 4.50.

Reactions of Zwitterion 4 with Alcohols. − General Procedure: The alcohol (0.35 mmol) was injected into a solution of **4** (110 mg, 0.33 mmol) in dichloromethane (4.0 mL), causing immediate decolourisation of the reaction mixture. After stirring for 2 h at 20 °C the solvent was partially evaporated to approximately 25% of its original volume, and diethyl ether (3 mL) was added. Extraction with 0.35 mL aqueous HCl (1 N) removed the 4-(dimethylamino)-pyridine. The organic layer was pipetted off and the aqueous solution again extracted twice with ether (2 × 1 mL). The combined ether solutions were dried over sodium sulfate. Careful evaporation of the ether at 20 °C afforded the crude products, which could be recrystallized from *n*-hexane and should be stored under a dry atmosphere.

Methyl Dipivaloylacetate (7a): M.p. 49−50 °C; for analytical and spectroscopic data see ref. [9a] and [10b].

Ethyl Dipivaloylacetate (7b): M.p. 59−61 °C; for analytical and spectroscopic data see ref. [9a] and [10b].

***tert*-Butyl Dipivaloylacetate (7c):** M.p. 76−78 °C. − IR (KBr): $\tilde{\nu}$ = 3240, 3020−2800, 1710, 1685, 1600 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.20 (s, 18 H, *t*Bu), 1.49 (s, 9 H, *t*Bu), 5.77 (s, 1 H, CH). − $C_{16}H_{28}O_4$ (284.3932): calcd. C 67.57, H 9.92; found C 67.65, H 10.01.

6-*tert*-Butyl-2,2-dimethyl-5-pivaloyl-1,3-dioxin-4-one (8): Dry acetone (22 µL, 0.3 mmol) was injected with the aid of a syringe into a solution of **4** (100 mg, 0.3 mmol) in dichloromethane (3.0 mL). The solution decolourised slowly and after stirring for 3 h at 20 °C the solvent was evaporated to a volume of approximately 1 mL. Diethyl ether (3 mL) was added, and the further workup followed the procedure described for the preparation of compounds **7**. Yield 65 mg (81%), m.p. 56−58 °C. − $C_{15}H_{24}O_4$ (268.35): calcd. C 67.14, H 9.01; found C 66.93, H 9.07. The spectroscopic data exactly match those reported in ref.[18]

6-*tert*-Butyl-5,6-dihydro-2,3-diphenyl-5-pivaloyl-1,3-oxazin-4-one (9): Compound **4** (100 mg, 0.3 mmol) was treated with benzylideneaniline (55 mg, 0.3 mmol) exactly following the experimental procedure described for **8**. Yield 90 mg (76%); m.p. 160−162 °C. − $C_{25}H_{29}NO_3$ (391.51): calcd. C 76.70, H 7.47, N 3.58; found C 76.75, H 7.51, N 3.44. The spectroscopic data were identical with those presented in ref.[18]

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