The First Synthesis of Thermally Stable Acylamino-substituted 1,2-Dioxetanes

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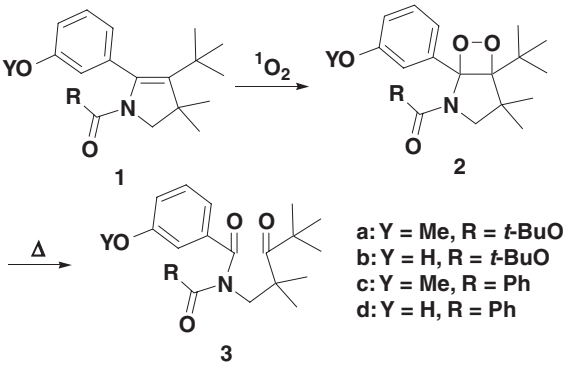
(Received May 10, 2006; CL-060557; E-mail: matsumo-chem@kanagawa-u.ac.jp)

Singlet oxygen added smoothly to *N*-acyl-5-aryl-4-*tert*-butyl-3,3-dimethyl-2,3-dihydropyrroles **1** to give the corresponding bicyclic dioxetanes fused with *N*-acylpyrrolidine **2**, which possessed marked thermal stability.

Enol ethers undergo 1,2-cycloaddition of singlet oxygen to give oxy-substituted dioxetanes, the thermal stability of which ranges in half-life from shorter than a second to more than a hundred years at room temperature.[1–3] On the other hand, there has been little known of amino-substituted dioxetanes stable enough to be isolated at room temperature, though singlet oxygen adds also easily to the enamine precursors.[1–5] In the course of our investigation of novel chemiluminescent compounds, we found that singlet oxygen added smoothly to *N*-acyl-5-aryl-4-*tert*-butyl-3,3-dimethyl-2,3-dihydropyrroles **1** to give the corresponding acylamino-substituted dioxetanes **2**, which possess marked thermal stability.

When *N*-(*t*-butoxycarbonyl)dihydropyrrole **1a** (200 mg) was irradiated together with a catalytic amount of tetraphenylporphin (TPP) in CH_2Cl_2 (10 mL) with Na-lamp under O_2 atmosphere at 0 °C for 1 h, dioxetane fused with pyrrolidine ring **2a** was produced exclusively (Scheme 1). Chromatographic purification of the photolysate gave pure **2a** as colorless plates (mp 133.5–134.0 °C, from CH_2Cl_2–hexane), the structure of which was determined by ^{1}H NMR, ^{13}C NMR, IR, Ms (EI), and HRMs (ESI) spectral analysis.[6] Furthermore, X-ray single crystallographic analysis of **2a** was successfully attained as illustrated in Figure 1.[7] Dihydropyrrole-analogs **1b**–**1d** were similarly dioxygenated with singlet oxygen to afford the corresponding bicyclic dioxetanes **2b**–**2d** in high isolated yields.

The dioxetanes **2a**–**2d** decomposed into the corresponding keto imides **3a**–**3d** quantitatively by first-order kinetics in *p*-xylene-d_{10} at 90, 100, and 110 °C. Their thermodynamic parameters, namely, activation enthalpy ($\Delta H_0^{\ddagger}$), activation entropy ($\Delta S_0^{\ddagger}$), activation free energy ($\Delta G_0^{\ddagger}$), and half-life ($t_{1/2}$) at 25 °C, were estimated from Arrhenius plots. The results are summarized in Table 1 together with activation parameters for thermolysis of related dioxetane **4** fused with a tetrahydrofuran ring (Scheme 2).[8] Table 1 shows that acylamino-substituted dioxetanes **2a**–**2d** possess marked thermal stability ($t_{1/2} > 20$ y at 25 °C), and that they and their oxy-analog **4** belong to the class of dioxetanes with the highest thermal stability among hundreds of dioxetanes hitherto known.[1–3] Considering that *N*-*t*-butoxycarbonyl (*N*-*t*-Boc) analogs **2a** and **2b** are more stable thermally than *N*-benzoyl analogs **2c** and **2d**, it is presumed that the unusual thermal stability of **2** is attributed mainly to the effect of an annelated five-membered ring, which prevents the dioxetane ring from cleaving through distortion; an electron-withdrawing acyl group on a nitrogen should contribute also to the stabilization of dioxetanes **2**.



