Dipivaloylketene and Its Dimers. [2 + 4] versus [2 + 2] Cycloaddition Reactions of α-Oxo Ketenes

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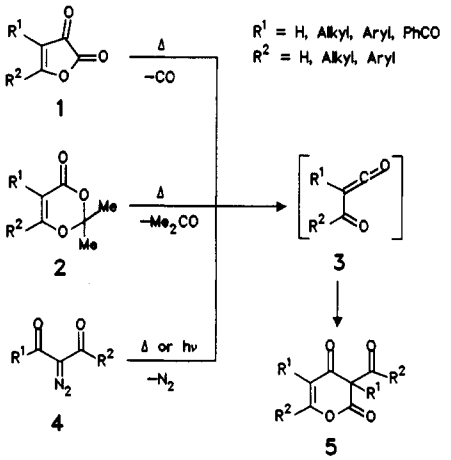
Dipivaloylketene (8) is generated by preparative flash vacuum pyrolysis of furandione **6**. While dimerization of 8 in apolar and several polar solvents leads to the previously reported [2 + 4] dimer **7**, dimerization in the presence of DMSO, tributylphosphine oxide, or pyridine instead surprisingly occurs across the C=O bond of the ketene function, affording dioxinone **9**. This is a novel type of α-oxo ketene dimerization. The reversibility of both dimerizations and mechanistic pathways for the formation of **9** are discussed. Cycloaddition reactions of 8 with heterocumulenes **10a,b** and **12a–c** yield [2 + 4] cycloadducts **11a,b** and **13a–c**, respectively. Oxazinones **13a–c** can add a second molecule of 8 to generate novel spiro heterocycles **14a–c**. In contrast, oxo ketene **7** reacts with carbodiimides **12a,b**, to furnish [2 + 2] adducts **15a,b**. This is the first unequivocal example of a direct [2 + 2] cycloaddition reaction of an α-oxo ketene. The unexpected formation of these compounds was confirmed by X-ray crystallography (**15a**). General aspects of [2 + 2] versus [2 + 4] cycloaddition in α-oxo ketenes are discussed.

α-Oxo ketenes (acylketenes) are highly reactive molecules that cannot normally be isolated or observed under ordinary reaction conditions, although several examples have been detected by low-temperature IR spectroscopy, e.g., in Ar matrix.[1] These ketenes are of considerable current interest, not only because of mechanistic and theoretical considerations[1,2] but also because of their use as synthetic building blocks in organic synthesis.[3–7]

Synthetically useful procedures for the generation of α-oxo ketenes **3** generally involve solution thermolysis of 2,3-dihydrofuran-2,3-diones **1**[3] or 1,3-dioxin-4-ones **2**[2g–i,4,5c] and thermolysis or photolysis of 2-diazo-1,3-dicarbonyl compounds **4**.[5] In these reactions, the reactive ketenes are generated in situ from their respective precursors and are trapped immediately with nucleophiles, or in [2 + 4] cycloaddition reactions. These methods however are not always applicable and have some disadvantages, as under these conditions (the thermolysis of **1**, **2**, and **4** usually requires temperatures of 80–130 °C) side reactions such as dimerization of the α-oxo ketenes (**3** → **5**)[1c,f,g,2g,h,6] may occur, thus resulting in only moderate yields of cycloadducts.



Recently, we reported the generation of dipivaloylketene (8) by flash vacuum pyrolysis (FVP) of furandione **6**.[1d] This sterically hindered diacylketene is extraordinarily stable and was characterized by low-temperature IR and

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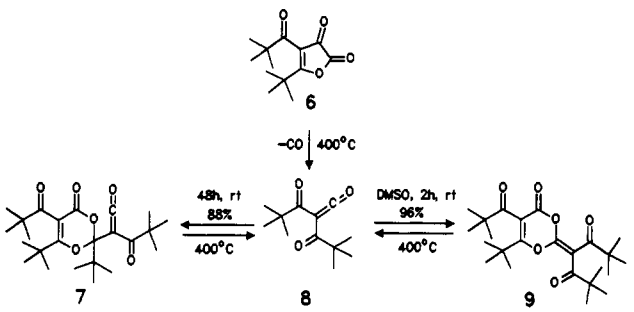
NMR spectroscopies.[1d] At room temperature it slowly dimerizes in an unusual [2 + 4] cycloaddition reaction to the dioxinone 7 which, although still an α-oxo ketene, is



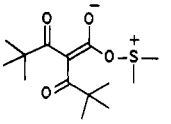
stable and not attacked by oxygen or moisture.[1d] While our previous work in this area was mainly analytical in intent, we have now utilized preparative FVP to prepare neat dipivaloylketene (8) on a multigram scale and study the chemistry of this persistent diacylketene. Herein we report the formation of another dipivaloylketene dimer, viz. 9, as well as the cycloaddition reactions of α-oxo ketenes 8 and 7 with carbodiimides. It is the first time that the cycloaddition chemistry of α-oxo ketenes of type 3 has been studied under such mild conditions. In other research, we have demonstrated that α-oxo ketene 7 is a valuable starting material for the synthesis of functionalized 2,6,9-trioxabicyclo[3.3.1]nona-3,7-dienes.[7]

