THERMAL CYCLOADDITION OF AROYLKETENE TO 1-ARYL-1-TRIMETHYLSILYLOXYETHYLENE: A SIMPLE SYNTHESIS OF 2,6-DIARYL-4*H*-PYRAN-4-ONE

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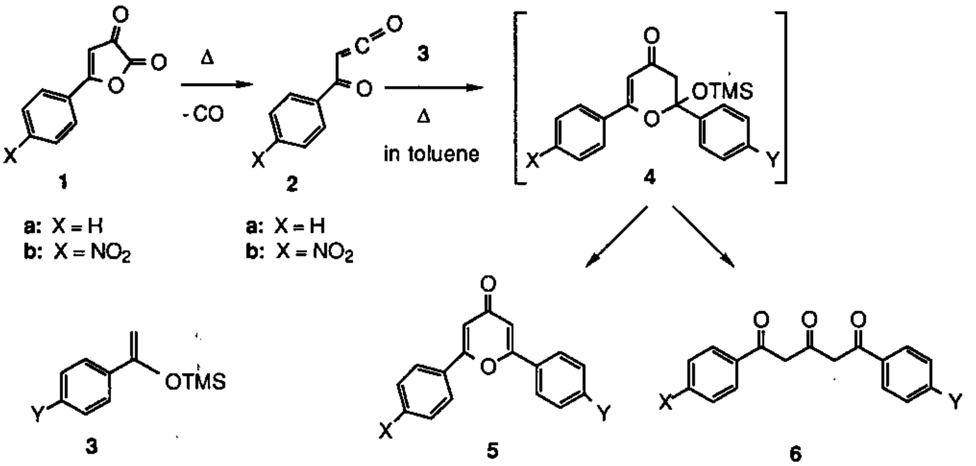
Abstract - Aroylketene (**2**) generated by pyrolytic decarbonylation of 5-aryl-2,3-dihydro-2,3-furandione (**1**) reacted with 1-aryl-1-trimethylsilyloxyethylene (**3**) in a regioselective manner to give 2,6-diaryl-4*H*-pyran-4-one (**5**) and/or 1,5-diarylpentane-1,3,5-trione (**6**). This reaction provides a simple synthetic method of 2,6-diaryl-4*H*-pyran-4-one with various substituents in the aryl group.

Acylketenes readily react with a variety of hetero-olefins including imine,[1,2] cyanide,[1,3,4] diimine,[1,4] ketone,[1,5,6] thioamide,[7] and isocyanate[1,3,5,8] as a heterodiene in the [4 + 2] cycloaddition reaction. Furthermore, it has been demonstrated that acylketenes undergo [4 + 2] cycloaddition to electron-rich olefins such as enol ethers[9~11] and ketene acetals[9,10] which provide a versatile synthetic method of 2-alkoxy-2,3-dihydro-4*H*-pyran-4-one and of 4*H*-pyran-4-one. In this paper, we describe a potentially versatile approach to the 2,6-diaryl-4*H*-pyran-4-ones, based on the reaction in which aroylketene (**2**) and 1-aryl-1-trimethylsilyloxyethylene (**3**) undergo [4 + 2] cycloaddition.

Benzoylketene (**2a**) and *p*-nitrobenzoylketene (**2b**) used for the reaction were thermally generated *in situ* from the 5-phenyl-2,3-dihydro-2,3-furandione (**1a**)[12] and 5-*p*-nitrophenyl derivative (**1b**), respectively. The reactions with 1-aryl-1-trimethylsilyloxyethylene (**3**) were performed simply by heating a mixture of the precursor (**1**) and the olefin (**3**) in dry toluene at 100°C for 1 h in a sealed tube. The reaction mixture was purified by silica gel column chromatography to afford 2,6-diaryl-4*H*-pyran-4-one (**5**) and/or 1,5-

diarylpentane-1,3,5-trione (6). The structures of the products were confirmed by their mass, ir, uv, ^{1}H- and ^{13}C-nmr spectral data. The 1,5-diarylpentane-1,3,5-trione existed exclusively as the keto-enol tautomers, as evidenced from the ^{1}H-nmr spectrum of (6a) ($CDCl_3$). The results are summarized in the table .



