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Bis(ketenyl)benzenes: preparation, observation, and reaction with tetramethylpiperidin-1-yloxyl

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1,2- and 1,3-Bis(ketenyl)benzenes formed by double dehydrochlorination and by double Wolff rearrangement, respectively, gave ketenyl IR absorption at 2115, and 2122, and 2116 cm^{-1}, respectively. Reaction of these bisketenes with the aminoxyl radical tetramethylpiperidin-1-yloxyl (TEMPO) gave the corresponding tetraadducts as mixtures of *meso*- and *d,l*-isomers. The kinetics of the reaction of 1,3-bis(ketenyl)benzene with TEMPO gave a rate constant comparable to that of the monoketene PhCH=C=O. The reactions proceed by the initial attack of TEMPO on the carbonyl carbon of one ketenyl group followed by fast capture of the intermediate radical by a second TEMPO, and then reaction of the remaining ketene.

Key words: ketenes, diazoketones, Wolff rearrangement, nitroxyl radical TEMPO.

Diphenyketene ($Ph_2C=C=O$) prepared[1] from the reaction of $Ph_2CClCOCl$ with zinc (Scheme 1) was the first ketene to be isolated and characterized. This was followed by the preparation of the isolable fluorenylideneketene by the same route.[2] However, when PhCH=C=O (**1**) was prepared by this method[3] the ketene could not be isolated, although there was evidence for its presence in solution from trapping reactions. The difficulty in isolation of ketene **1** is due to its tendency for dimerization and its reactivity toward water and other nucleophiles.

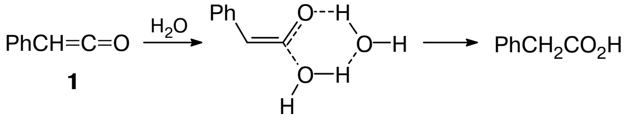
Scheme 1

$$Ph_2CClCOCl \xrightarrow{Zn} Ph_2C=C=O$$

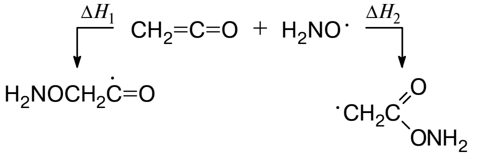
Later[4—8] the technique of flash photolysis was applied to the preparation of ketene **1**, allowing direct observation by fast UV spectroscopy[5,6] and time-resolved IR spectroscopy.[7] Kinetic studies of the reactivity of compound **1** with water and with amines showed this ketene was highly reactive, with a rate constant for reaction with H_2O greater than that for $CH_2=C=O$ by a factor of 100.[5,6] This rate effect is attributed to delocalization of charge by the phenyl group in the transition state for hydration (Scheme 2).[8]

Recently[9—14] we have undertaken the study of radical reactions of ketenes, and predicted on the basis of B3LYP/6-31G* calculations that the reaction of $CH_2=C=O$ at the α-carbon would be exothermic ($\Delta H_2 = -18.7$ kcal mol^{-1}) (Scheme 3).[10]

Scheme 2

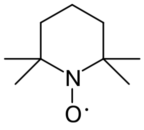


Scheme 3



$\Delta H_1 = 7.5$ kcal mol^{-1}
$\Delta H_2 = -18.7$ kcal mol^{-1}

This prediction was confirmed experimentally by the discovery that ketenes such as **1** undergo facile reaction with the aminoxyl radical tetramethylpiperidin-1-yloxyl (TEMPO, TO$^\cdot$) forming 1,2-bis(addition) products (Scheme 4), or in some cases products resulting from allylic rearrangements, cyclizations, or free radical rearrangements.[10—14] These reactions were all interpreted as involving rate limiting attack of TEMPO on the carbonyl carbon as shown in Scheme 4, and in the case of ketene **1** this was



TEMPO (TO$^\cdot$)

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followed by fast capture of the resulting radical by a second TEMPO.[11,12]

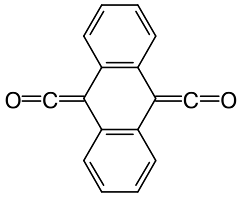
Scheme 4

$$PhCH{=}C{=}O \xrightarrow{TO^{\cdot}} Ph\dot{C}HCO_2T \xrightarrow{TO^{\cdot}} PhCH(OT)CO_2T$$