Results and Discussion

Neat dipivaloylketene (8) was generated by preparative FVP of *tert*-butylpivaloylfurandione 6 at 400 °C (10^{-2} mbar) and trapping of the pyrolyzate on a cold finger at 77 K. After the solution was warmed to room temperature, 8, mp 10–12 °C, was collected as a colorless oil in quantitative yield. When a sample of neat dipivaloylketene (8) was allowed to stand at room temperature for 48 h, the highly hindered ketene 7 was obtained, analogously to the previously reported experiment.[1d] Much to our surprise, however, when the dimerization was carried out in the presence of DMSO or tributylphosphine oxide (1 equiv), a crystalline product began separating from the reaction mixture within 30 min. From the spectroscopic properties of this compound, in particular the IR spectrum (no ketene absorption was present), it became evident that a different dimer, viz. 9, had formed. Final confirmation of the proposed structure was obtained from an X-ray crystallographic analysis.

The formation of dimers 7 and 9 is most unusual, and distinctly different from all other known acyl- and diacylketene dimerizations, that proceed via [2 + 4] cyclodimerization of one α-oxo ketene molecule to the C=C bond of another to give α-pyrones (3 → 5).[1c,f,g,2g,h,6] In the case of the uncatalyzed dipivaloylketene dimerization, the [2 + 4] cycloaddition instead involves one molecule of acylketene as the four-electron component adding to one of the C=O bonds of the pivaloyl groups, thus leading to dioxinone 7. If catalyzed by DMSO, one molecule of acylketene now adds to the C=O bond of the ketene function, thereby generating dioxinone 9.

A reasonable explanation for this unexpected change of mechanism in the dipivaloylketene dimerization process might be that the reaction sequence 8 → 9 proceeds via a zwitterionic intermediate, which is stabilized by dipolar solvents (i.e., DMSO). Other examples of such solvent-induced alterations of mechanisms for cycloaddition reactions of ketenes are known.[8] However, in the present case, this effect was not observed with other dipolar aprotic solvents such as acetonitrile or DMF, where dimer 7 is still formed. This suggests that the interaction between dipivaloylketene and DMSO (or tributylphosphine oxide) is, in fact, a more specific one. Since the dimerization 8 → 9 is apparently faster than that forming 7, the oxo ketene 8 may be activated by interaction with DMSO (or tributylphosphine oxide), eventually leading to a dipolar intermediate:



A model shows that the oxy anion so generated is in fact quite unhindered sterically and thus may attack a second molecule of oxo ketene 8, ultimately giving 9 rather than 7.

These results prompted us to study the dimerization of dipivaloylketene (8) also in the presence of pyridine. Tertiary amines have been found to catalyze the dimerization of ketenes, presumably through pathways involving zwitterionic intermediates similar to the one shown above.[9] Only recently has direct spectroscopic evidence for the existence of such zwitterionic ketene–pyridine complexes been reported.[10] Indeed, when 8 was treated with 1 equiv of pyridine, dimer 9 was formed within seconds. From the above we conclude that zwitterionic intermediates are likely to play a significant role in all dimerization reactions leading to 9. Note that both dimers 7 and 9 are formed in high yield and with complete regioselectivity.

As 1,3-dioxin-4-ones, both dimers should be thermally cleavable to α-oxo ketenes. Indeed, when subjected to FVP at 400 °C (10^{-3} mbar) monomeric dipivaloylketene (8) was regenerated from both 7 and 9.

The apparent reluctance of dipivaloylketene to undergo cyclodimerization in the "normal" way, by attacking the C=C bond of the ketene function (cf. 3 → 5), can be ascribed to the severe steric hindrance coming from the adjacent pivaloyl groups. However, dipivaloylketene can add to the C=C bond of other ketenes, such as diphenylketene (10a). When dipivaloylketene (8) was treated with 10a at room temperature, 2,4-pyranedione 11a was obtained. The structure of 11a was established by IR and ^{13}C NMR spectroscopy. Related oxo ketene–di-

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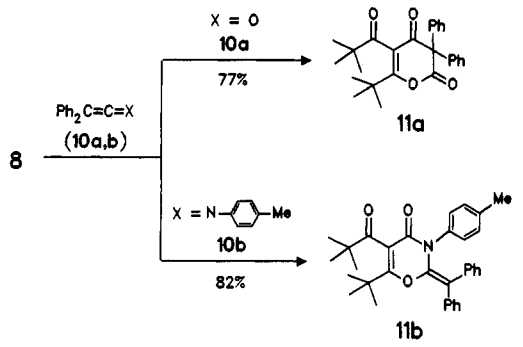
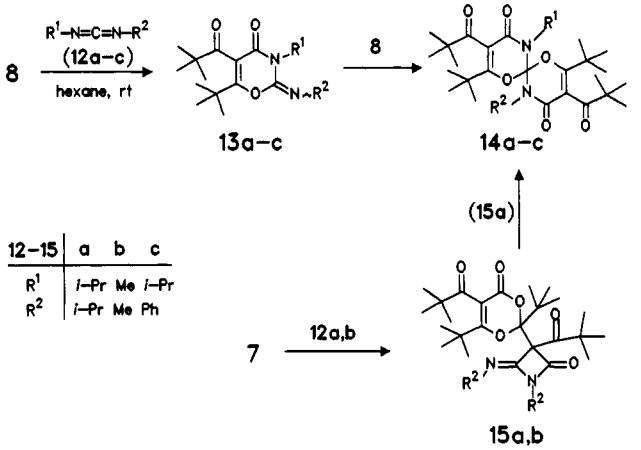


phenylketene adducts have been reported.[6g,h] In a similar experiment, 8 was treated with keteneimine **10b**. Here, addition takes place at the C=N bond of the keteneimine, in agreement with previous work on the addition of acylketenes to keteneimines.[11]

