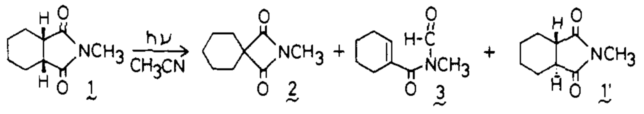
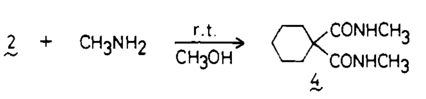
Azetidine-2,4-diones via Photoinduced Ring Contraction of Succinimides

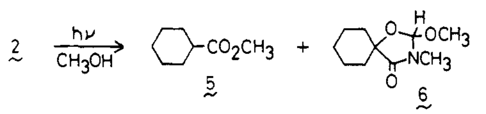
Sir:

In recent years the photochemistry of alicyclic imides has received considerable attention. Chiefly, the formation of oxetanes with olefins,[1] hydrogen abstraction,[2] and α-cleavage reactions[2c,3] have been reported, in which some interesting properties characteristic of imides are disclosed. In this communication we report a photoinduced ring-contraction reaction of 1,3,4-trialkyl-substituted succinimides.

After irradiation of an acetonitrile solution (0.12 M) of *cis-N*-methylcyclohexane-1,2-dicarboximide (**1**) with a 120-W low-pressure Hg lamp for 7 h, chromatography of the products on silica gel gave a ring-contracted product, *N*-methylcyclohexane-1,1-dicarboximide (**2**, 43%), together with a small amount of *N*-formyl-*N*-methyl-1-cyclohexene-1-carboxamide (**3**, 7%) (yields are based on the amount of **1** consumed).[4] The starting material recovered (60%) was partly isomerized to its trans isomer **1′**. The structure of **2** was deduced from its spectroscopic properties: ^{1}H NMR ($CDCl_3$) δ 1.2–2.0 (m, 10 H), 2.89 (s, 3 H); IR (KBr)[5] 1822 (w), 1710 (s), 945 cm^{-1}; *m/e* (rel intensity) 167 (M$^+$, 0.7), 110 (100).[6] When treated with methylamine, **2** gave **4** quantitatively, and further photolysis of **2** in methanol gave **5** (35%) and **6** (60%),[7] the reported characteristics of azetidine-2,4-diones.[3a,5a] The ring-opened imide **3** showed reasonable spectral properties: ^{1}H NMR ($CDCl_3$) δ 1.6–1.9 (m, 4 H), 2.1–2.5 (m, 4 H), 3.15 (s, 3 H), 6.24 (m, 1 H), 9.21 (s, 1 H); IR 1718, 1660 (s) cm^{-1}; *m/e* 167 (M$^+$). It was identical with a sample prepared from 1-cyclohexenecarbonyl chloride and *N*-methylformamide. Similarly, irradiation of succinimide derivatives **7–12** gave the corresponding azetidine-2,4-diones **13–18**, respectively (Table I).[8]







This photoinduced ring-contraction reaction is most reasonably explained in terms of a mechanism shown in Scheme I. First, **1** undergoes α-cleavage reaction to give a biradical **19** followed by two pathways: i.e., (i) reproduction of **1** or isomerization to its trans isomer **1′**, and (ii) formation of **3** via hydrogen abstraction by the carbamoyl radical from C-4 position.[9] The generated compound **3** will absorb light once again to give a 1,4 biradical **20**, which finally could collapse to azetidine-2,4-dione **2**.[10] The following experiments support this mechanism. First, at 254 nm the extinction coefficient of **3** (ε 1023) is about ten times larger than that of **1** (ε 100). Secondly, irradiation of an acetonitrile solution of **3** with a low-pressure Hg lamp gave **2** in 85% yield.[11] Thirdly, following the reaction by high pressure liquid chromatography, we found that the amount of **3** increases initially, but reaches a maximum after 1 h and then decreases gradually. The feature of the time-dependent variation of the products in the reaction mixture is depicted in Figure 1. From Figure 1 we can see that the production rate of **2** rises slightly for the first hour, but then decreases; that is, there is an inflection point at ~1 h from the beginning of the reaction and this point just corresponds to the maximum point for **3**. The fact suggests that **2** could be formed via **3**, though the other possibilities can not be excluded at the present. Since the isomerization of **1** to **2** was quenched by adding 1,3-butadiene to a reacting mixture the α-cleavage reaction seems to proceed only from a triplet excited state.