1

Our study of ketene **1** was greatly facilitated by the discovery that this and other reactive ketenes could be prepared by Wolff rearrangements in dilute solutions in hydrocarbon solvents as relatively long-lived species at room temperature, and their presence could be established using conventional IR spectroscopy. Thus ketene **1** was identified[11,12] by its IR band at 2117 cm^{-1}, in good agreement with the value found by TRIR studies.[7]

The preparation of bisketenes[15] has been a major goal of chemical research since first reports[16] on systematic efforts to prepare α,ω-bisketenes of the type $O{=}C{=}CH(CH_2)_nCH{=}C{=}O$ beginning with the first term of the series $(CH{=}C{=}O)_2$ for $n = 0$, which may be termed a 1,2-bisketene. These species have been of great interest because of their potential as precursors for polyester and polyamide preparation, but although carbon suboxide ($O{=}C{=}C{=}C{=}O$) was reported previously,[17,18] efforts to prepare α,ω-bisketenes of the type indicated above as observable intermediates have been unsuccessful.[8,15] Bisketenes of the aromatic series have been examined,[19] including that of the type **A**,[20] which can be isolated and is the most highly studied aryl bisketene.



A

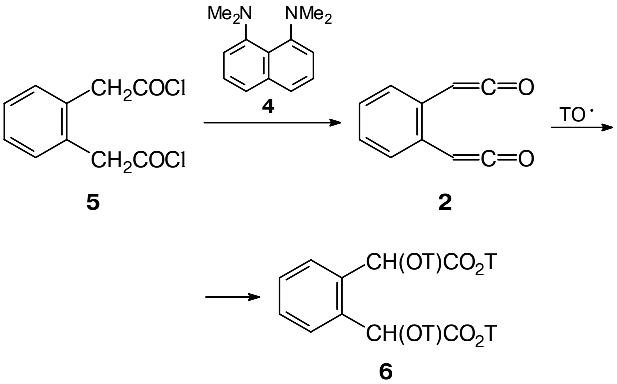
Our successful preparation of the highly reactive aldoketene **1** as an observable intermediate in solution encouraged us to believe that the replacement of more than one ketenyl group on an aromatic scaffold might be possible, and this goal has now been reached. We report the successful preparation, observation, and study of 1,2- and 1,3-bis(ketenyl)benzenes (**2**, **3**). The keys to this success are the use of dilute solutions and moderate temperatures to prevent dimerization reactions, and dry hydrocarbon solvents to prevent reaction with water.

Results and Discussion

Dehydrochlorination by a known procedure[21] with 1,8-bis(dimethylamino)naphthalene (**4**) has been used for bisketene **2**, and compound **3** has been prepared by the classical Wolff rearrangement, as we have recently demonstrated for monoketenes.[11–13]

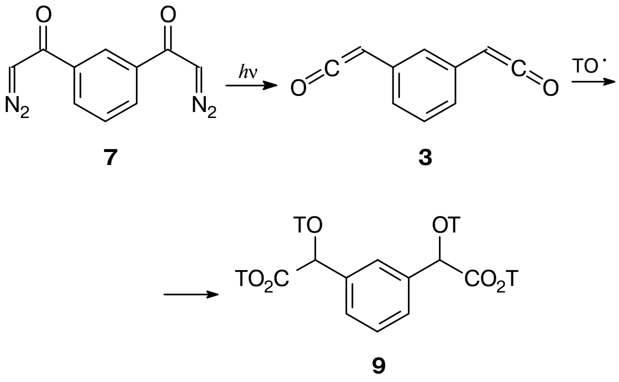
Reaction of the bis(acyl chloride) **5**[22] with amine **4** and Et_3N in toluene at −78 °C gave immediate formation of an IR band at 2115 cm^{-1} indicative of formation of bisketene **2**. The successive addition of TEMPO gave the tetraadduct **6** (23%), as a 2 : 1 mixture of *meso*- and *d*,*l*-isomers that were not differentiated (Scheme 5). The rapid formation of the ketene IR band, and the capture of the intermediate as **6**, are strong evidence for the intermediacy of bisketene **2**.