In connection with the studies on the cyclodimerization of dipivaloylketene, we became interested in cycloaddition reactions of α-oxo ketenes 7 and 8 in general: α-Oxo ketenes show a pronounced tendency to form [2 + 4] Diels–Alder adducts when trapped with dienophiles.[3-6,11,12] Carbodiimides are particularly reactive and lead to 1,3-oxazin-4-ones.[3k,4b,6e,f,12] When dipivaloylketene (8) was treated with 1 equiv of diisopropylcarbodiimide (**12a**) in hexane, the expected oxazinone **13a** was obtained in almost quantitative yield. When the reaction was carried out in



the absence of any solvent and 2 molar equiv of 8 was employed, a strongly exothermic reaction took place, affording a 2:1 adduct. The ^{13}C NMR spectrum of this material was in general agreement with structure **14a**, exhibiting resonances at similar shift values as observed for **13a**, in addition to the spiro carbon at 115.5 ppm. Analogously, 2 equiv of 8 added to dimethylcarbodiimide (**12b**) to furnish **14b**. The chirality of these novel dissymetric molecules, having a 2-fold rotational axis as the only element of symmetry, was established by ^1H NMR studies using chiral shift reagents. Thus, in the presence of $Eu(hfc)_3$, a clearcut splitting in the ratio of 1:1 of all three signals in the proton spectrum of **14b** was observed (see Experimental Section).

In the case of the unsymmetrical carbodiimide **12c**, reaction with 8 in hexane yielded a mixture of **13c** and **14c**, readily separable by crystallization. Of the two possible isomeric 1:1 adducts, only **13c** (R^1 = *i*-Pr) was isolated. The structure of this compound was deduced from *J*-($^{13}C,^1H$) values in the proton-coupled ^{13}C NMR spectrum, where a distinct doublet with $^3J_{CH}$ = 5 Hz was observed for C-4 at 160.8 ppm. The same indicative long-range coupling of C-4 with the α-protons of the isopropyl groups at N-3 was also seen in **13a** and **14a**, but not in, e.g., **11b** where a sharp singlet for C-4 at 162.0 ppm was observed. While we could not isolate the isomeric oxazinone **13** (R^1 = Ph, R^2 = *i*-Pr) in the reaction of 8 with **12c**, its initial formation, and subsequent transformation to **14c**, cannot be rigorously excluded. Treatment of **13c** with an equimolar amount of 8 at room temperature gave the expected spiro compound **14c**. Although several examples of cycloaddition reactions of "in situ" acylketenes with carbodiimides are known (carried out at much higher temperatures than here),[3k,4b,6e,f,12] surprisingly, the formation of 2:1 adducts has never before been observed.

While the cycloaddition reactions of dipivaloylketene (8) proceeded with remarkable ease, α-oxo ketene **7** was more reluctant to undergo reactions with dienophiles: when **7** was treated with carbodiimide **12a** at 60 °C for 48 h a mixture of two compounds was obtained. The minor product (24%) was readily identified as oxazinone **13a** by comparison with authentic material. The formation of **13a** can be explained in terms of partial monomerization of dimer **7** under the reaction conditions employed. The major product (58%) was identified as a 1:1 adduct of dimer **7** with **12a** by elemental analysis. Instead of the expected [2 + 4] adduct, however, this material was shown to be the [2 + 2] cycloadduct **15a**. The first evidence for the presence of a four-membered ring in **15a** was adduced by its IR spectrum, showing an absorption at 1820 cm^{-1}, characteristic of the C=O band in 4-iminoazetidin-2-ones.[13] In the ^{13}C NMR spectrum all signals appeared to be "doublets", thus indicating either the presence of diastereomers or the existence of *E*/*Z* isomers (C=NR^2). Note that the [2 + 2] addition (*rac*-**7** + **12** → **15**) only generates two neighboring asymmetric carbon atoms and therefore may lead to diastereoisomers. When the highly reactive dimethylcarbodiimide (**12b**) was employed, reaction took place at room temperature within 8 h leading to **15b** in 76% yield. Due to the mild reaction conditions used here, the formation of oxazinone **13b** as side product was not observed. The ^1H NMR spectrum of **15b** at 20 °C exhibited 4 singlets for the two *N*-methyl groups. A temperature-dependent NMR study showed that these 4 singlets collapsed into two signals upon warming to 60 °C (reversible). This confirms that the splitting is, in fact, due to the appearance of *E*/*Z* isomers, which was observable at room temperature (see Experimental Section). Final structural confirmation of [2 + 2] adducts **15** was obtained from an X-ray crystallographic analysis of **15a** (Figure 1).[14]