	a	b	c	d	e	f
Y:	H	CH_3	OCH_3	OTMS	Cl	NO_2

	a	b	c	d	e	f	g	h	i	j	k	l
X:	H	NO_2	H	NO_2	H	NO_2	H	NO_2	H	NO_2	H	NO_2
Y:	H	H	CH_3	CH_3	OCH_3	OCH_3	OH	OH	Cl	Cl	NO_2	NO_2

Table Cycloaddition of Aroylketene (2) to 1-Aryl-1-trimethylsilyloxyethylene (3)

Aroylketene (2)	Olefin (3)	Yield (%)	
X	Y	Pyran-4-one (5)	Triketone (6)
H (2a)	H (3a)	27 (5a)	5 (6a)
NO_2 (2b)	H (3a)	51 (5b)	5 (6b)
H (2a)	CH_3 (3b)	--	2 (6c)
NO_2 (2b)	CH_3 (3b)	26 (5d)	10 (6d)
H (2a)	OCH_3 (3c)	19 (5e)	8 (6e)
NO_2 (2b)	OCH_3 (3c)	61 (5f)	5 (6f)
H (2a)	OTMS (3d)	37 (5g)	--
NO_2 (2b)	OTMS (3d)	63 (5h)	--
H (2a)	Cl (3e)	--	23 (6i)
NO_2 (2b)	Cl (3e)	7 (5j)	20 (6j)
H (2a)	NO_2 (3f)	--	3 (6k)*
NO_2 (2b)	NO_2 (3f)	--	3 (6l)

*6k was identical with 6b

Substituents introduced at the *para*-position of the phenyl group in the trimethylsilyloxyethylene (3) affected this reaction. In the reaction of benzoylketene (**2a**) with the olefin (**3**), the trimethylsilyloxy substituted **3d** gave the pyran-4-one (**5g**) in slightly higher yield (37%) than the non-substituted **3a** which gave the pyran-4-one (**5a**) (27%) and (**6a**) (5%). The methoxy substituted **3c** little affected the reaction (19% for **5e** and 8% for **6e**). The chlorine derivative (**3e**) gave only the triketone (**6i**) as a characterizable product in 23% yield. The methyl derivative (**3b**), in contrast to the expectation inferred from its electron releasing property, showed poor reactivity for **2a**, giving the triketone (**6c**) in only 2% yield as a characterizable product. The result is similar to that of the nitro derivative (**3f**) (**6k**: 3%) which is predictable from the electron-withdrawing property of the nitro group.

As shown in the table, the *p*-nitrobenzoylketene (**2b**) was evidenced to have higher reactivity for this cycloaddition reaction. The olefins (**3c**) and (**3d**) with electron-releasing substituents (OMe and OTMS) gave the pyran-4-ones (**5f**) and (**5h**) in the yield of 61% and 63%, respectively. Although the methyl derivative (**3b**) showed the poor result in the reaction with **2a** as described above, the reaction with **2b** was appreciably improved, thus giving the pyran-4-one (**5d**) in 26% yield and the triketone (**6d**) in 10% yield. However, in the reaction with the chlorine derivative (**3e**) the nitro substituted **2b** introduced into the aryl group of the aroylketene did not improve the reaction as expected, giving the triketone (**6j**) (20%) as a major product together with the pyran-4-one (**5j**) (7%). The nitro derivative (**3f**), as predicted, gave a poor result, yielding the triketone (**6l**) in only 3% yield.

The formation of such products is rationalized when it is assumed that aroylketene (**2**) generated by pyrolytic decarbonylation of 5-aryl-2,3-dihydro-2,3-furandione (**1**) undergoes cycloaddition in terms of the inverse Diels-Alder reaction. In this [4 + 2] cycloaddition reaction the aroylketene behaves as an electron-deficient diene and 1-aryl-1-trimethylsilyloxyethylene as an electron-rich olefin, which is evidenced by the fact that this cycloaddition reaction is facilitated either by the electron-withdrawing group (X) in the 5-aryl-2,3-dihydro-2,3-furandione or by the electron-releasing group (Y) in the 1-aryl-1-trimethylsilyloxyethylene. The cycloaddition proceeds in a highly regioselective manner to afford the dihydropyran-4-one (**4**) which then undergoes either pyrolytic desilyloxylation or ring opening with concomitant desilylation to yield the pyran-4-one (**5**) or the triketone (**6**). Since the pyran-4-one (**5**) is obtainable from the triketone (**6**) by acid catalysed ring closure,[13,14] this approach provides a potentially versatile synthetic method of 2,6-diaryl-4*H*-pyran-4-ones with various substituents in the aryl group.