Scheme 5



Photolysis with 350-nm light of a $7 \cdot 10^{-5}$ *M* solution in isooctane of the bis(diazoketone) **7**[23,24] derived from isophthalic acid resulted in the disappearance of the IR absorption of diazoketone **7** at 2110 cm^{-1} and the appearance of a pair of bands at 2122 and 2116 cm^{-1} (rel. intensity 43 : 57) ascribed to bisketene **3**. Addition of Bu^nNH_2 to the preformed **3** gave bisamide **8** described previously.[25,26] Addition of TEMPO to a solution of **3** gave after chromatography adduct **9** (68%), as a 55 : 45 mixture of *meso*- and *d*,*l*-isomers that were not differentiated (Scheme 6). The complete conversion of

Scheme 6



the IR absorption of the bands of diazoketone **7** to ketenyl bands, and the capture of the intermediate with both Bu^nNH_2 and with TEMPO are convincing evidence for the formation of **3**.

The kinetics of this reaction (see Scheme 6) were monitored as previously,[11—13] and gave single exponential decay and a derived value of the rate constant (k_2) of 2.44 L mol^{-1} s^{-1}, which is comparable to a value for PhCH=C=O (1.26 L mol^{-1} s^{-1}).[10,11] This result indicates that bisketene **3** reacts with TEMPO by initial reaction on one ketenyl moiety followed by reaction of the second ketene with a rate constant either similar to or faster than the first.

In summary the highly reactive bis(ketenyl)benzenes **2** and **3** have been prepared as observable and relatively long lived intermediates for the first time, and utilized in synthetic and mechanistic investigations. The way is now open for the preparation of further examples, and for the exploitation of their multifunctional reactivity.

Experimental

Reactions were carried out under an atmosphere of argon or nitrogen. ^{1}H NMR spectra were obtained at 200 MHz (Varian Gemini), 300 MHz (Varian Mercury), and 400 MHz (Varian Unity). ^{13}C NMR spectra were obtained on a Varian Unity instrument (100 MHz). IR spectra were obtained on a Perkin—Elmer FT-IR Spectrum 1000 spectrum. Bis(acyl chloride) **5** was synthesized[22] from 1,2-benzenediacetic acid (Aldrich) by reaction with $SOCl_2$ and purified by sublimation. Bis(diazo ketone) **7** (^{1}H NMR ($CDCl_3$), δ: 5.98 (s, 2 H); 7.50—7.56 (m, 1 H); 7.92—7.96 (m, 2 H); 8.13—8.16 (m, 1 H)) was obtained[23,24] from bis(acyl chloride) of isophthalic acid (Aldrich). Commercial 1,8-bis(dimethylamino)naphthalene (Aldrich) was used. Photolyses were conducted using a Rayonet photoreactor. Chromatography was carried out on SiO_2 (Aldrich).

1,2-Bis(ketenyl)benzene (2) and its reaction with TEMPO. To chloride **5** (100 mg, 0.4 mmol) in toluene (3 mL) at −78 °C was added amine **4** (195 mg, 0.90 mmol) in toluene (2 mL), and then Et_3N (10 μL) was added. There was immediate formation of a yellow color and precipitation of the hydrochloride salt of **4**, and generation of a ketene IR band at 2115 cm^{-1}. TEMPO (277 mg, 177 mmol) in toluene (2 mL) was added, and the solution was stirred for ~15 h at ~20 °C, filtered, and evaporated. Aqueous 1 *N* HCl was added to the residue, and the mixture was extracted with ether. The organic layer was dried, concentrated, and chromatographed (eluent EtOAc—hexane, 1 : 3) to give tetraadduct **6** (78 mg, 23%) as a 2 : 1 mixture of the *meso*- and *d*,*l*-isomers (not differentiated). ^{1}H NMR ($CDCl_3$), δ: 0.6—1.6 (m, 72 H); 5.88 (s, CHOT, minor isomer); 6.00 (s, CHOT, major isomer); 7.3—8.0 (m, 4 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 16.8, 16.9, 17.0, 20.1, 20.4, 20.5, 20.6, 21.2, 31.5, 31.8, 33.2, 34.0, 39.2, 39.3, 39.5, 40.1, 40.2, 40.8, 60.0, 60.3, 60.5, 76.9, 77.2, 77.5, 82.2, 83.8, 127.4, 128.1, 128.9, 129.7, 135.9, 136.3, 169.0, 169.7. IR ($CDCl_3$), ν/cm^{-1}: 1771, 1757. MS (EI), *m*/*z* (I_{rel} (%)): 642 $[M - T]^+$ (0.6), 156 (80), 140 (100). HRMS (EI), found: *m*/*z* 642.4492. $C_{37}H_{60}N_3O_6$. Calculated: M = 642.4482.