The surprising occurrence of [2 + 2] cycloadducts **15** in the reaction of α-oxo ketene **7** with carbodiimides deserves further comment: Although [2 + 2] cycloadditions forming

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(14) While several examples of ketene–carbodiimide [2 + 2] cycloadducts (4-iminoazetidin-2-ones) are known,[13] an X-ray analysis of this four-membered ring system has never been reported. For comparison of X-ray data with other azetidines, and β-lactams in particular, see: (a) Trefonas, L. M.; Majeste, R. J. X-Ray Studies of Small-Ring Nitrogen Heterocycles in *Physical Methods in Heterocyclic Chemistry*; Gupta, R. R., Ed.; Wiley: New York, 1984; pp 313–354. (b) Cf. Buchanan, G. L.; Sim, G. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 801.

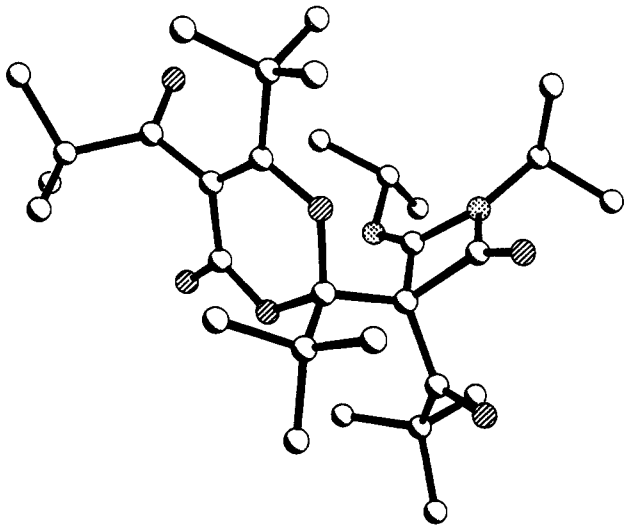
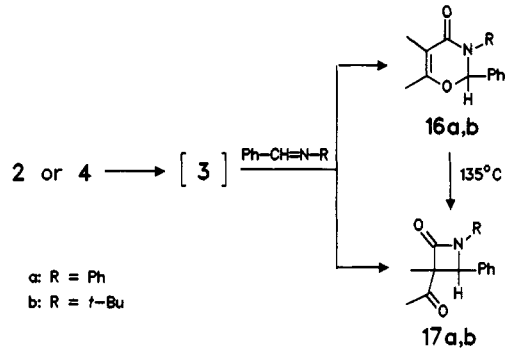


Figure 1. Molecular structure of **15a**. Circles shaded from top right to bottom left represent oxygen atoms, stippled circles nitrogen atoms. Hydrogen atoms have been omitted for clarity.

four-membered rings are characteristic reactions of ketenes,[15] this tendency is apparently overridden in α-oxo ketenes by the availability of [2 + 4] cycloaddition pathways. Compared to the vast number of papers dealing with [2 + 4] adducts,[1c,d,f,g,2g-i,3-6,11,12] reports on [2 + 2] cycloadditions to the ketene function of acylketenes are extremely rare.[16] Stetter and Kiehs[16a] reported the formation of small amounts of a β-lactam (**17a**, 16%) along with the [2 + 4] adduct **16a** in the thermolysis of 2-diazacyclohexane-1,3-dione (cf. **4**) with *N*-benzylideneaniline. Similarly, Kato et al.[16b] also found β-lactams (e.g., **17b**, 6%) in the reaction of acetylketene **3** generated from dioxinone (cf. **2**) with related *N*-benzylideneamines. However, Kato et al.[16b] were able to demonstrate that these azetinones **17** could have arisen by thermal rearrangement of [2 + 4] primary products of **16**.



In the case of dipivaloylketene dimer **7**, we ascribe the tendency to form [2 + 2] adducts rather than [2 + 4] adducts to the highly hindered nature of the ketene functionality, in particular to the fact that the α-oxo ketene moiety has s-*E* conformation, as established by X-ray crystallography[1d] and indicated in formula **7**. Although this does not strictly exclude isomerization to the s-*Z* conformer under the reaction conditions (60 °C, 48 h), it nevertheless makes a concerted [2 + 4] cycloaddition sterically less favorable. Also note that, although in the crystal the s-*E* structure is nearly planar, strongly skewed forms may exist in solution.[2m,17a]

Attempts to selectively cleave the dioxinone ring in **15a** to generate **8** and a simple azetinone failed. Instead, when **15a** was subjected to FVP at 400 °C (10^3 mbar) spiro compound **14a** was isolated in good yield. This unusual transformation of [2 + 2] adduct **15a** into isomeric **14a** is most likely to proceed via complete cycloreversion of both rings to **8** and **12a**, followed by 2-fold [2 + 4] addition of dipivaloylketene (**8**) to carbodiimide **12a** on warm-up of the cold finger.

When dimer **9** was treated with diisopropylcarbodiimide at 55 °C, monomerization occurred (**9** → **8**), and oxazinone **13a** was obtained in good yield. This illustrates again the reversibility of both dimerizations and also confirms that dimer **9** may be used as another precursor of dipivaloylketene.