Scheme I

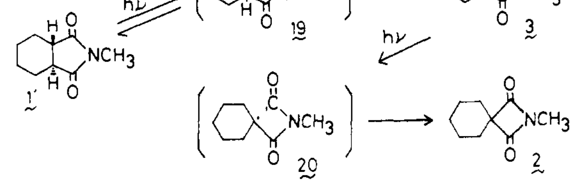
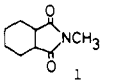
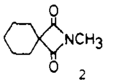
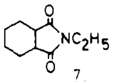
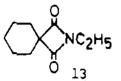
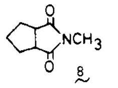
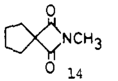
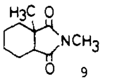
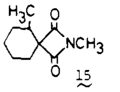
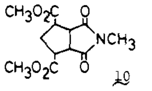
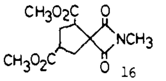
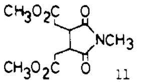
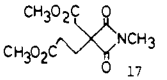
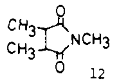
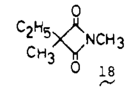
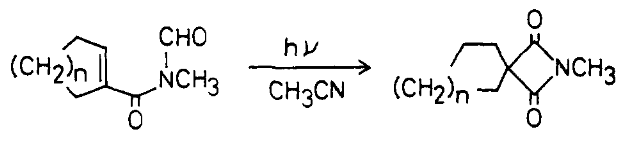


Table I. Yields[a] of Azetidine-2,4-diones from Succinimides

Succinimides	Azetidine-2,4-diones	mp (°C)	Yield (%)
 **1**	 **2**	96–7	43
 **7**	 **13**	62–5	22
 **8**	 **14**	38–42	51
 **9**	 **15**	58–9	26
 **10**	 **16**	99–100	50
 **11**	 **17**	oil	25
 **12**	 **18**	oil	9

[a] Yields are based on the amount of succinimides consumed.

Table II. Yields[a] of **2** or **15** from **3** or **21**



	Material	Product	Yield (%)
n=2	**3**	**2**	85
n=1	**21**	**15**	81

[a] Yields are based on the amount of materials consumed.

In 1914 azetidine-2,4-dione was prepared for the first time by Staudinger and his co-workers,[12] and some other synthetic methods have been investigated.[5,13] It is also known that azetidine-2,4-diones are pharmacologically highly active and that 3,3-dialkyl-substituted derivatives have the especially short

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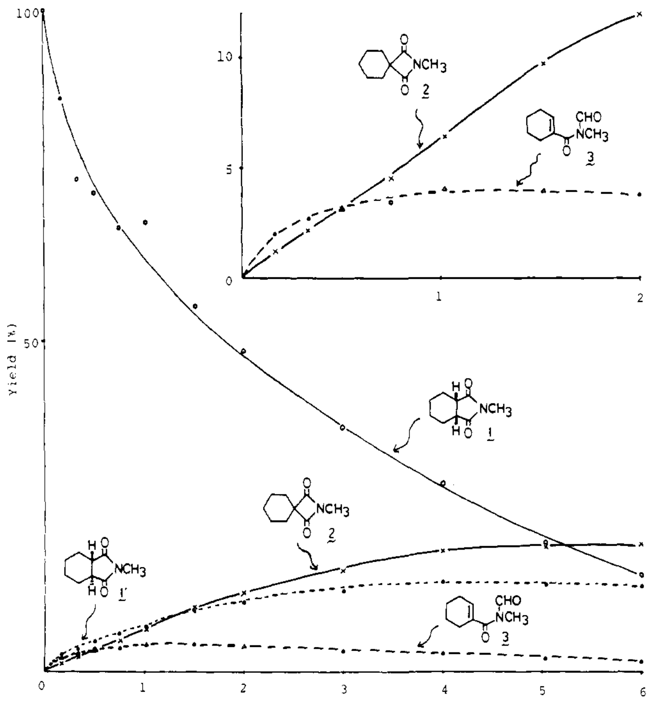

Figure 1. The time dependent variation of products in the reaction followed by LC. An acetonitrile solution (0.06 M) of **1** was irradiated with a 120-W low-pressure Hg lamp at 4 °C.

hypnotic effect.[5a] The previously reported synthetic methods involve sluggish reactions and the yields are generally poor. Since our synthetic approach to azetidine-2,4-diones simply consists of photolysis of the related succinimides which are readily available and the products can be isolated on silica gel column chromatography with ease, this reaction provides a convenient synthetic method of 1,3,3-trialkyl-substituted azetidine-2,4-diones. Further, photolysis of ring-opened imides like **3** or **21** with a low-pressure Hg lamp results in much better yields (Table II). So far the reported photoinduced α-cleavage reactions of acyclic imides[14] and lactams[15] were primarily related to the fission of the C(O)-N bond, and that of the C(O)-C bond was significant in a few exceptional imides.[3] The present example shows the generality and importance of α-cleavage reaction, especially the C(O)-C bond fission of alicyclic imides. Its scope and limitation are being studied.