1,3-Bis(ketenyl)benzene (3) and its reactions with Bu^nNH_2 and TEMPO. Bis(diazo ketone) **7** [23,24] (6 mg, 0.026 mmol) in hexane (380 mL) was irradiated for 5 min with λ = 300 and 350 nm light. Then Bu^nNH_2 (5.1 mmol) was added, and the solvent was evaporated. The known[25,26] *N*,*N′*-dibutylbenzene-1,3-bisacetamide (**8**) (m.p. 144—145 °C) was isolated in 26% yield upon chromatography eluting first with ether—$CHCl_3$, 1 : 1 and then with MeOH—$CHCl_3$, 1 : 9. ^{1}H NMR ($CDCl_3$), δ: 0.88 (t, 6 H); 1.22—1.32 (m, 4 H); 1.37—1.47 (m, 4 H); 3.17—3.25 (m, 4 H); 3.54 (s, 4 H); 5.40 (br.s, 2 H); 7.2—7.4 (m, 4 H). ^{13}C NMR ($CDCl_3$), δ: 13.7, 20.0, 31.6, 39.5, 43.7, 128.3, 129.5, 130.5, 135.8, 170.5. IR ($CDCl_3$), ν/cm^{-1}: 1662. MS (EI), *m*/*z* (I_{rel} (%)): 304 $[M]^+$ (12), 232 (12), 205 (100). HRMS (EI), found: *m*/*z* 304.2153. $C_{18}H_{28}N_2O_2$. Calculated: M = 304.2151. Similar irradiation of a 0.07 m*M* solution of **7** in isooctane for 8 min resulted in the disappearance of the IR absorption of **7** at 2110 cm^{-1} and the appearance of bands at 2122 and 2116 cm^{-1}, which disappeared upon the addition of Bu^nNH_2.

A solution of diazoketone **7** (6 mg, 0.026 mmol) in hexane (370 mL) was irradiated for 5 min with λ = 300 and 350 nm light, and TEMPO (50 mg, 0.32 mmol) in hexane (0.05 mL) was added. After 12 h the solvent was evaporated and the residue chromatographed successively with CH_2Cl_2, ether, and MeOH. In the MeOH fraction was found adduct **9** (14 mg, 68%) as a clear liquid which on addition of MeOH crystallized, m.p. 183—186 °C (*meso*- and *d*,*l*-isomers in a ratio of 59 : 41, not separated). ^{1}H NMR ($CDCl_3$), δ: 0.4—1.7 (m, 72 H); 5.25 (s, CHOT, major isomer); 5.27 (s, CHOT, minor isomer); 7.3—7.7 (m, 4 H). ^{13}C NMR ($CDCl_3$), δ: 16.6, 16.8, 19.6, 20.6, 31.3, 32.0, 33.3, 34.6, 39.1, 40.1, 59.2, 60.4, 87.3, 87.7, 126.0, 127.1, 127.2, 127.5, 127.7, 138.9, 139.1, 170.2, 170.25. IR ($CDCl_3$), ν/cm^{-1}: 1774, 1751 (sh). MS (EI), *m*/*z* (I_{rel} (%)): 626 $[M - TO]^+$ (0.5), 156 $[TO]^+$ (65), 69 (100). HRMS, found: *m*/*z* 626.4550. $C_{37}H_{60}N_3O_5$. Calculated: M = 626.4533. MS (electrospray), *m*/*z*: 783.5 $[MH]^+$.

Kinetics of the reaction of bisketene 3 with TEMPO. Ketene solutions ($2 \cdot 10^{-6}$ *M*) in isooctane from irradiation of diazoketene **7** were reacted with $(1.6—8.0) \cdot 10^{-4}$ *M* TEMPO solutions and the decrease in the concentration of **3** at λ = 244 nm was monitored. The k_2 rate constant (L mol^{-1} s^{-1}) was derived from a plot of k_{obs} (s^{-1}) *vs.* [TEMPO] (mol L^{-1}) described by the equation

$$k_{obs} = (2.44\pm0.22)\cdot[\text{TEMPO}] + (7.59\pm1.21)\cdot10^{-4}$$

(dimensionality of the last term of the equation is s^{-1}).

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