In conclusion, we have shown that the chemistry of neat dipivaloylketene (**8**), generated by FVP and studied at room temperature, is somewhat different from reactions of other acylketenes generated in situ at higher temperatures. This is particularly true for dimerization reactions which, in the case of **8**, can lead to dioxinones **7** or **9** depending on the reaction medium. We have shown that **8** reacts with a number of dienophiles, giving [2 + 4] cycloadducts. These reactions proceed smoothly at room temperature, generally affording products in high yields. Some of these adducts could also be obtained by solution thermolysis of furandione **6** in the presence of the corresponding dienophiles; however, yields are rather poor in the latter reactions and a number of side products are formed.[17b] Surprisingly, α-oxo ketene **7** forms [2 + 2] adducts **15** in the reaction with carbodiimides. Few [2 + 2] cycloaddition reactions of α-oxo ketenes have been reported in the literature.[16] In fact the reaction **7** → **15** is the first example where the *direct* formation of a [2 + 2] cycloadduct from reaction of an acylketene and a multiple bond system has been unambiguously established.

Further studies on the chemistry of these intriguing ketenes are under way, and results will be reported in due course.

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 298 spectrophotometer. ^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra at 50 MHz on a Varian XL-200 instrument. Mass spectra were obtained on a Kratos MS25RFA instrument. Microanalyses were performed on a C,H,N-automat Carlo Erba 1106.

Dipivaloylmethane, diisopropylcarbodiimide, tributylphosphine oxide, tris[3-(heptafluoropropyl)hydroxymethylene))-*d*-camphorato]europium (Eu[hfc]$_3$), and anhydrous $MgCl_2$ were purchased from Aldrich Chemical Co and used without further purification. Diethyl ether and hexane were dried over sodium wire and DMSO was dried over 4-Å molecular sieves. All reactions were carried out in a dry N_2 atmosphere to minimize contact with moisture. Cycloaddition reactions were performed in sealed flasks.

For preparative FVP experiments compounds were sublimed through an unpacked 300 × 20 mm (i.d.) horizontal quartz tube heated by a conventional high-temperature tube furnace (heating

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zone 250 mm). Products were collected on a cold finger cooled with liquid nitrogen and directly connected to a vacuum line equipped with an oil diffusion pump capable of a vacuum of 10^{-3}–10^{-4} mbar.

5-*tert*-Butyl-4-pivaloyl-2,3-dihydrofuran-2,3-dione (6). Improved Procedure.[18] To a solution of dipivaloylmethane (3.68 g, 20 mmol) in dry diethyl ether (50 mL) containing a catalytic amount of anhydrous $MgCl_2$ (ca. 10 mg) was added freshly distilled oxalyl chloride (2.67 g, 1.84 mL, 20.5 mmol) dropwise under intensive stirring within 2 h ($CaCl_2$ tube). Then the mixture was stirred for an additional hour and filtered, and the solvent was removed on a rotary evaporator at 20 °C. When the ether was completely evaporated, the bath temperature was raised to 50 °C whereupon the yellow oily residue crystallized. The crude product was digested with cold hexane and filtered to give 3.90 g (82%) of **6**. The material obtained was sufficiently pure for pyrolysis purposes; an analytical sample may be obtained by crystallization from hexane or by sublimation (50 °C/10^{-1} mbar). **6** is sensitive to moisture and should be stored in a vacuum dessicator over P_4O_{10}: mp 97 °C; IR (KBr) 1835, 1730, 1685, 1600 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 27.8, 28.1, 38.3, 46.6, 121.6 (s, C-4), 154.8 (s, C-2), 179.8 (s, C-3), 191.5 (m, C-5), 208.3 (m, pivaloyl CO) ppm. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.76; H, 7.59.

Dipivaloylketene (8). Furandione **6** (240 mg, 1 mmol) was sublimed at 60 °C into the preparative pyrolysis apparatus (400 °C, 10^{-2} mbar) within the course of 1 h and the product collected on a cold finger at 77 K. After the pyrolysis was completed, the cold finger was allowed to warm until 8, mp 10–12 °C, started to melt. At this point the apparatus was pressurized to 1 atm with dry N_2, and dipivaloylketene was collected in a flask beneath the cold finger. The neat ketene can be stored for several months at −20 °C without any changes in spectroscopic properties. Solutions of **8** in hexane (5%) can be handled for several hours at room temperature under anhydrous conditions without any significant degree of dimerization or hydrolysis. With the apparatus described above up to 3 g of **8** could be obtained in one experiment within 4–5 h. IR and NMR data have been reported earlier.[1d]

2-[3,3-Dimethyl-2-oxo-1-(oxomethylene)butyl]-2,6-di-*tert*-butyl-5-pivaloyl-1,3-dioxin-4(2*H*)-one (7).[1d] A neat sample of **8** was kept in a dry N_2 atmosphere for 48 h at 20 °C or for 16 h at 40 °C. The resulting crystalline product was digested with cold hexane and filtered to give 88% of **7**.

FVP of this material at 400 °C (10^{-3} mbar, sublimation temperature 90 °C) gave dipivaloylketene (**8**) in 90% yield.