Scheme 1.

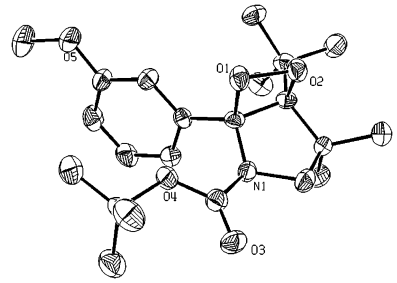
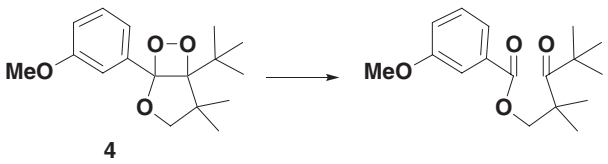


Figure 1. ORTEP view of dioxetane **2a**.

Table 1. Thermodynamic parameters for thermal decomposition of acylamino-substituted dioxetanes **2a**–**2d** in *p*-xylene-d_{10}[a]

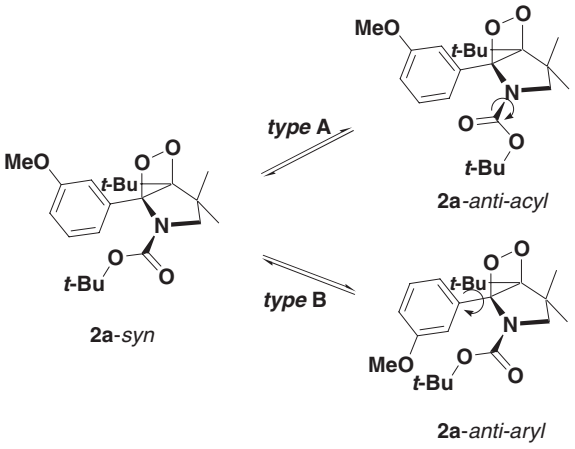
Dioxetane	$\Delta H_0^{\ddagger}$ /kJ mol^{-1}	$\Delta S_0^{\ddagger}$ /J K^{-1} mol^{-1}	$\Delta G_0^{\ddagger}$ /kJ mol^{-1}	$t_{1/2}$ at 25 °C/y
2a	132	17.6	127	51.5
2b	124	−5.0	126	33.7
2c	122	−7.5	124	21.7
2d	123	−5.0	125	27.8
4	124	−4.2	125	49.8

[a]Time course of thermal decomposition of dioxetanes **2a**–**2d** was monitored by the use of ^{1}H NMR.

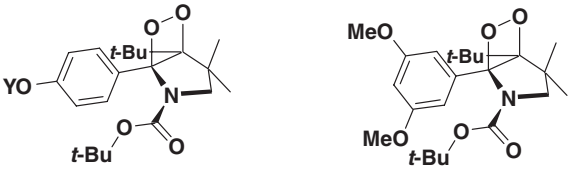


Scheme 2.

It should be noted here that dioxetanes **2a**–**2d** exist as a mixture of two conformers (40:60–45:55) in a solution, based on the ^{1}H NMR analysis. Crystalline **2a** used for the X-ray single crystallographic analysis displayed ^{1}H NMR spectrum of con-



Scheme 3.



Scheme 4.

formers similarly to the case mentioned above. Thus, dioxetanes **2** exist as an equilibrium mixture of conformers in the solution. There was little change in the ratio of two conformers through thermolysis in *p*-xylene-d_{10}, so that the isomerization between the conformers should occur easily. If one of the conformers for **2a** possesses the structure **2a**-*syn* like the ORTEP view in Figure 1, two types of conformational isomerism are possible; one (type **A**) occurs around the axis joining *t*-Boc carbonyl to nitrogen to give conformers **2a**-*syn* and **2a**-*anti-acyl*, whereas the other (type **B**) occurs around the axis joining 3-methoxyphenyl to a dioxetane carbon to afford conformers **2a**-*syn* and **2a**-*anti-aryl* (Scheme 3).