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(4) Quantum yield of disappearance of **1** was 0.5_9 and that of formation of **3** was 0.3_1 at an early stage.
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(6) This peak (*m/e* 110) can be attributed to the cation radical of carbonylcyclohexane formed by the cycloreversion of **2**. Compernolle, F.; De Schryver, F. C. *J. Am. Chem. Soc.* **1975,** *97*, 3909.
(7) **4**, **5**, and **6**, showed reasonable spectral data.
(8) Characterization data follow. **13**: ^{1}H NMR (CCl_4) δ 1.26 (t, 3 H, *J* = 7 Hz), 1.3–1.9 (m, 10 H), 3.24 (q, 2 H, *J* = 7 Hz); IR (KBr) 1712 (s), 964 cm^{-1}. **14**: ^{1}H NMR ($CDCl_3$) δ 1.8–2.2 (m, 10 H), 2.87 (s, 3 H); IR (KBr) 1840 (w), 1710 (s), 955 cm^{-1}. **15**: ^{1}H NMR (CCl_4) δ 0.96 (d, 3 H, *J* = 6 Hz), 1.1–2.1 (m, 9 H), 2.88 (s, 3 H); IR (KBr) 1720 (s), 950 cm^{-1}. **16**: ^{1}H NMR ($CDCl_3$) δ 2.2–2.5 (m, 4 H), 2.8–3.1 (m, 1 H), 2.95 (s, 3 H), 3.25 (dd, 1 H), 3.72 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 24.8 (q, *N*-CH_3), 31.9, 32.1 (t, $-CH_2-$), 42.0, 46.3 (d, >CH–), 52.1, 52.4 (q, *O*-CH_3), 69.0 (s, quaternary C), 170.6, 171.7, 172.6, 173.1 (s, >C=O); IR (KBr) 1730 (s), 963 cm^{-1}. **17**: ^{1}H NMR ($CDCl_3$) δ 2.21 (t, 2 H, *J* = 8 Hz), 2.42 (t, 2 H, *J* = 8 Hz), 2.74 (s, 3 H), 2.94 (s, 3 H), 3.67 (s, 6 H); IR ($CHCl_3$) 1734 (s), 960 cm^{-1}. **18**: ^{1}H NMR (CCl_4) δ 0.98 (t, 3 H, *J* = 8 Hz), 1.30 (s, 3 H), 1.68 (q, 2 H, *J* = 8 Hz), 2.86 (s, 3 H); IR 1805 (w), 1720 (s), 945 cm^{-1}.
(9) In the photochemistry of cyclic ketones analogous examples are reported. Chapman, O. L.; Weiss, D. S. "Organic Photochemistry", Vol. 3; Marcel Dekker: New York, 1973; p 228.
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(11) Quantum yield of formation of **2** was 0.3_3.
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(13) (a) Testa, E.; Fontanella, L.; Cristiani, G. F.; Mariani, L. *Helv. Chim. Acta* **1959,** *42*, 2370. (b) Poshkus, A. C.; Herweh, J. E. *J. Org. Chem.* **1965,** *30*, 2466.
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Kazuhiro Maruyama,* Takeshi Ishitoku, Yasuo Kubo
Department of Chemistry, Faculty of Science
Kyoto University, Kyoto 606, Japan

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S_1 vs. T_2 Photoreactivity of β,γ-Unsaturated Ketones. Temperature Dependent Photo-CIDNP of 2-Cyclopentenyl Methyl Ketones[1]

Sir:

Among the diverse facets of the photochemistry of β,γ-unsaturated ketones (β,γ-UK),[2] the mechanism of the allylic 1,3-acyl shift (AS), most commonly observed on direct irradiation only, has persisted as a prominent matter of debate. On the basis of earlier results, the AS was assumed to occur from the singlet n,π* state (S_1) via a concerted process.[2] Only for β,γ-unsaturated phenyl ketones has the AS been shown to proceed via a radical-pair mechanism, predominantly from the n,π* triplet, which is the lowest lying excited state of these compounds.[3] Subsequently, AS from a short-lived T_2 state of prevalent n,π* character has also been taken into consideration for β,γ-UK's with a lowest lying triplet π,π* state.[2b,c,4,5] While results of fluorescence studies remained inconclusive on this point,[4,5] it has been unequivocally shown recently that the AS can indeed occur from the T_2(n,π*) state of a β,γ-UK, **1c**.[6] CIDNP effects have been taken as evidence for all three of the current views on the AS mechanism.[2c,3,7,8]

We now report results on the β,γ-UK's **1a–c** which allow the assembly of a more coherent, mechanistic picture of the S_1 vs. T_2 reactivity of these ketones. Photo-CIDNP effects from **1a–c** exhibited a remarkable temperature dependence in the range of −60 to 140 °C. *They are interpreted in terms of an AS via radical pairs that originate from both the S_1 and T_2 states depending on the reaction temperature.*

When a 0.1 M solution of **1a**[9,10a] in CD_3OD was irradiated at 45 °C in the modified ^{1}H probe of an FT NMR spectrometer,[11] CIDNP effects of the starting ketone (**1a**) and acetaldehyde (**2**) were observed (Figure 1B).[13] Additional enhanced resonances were assigned to 1,2-dimethyl-3-methylenecyclopentene, R_{-H}, on the basis of previous evidence.[3] Both CIDNP and product structures are in accord with the reactions summarized in Scheme I. At 45 °C, these reactions of **1a** occur predominantly from S_1: all polarizations are readily rationalized in terms of reactions from a singlet radical pair, $\overline{R\cdot\cdot R'}^{1}$ when Kaptein's rules[14] are applied using the respective radical parameters.[15]

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