6-*tert*-Butyl-2-(dipivaloylmethylene)-5-pivaloyl-1,3-dioxin-4(2*H*)-one (9). (a) From 8 and DMSO. To a 210 mg (1 mmol) portion of **8** was added 110 mg (1 mmol) of dry DMSO. After the reaction mixture was kept in a sealed flask for 2 h at 20 °C, unreacted DMSO was removed from the crystalline product in vacuum (10^{-3} mbar). IR investigations showed that this crude product (400 mg, 96%) was very pure and uncontaminated with isomeric **7**. An analytical sample was obtained by recrystallization from hexane, mp 144 °C.

(b) From 8 and Tributylphosphine Oxide. To 210 mg (1 mmol) of **8** was added 220 mg (1 mmol) of phosphine oxide. After the reaction mixture was kept in a sealed flask for 2 h at 20 °C, hexane (5 mL) was added to dissolve the phosphine oxide. The remaining solid was filtered and washed with hexane to give 365 mg (87%) of **9**.

(c) From 8 and pyridine: analogously to procedure a, yield 87%, reaction time 5 min; mp 144 °C; IR (KBr) 1765, 1705, 1690, 1625, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (s, 18 H, 2 *t*-Bu), 1.23, and 1.26 (2 s, 9 H each, 2 *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 26.9, 27.1, 28.5, 28.6, 38.3, 45.7, 46.5, 46.7, 107.2 and 109.2 (2 s, exocyclic =C and C-5), 148.8 (s, C-2), 154.4 (s, C-4), 173.5 (m, C-6), 203.8, 204.1, and 207.5 (3 m, 3 pivaloyl CO) ppm; EIMS *m/z* (rel intensity) 420 (M^+, 0.5), 405 (1), 363 (11), 295 (13), 211 (77), 154 (35), 126 (21), 111 (31), 85 (65), 57 (100). Anal. Calcd for $C_{24}H_{36}O_6$: C, 68.64; H, 8.63. Found: C, 68.71; H, 8.48.

FVP of this material at 400 °C (10^{-3} mbar, sublimation temperature 125 °C) gave dipivaloylketene (**8**) in 90% yield.

6-*tert*-Butyl-3,3-diphenyl-5-pivaloylpyran-2,4-dione (11a). To 210 mg (1 mmol) of **8** were added 194 mg (1 mmol) of diphenylketene[19] (**10a**) and one crystal of hydroquinone. The reaction mixture was kept at room temperature for 1 day. By treating the oily residue with hexane a colorless solid separated which was recrystallized from hexane to give 310 mg (77%) of **11a**, mp 139–141 °C: IR (KBr) 1770, 1695, 1675, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06, 1.20 (2 s, 9 H each, 2 *t*-Bu), 7.06–7.41 (m, 10 H, Ar-H); ^{13}C NMR ($CDCl_3$) δ 28.5, 38.0, 45.7, 72.4 (C-3), 120.5 (C-5), 128–136 (Ar-C), 168.4, and 170.6 (C-2 and C-6), 192.7 (C-4), 209.8 (pivaloyl CO) ppm. Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.20; H, 6.98. Found: C, 76.99; H, 6.80.

6-*tert*-Butyl-2-(diphenylmethylene)-3-(4-methylphenyl)-5-pivaloyl-1,3-oxazin-4-one (11b). This compound was obtained analogously to **11a** (4 h, 45 °C) using diphenylketene *N*-(4-methylphenyl)imine[20] (**10b**) as dienophile, 82% yield, mp 150–152 °C (hexane): IR (KBr) 1700, 1670, 1635, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01, 1.32 (2 s, 9 H each, 2 *t*-Bu), 2.13 (s, 3 H, Me), 6.72–7.72 (m, 14 H, Ar-H); ^{13}C NMR ($CDCl_3$) δ 23.1, 28.8, 37.3, 46.2, 115.5 (s, C-5), 118.0 (m, $=CPh_2$), 127.0–141.4 (Ar-C), 145.2 (s, C-2), 162.0 (s, C-4), 172.7 (m, C-6), 210.5 (m, pivaloyl CO) ppm. Anal. Calcd for $C_{33}H_{35}NO_3$: C, 80.29; H, 7.15; N, 2.84. Found: C, 80.60; H, 6.94; N, 2.93.

6-*tert*-Butyl-3-isopropyl-2-(isopropylimino)-5-pivaloyl-1,3-oxazin-4-one (13a). (a) To a solution of 210 mg (1 mmol) of **8** in hexane (2 mL) was added 130 mg (1 mmol) of diisopropylcarbodiimide (**12a**) at room temperature. After 1 h the solvent was evaporated, yielding 330 mg (98%) of pure **13a**. An analytical sample was obtained by sublimation at 80 °C (10^{-1} mbar): mp 100–105 °C; IR (KBr) 1700, 1690, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (d, *J* = 6 Hz, 6 H, $CH(CH_3)_2$), 1.22 and 1.27 (2 s, 9 H each, 2 *t*-Bu), 1.41 (d, *J* = 6 Hz, 6 H, $CH(CH_3)_2$), 3.91 and 5.02 (2 hept, *J* = 6 Hz, 1 H each, 2 $CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 17.9, 23.6, 27.8, 36.7, 44.4, 45.2, 45.9, 112.8 (s, C-5), 137.6 (m, C-2), 160.4 (d, *J* = 5 Hz, C-4), 166.0 (m, C-6), 209.8 (m, pivaloyl C=O) ppm. Anal. Calcd for $C_{19}H_{32}N_2O_3$: C, 67.82; H, 9.59; N, 8.33. Found: C, 67.67; H, 9.76; N, 8.32.