Bicyclic dioxetanes bearing a 4-methoxyphenyl **5a**, 4-hydroxyphenyl **5b**, or 3,5-dimethoxyphenyl **6** can not exhibit the isomerism due to the rotation of the aromatic ring like the one between **2a**-*syn* and **2a**-*anti-aryl* (Scheme 4). Thus, dioxetanes **5a**, **5b**, and **6** were synthesized similarly to the case of **2a**–**2d**: **5a** and **5b** were less stable thermally than **2a**–**2d**,[9] though their stability was enough to permit handling at room temperature. The ^{1}H NMR spectra of **5a**, **5b**, and **6** exhibited that they existed as one observable conformer but not as a mixture of isomers. This result suggests strongly that the rotation of the 3-oxyphenyl group causes the isomerism between **2**-*syn* and **2**-*anti-aryl,* but not between **2**-*syn* and **2**-*anti-acyl*.

We should point out finally that acylamino-substituted dioxetanes, **2b** and **2d**, underwent intramolecular charge-transfer-induced chemiluminescent decomposition (CTICL),[10] on treatment with tetrabutylammonium fluoride in DMSO, to give light with maximum wavelength at 571 and 600 nm, respectively.

References and Notes

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6 Selected data for **2a**: ^{1}H NMR (400 MHz, as a mixture of 57:43 conformational isomers in $CDCl_3$) δ_H 1.00 (s, 9H), 1.05 (s, 9H × 0.57), 1.06 (s, 9H × 0.43), 1.12 (s, 3H), 1.40 (s, 3H × 0.57), 1.40 (s, 3H × 0.43), 3.62 (d, J = 10.0 Hz, 1H), 3.78 (s, 3H × 0.43), 3.83 (s, 3H × 0.57), 4.06 (d, J = 10.0 Hz, 1H), 6.82–6.94 (m, 2H), 7.18–7.32 (m, 2H); ^{13}C NMR (125 Hz, as a mixture of 57:43 conformational isomers in $CDCl_3$) δ_C 20.6 and 20.6, 25.7 and 25.8, 27.2 and 27.3, 27.6 and 27.7, 37.8 and 37.8, 43.0, 55.3, 62.8, 80.6 and 80.7, 104.5 and 104.6, 106.1 and 106.1, 113.0 and 113.7, 113.8 and 114.5, 119.7 and 121.4, 128.4 and 128.6, 139.4 and 139.5, 154.3, 159.0 and 159.1; Ms (EI, m/z, %) 391 (M^+, 0.3), 359 (0.4), 234 (46), 206 (15), 135 (100); HRMs (ESI, m/z) found 414.2223, calcd for $C_{22}H_{33}NO_5Na$ [M^+ + Na] 414.2256.

7 Crystal data for compound **2a**: $C_{22}H_{33}NO_5$: M_r 391.51, colorless platelet, 0.30 × 0.20 × 0.10 mm^3, orthorhombic, space group $Pca2_1$ (#29), a = 21.23(2), b = 9.11(2), c = 11.208(9) Å, V = 2168.9(46) Å^3, Z = 4, D_{calcd} = 1.199 g cm^{-3}, T = 173 K, $2\theta_{max}$ = 54.9°, $F(000)$ = 848.00, reflections collected/unique 23043/4914 (R_{int} = 0.048), μ(Mo Kα) = 0.84 cm^{-1}. An empirical absorption correction was applied which resulted in transmission factors ranging from 0.8694–1.0000. The data were corrected for Lorentz and polarization effects. Final R indices $R1$ = 0.057 [$I > 2\sigma(I)$], wR_2 = 0.145 (all data), GOF on F^2 = 1.000, and residual electron density 0.42/−0.46 e Å^{-3} CCDC-297571 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2, 1EZ, UK; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

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Published on the web (Advance View) July 1, 2006; doi:10.1246/cl.2006.882