(b) From Dimer 9 and 12a. A mixture of 210 mg (0.5 mmol) of **9** and 170 mg (1.4 mmol) of **12a** was kept at 60 °C for 24 h. Excess carbodiimide was removed in vacuo, and the resulting crude product was treated with ice-cold hexane to yield 260 mg (78%) of **13a** (mp, IR).

2,8-Di-*tert*-butyl-5,11-diisopropyl-3,9-dipivaloyl-1,7-dioxa-5,11-diazaspiro[5.5]undeca-2,8-diene-4,10-dione (14a). To 420 mg (2 mmol) of **8** was added 130 mg (1 mmol) of diisopropylcarbodiimide (**12a**). After the strongly exothermic reaction ceased, the resulting solid was treated with hexane and then removed by filtration. Recrystallization from toluene gave 450 mg (82%) of **14a**: mp 200–202 °C; IR (KBr) 1700, 1660, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 and 1.28 (2 s, 18 H each, 4 *t*-Bu), 1.47 and 1.56 (2 d, *J* = 6 Hz, 6 H each, 2 $CH(CH_3)_2$), 3.82 (hept, *J* = 6 Hz, 2 H, 2 $CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 19.0, 21.2, 28.8, 29.0, 37.0, 45.3, 50.1, 113.2 (s, C-3, C-9), 115.5 (m, C-6), 162.5 (d, ^3J = 6 Hz, C-4, C-10), 164.2 (m, C-2, C-8), 210.2 (m, 2 pivaloyl CO) ppm; EIMS *m/z* (rel intensity) 546 (M^+, 1), 531 (1), 489 (3), 336 (26), 279 (48), 237 (19), 194 (14), 152 (7), 126 (16), 111 (46), 85 (28), 69 (20), 57 (100). Anal. Calcd for $C_{31}H_{50}N_2O_6$: C, 68.10; H, 9.22; N, 5.12. Found: C, 68.39; H, 8.94; N, 5.01.

2,8-Di-*tert*-butyl-5,11-dimethyl-3,9-dipivaloyl-1,7-dioxa-5,11-diazaspiro[5.5]undeca-2,8-diene-4,10-dione (14b). This compound was obtained analogously to **14a** using dimethylcarbodiimide[21] (**12b**) as dienophile (76%): mp 182–186 °C; IR (KBr) 1695, 1665, 1620 cm^{-1}; ^1H NMR (a) in $CDCl_3$ δ 1.16 and 1.29 (2 s, 18 H each, 4 *t*-Bu), 2.97 (s, 6 H, 2 CH_3); (b) with Eu[hfc]$_3$ δ 1.49 and 1.52 (2 s, 18 H, 2 *t*-Bu), 1.68 and 1.72 (2 s, 18 H, 2 *t*-Bu), 3.51 and 3.67 (2 s, 6 H, 2 Me) ppm. Anal. Calcd for $C_{27}H_{42}N_2O_6$: C, 66.10; H, 8.63; H, 5.71. Found: C, 66.11; H, 8.69; N, 5.72.

Reaction of Dipivaloylketene (8) with Carbodiimide 12c. 6-*tert*-Butyl-3-isopropyl-2-(phenylimino)-5-pivaloyl-1,3-oxazin-4-one (13c) and 2,8-Di-*tert*-butyl-5-isopropyl-11-phenyl-3,9-dipivaloyl-1,7-dioxa-5,11-diazaspiro[5.5]undeca-

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2,8-diene-4,10-dione (14c). To a solution of 210 mg (1 mmol) of **8** in hexane (2 mL) was added 160 mg (1 mmol) of isopropylphenylcarbodiimide[22] (**12c**). After 2 h at room temperature the precipitated crystals were filtered and recrystallized from hexane to give 130 mg (45% based on **8**) of **14c**, mp 156–158 °C. Evaporation of the mother liquor and recrystallization of this material from small amounts of hexane gave 180 mg (50%) of **13c**: mp 124–125 °C; IR (KBr) 1710, 1690, 1660, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 and 1.29 (2 s, 9 H each, 2 *t*-Bu), 1.57 (d, J = 6 Hz, $CH(CH_3)_2$), 5.19 (hept, J = 6 Hz, $CH(CH_3)_2$), 6.92–7.36 (m, 5 H, Ar-H); ^{13}C NMR ($CDCl_3$) δ 18.3, 28.4, 37.4, 45.3, 47.8, 114.1 (s, C-5), 122.5, 123.1, 128.5 (all Ar-C), 140.6 (d, ^3J = 5.6 Hz, C-2), 145.2 (m, quart, Ar-C), 160.8 (d, ^3J = 5 Hz, C-4), 166.9 (m, C-6), 209.9 (m, pivaloyl CO) ppm. Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71.32; H, 8.16; N, 7.56. Found: C, 71.49; H, 8.05; N, 7.33.

14c: IR (KBr) 1700, 1660, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) 0.51 and 1.42 (2 d, J = 6 Hz, 6 H, $CH(CH_3)_2$), 1.26–1.30 (m, 36 H, 4 *t*-Bu), 3.71 (hept, J = 6 Hz, 1 H, $CH(CH_3)_2$), 7.21–7.44 (m, 5 H, Ph) ppm. Anal. Calcd for $C_{37}H_{48}N_2O_6$: C, 70.32; H, 8.33; N, 4.82. Found: C, 70.49; H, 8.29; N, 4.81.

Treatment of a solution of **13c** in hexane with an equimolar amount of **8** afforded **14c** in 92% yield.

2-[1-Isopropyl-4-(isopropylimino)-2-oxo-3-pivaloylazetidin-3-yl]-2,6-di-*tert*-butyl-5-pivaloyl-1,3-dioxin-4(2*H*)-one (15a). A mixture of 420 mg (1 mmol) of ketene **7** and 200 mg (1.6 mmol) of diisopropylcarbodiimide (**12a**) was kept at 60 °C for 48 h and then 16 h at room temperature. The resulting solid was treated with hexane and filtered to yield 315 mg (58%) of **15a**, mp 150–152 °C (hexane). Evaporation of the hexane solution and sublimation of the resulting material at 80 °C (10^{-1} mbar) gave 130 mg (24% based on **12a**) of **13a**, identified by comparison of mp and IR with authentic material prepared from **8** and **12a**.

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15a: IR (KBr) 1820, 1730, 1705, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90–1.50 (complex m, 48 H, 4 *t*-Bu, 2 $CH(CH_3)_2$), 4.06 and 4.44 (2 m, 2 H, $CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 19.5–50.0 (aliphatic C), 83.4/83.5 (C-3'), 105.1/105.9 (C-2), 111.4/111.8 (C-5), 140.3/140.4 (C-4'), 156.9/157.5 (C-2'), 163.4/164.6 (C-4), 174.2/174.3 (C-6), 202.9/203.1 and 210.1/210.2 (2 pivaloyl CO) ppm. Anal. Calcd for $C_{31}H_{50}N_2O_6$: C, 68.10; H, 9.22; H, 5.12. Found: C, 68.06; H, 9.16; N, 5.12.

2-[1-Methyl-4-(methylimino)-2-oxo-3-pivaloylazetidin-3-yl]-2,6-di-*tert*-butyl-5-pivaloyl-1,3-dioxin-4(2*H*)-one (15b). Ketene **7** was dissolved in an excess of dimethylcarbodiimide[21] (**12b**) (molar ratio 1:5). After 8 h at 20 °C the oily residue was diluted with hexane, precipitating a colorless solid which was recrystallized from hexane to give 370 mg (76%) **15b**: mp 144–145 °C; IR (KBr) 1820, 1720, 1710, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.30 (m, 36 H, 4 *t*-Bu), 2.92 and 3.21 (2 s, 3 H, C=NMe), 3.30 and 3.38 (2 s, 3 H, ring NMe) ppm, assignments based on a ^1H,^{13}C HMQC experiment. Anal. Calcd for $C_{27}H_{42}N_2O_6$: C, 66.10; H, 8.63; H, 5.71. Found: C, 65.91; H, 8.68; N, 5.77.

FVP of 15a. **15a** (100 mg, 0.2 mmol) was gently sublimed at 120 °C and pyrolyzed at 400 °C (10^{-3} mbar). After the pyrolysis was completed (ca. 2 h), the cold finger was allowed to warm to ca. −40 °C, and at this point the apparatus was pressurized to 1 atm with dry N_2. After the cold finger had reached ambient temperature, the crystalline product, **14a**, was collected in 84% yield (mp, IR).

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Supplementary Material Available: X-ray crystallographic data for **9** and **15a** (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

N-(8-Quinolyl)-*N'*-(2-pyridylmethyl)malonamide Derivatives as a Novel Cu(II) Carrier with High Efficiency and Selectivity for Proton-Driven Uphill Transport through Liquid Membranes

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Several N,N'-disubstituted malonamide derivatives have been designed as a carrier for ion transport. Their ability to transport transition-metal ions through liquid membranes has been investigated. It has been found that *N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide derivatives can transport Cu(II) with high efficiency and selectivity against its concentration gradient from nearly a neutral aqueous phase (pH 6.2) to an acidic aqueous phase through a chloroform liquid membrane.

Introduction

Selective transport of transition-metal ions as well as alkali and alkaline earth metal ions through liquid membranes, i.e, carrier-mediated continuous solvent extraction, has become increasingly important and noteworthy as an attractive method for the separation, recovery, and condensation of available resources.[1] So far, a number of carriers for heavy metal ions have been reported, but few can transport them selectively and efficiently.[2-6] In the solvent extraction, transition-metal ions can be usually separated with extractants by varying the acidic pH range in the aqueous phase, but the ion-selectivity could not be expected near the neutral pH range. It might be important to realize the highly selective and efficient separation under the mild conditions.

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