EXPERIMENTAL

Unless otherwise stated, following procedures were adopted. Melting points were determined with Yanagimoto MP-S1 melting point apparatus and are uncorrected. Infrared spectra were measured with JASCO FT/IR-5000 Fourier transform infrared spectrophotometer using KBr and are given as cm^{-1}.

Ultraviolet spectra were measured with Hitachi U-3200 spectrophotometer in dioxane and are given as λ $_{max}$ nm (ε). ^{1}H- and ^{13}C-Nmr spectra were measured in $CDCl_3$ using tetramethylsilane as an internal standard with a JEOL JNM-EX90 (^{1}H: 90 MHz; ^{13}C: 22.5 MHz). High-resolution mass (HRms) and low-resolution mass (LRms) spectra were obtained on JEOL JMS-D300 at 30 eV by the direct inlet system.

Synthesis of 1-Aryl-1-trimethylsilyloxyethylenes (3)

The olefins (**3a-f**) were prepared by trimethylsilylation of acetophenone derivatives according to the known procedure.[15]

3a: ^{1}H-Nmr: 0.27 (9H, s), 4.43 (1H, d, *J*= 2 Hz), 4.91 (1H, d, *J*=2 Hz), 7.2-7.4 (3H, m), 7.5-7.7 (2H, m). **3b** : ^{1}H-Nmr: 0.26 (9H, s), 2.34 (3H, s), 4.37 (1H, d, *J*=2 Hz), 4.86 (1H, d, *J*=2 Hz), 7.11 (2H, d, *J*=8 Hz), 7.48 (2H, d, *J*=8 Hz). **3c** : ^{1}H-Nmr: 0.26 (9H, s), 3.81 (3H, s), 4.33 (1H, d, *J*=2 Hz), 4.79 (1H, d, *J*=2 Hz), 6.7-6.9 (2H, m), 7.4-7.6 (2H, m). **3d** : ^{1}H-Nmr: 0.26 (18H, s), 4.32 (1H, d, *J*=2 Hz), 4.78 (1H, d, *J*=2 Hz), 6.7-6.9 (2H, m), 7.4-7.6 (2H, m). **3e** : ^{1}H-Nmr: 0.26 (9H, s), 4.43 (1H, d, *J*=2 Hz), 4.88 (1H, d, *J*=2 Hz), 7.2-7.6 (4H, m). **3f** : ^{1}H-Nmr: 0.28 (9H, s), 4.60 (1H, d, *J*=2 Hz), 5.06 (1H, d, *J*=2 Hz), 7.6-7.8 (2H, m), 8.0-8.3 (2H, m).

Synthesis of 5-Aryl-2,3-dihydro-2,3-furandiones (1)

The 5-phenyl-(**1a**) and 5-(*p*-nitrophenyl)-2,3-dihydro-2,3-furandione (**1b**) were prepared by condensation of oxalyl chloride with **3a** and **3f** according to the known procedure.[12]

1a: Yield 76%. mp 124-127°C [lit.,[12] mp 130-132°C]. Ir: 1823, 1717. Uv: 348 (9000). ^{1}H-Nmr: 4.41 (1H, s), 7.5-8.0 (5H, m). LRms *m/z* 174 (M^+).

1b: Yield 70%. mp 141-142°C. Ir: 1829, 1734. Uv: 349 (8100). ^{1}H-Nmr: 6.55 (1H, s), 8.0-8.5 (4H, m). LRms *m/z* 219 (M^+).

General Procedure for Thermal Cycloaddition of Benzoylketene (2a) to 1-Aryl-1-trimethylsilyloxyethylene (3)

A mixture of **1a** (500 mg, 2.87 mmol) and **3** (2 mol eq.) in toluene (10 ml) was heated at 100°C for 1 h in a sealed tube. After the reaction mixture was concentrated to dryness *in vacuo*, the residue was chromatographed over SiO_2. Elution with benzene-CH_2Cl_2 (1:1) and recrystallizations of the eluate from appropriate solvents gave the pyran-4-one (**5**) and the triketone (**6**).

1) Reaction with 3a

5a: 191 mg (27%). Colorless needles from CH_2Cl_2-benzene, mp 136-140°C [lit.,[13,16] mp 138-140°C]. Ir: 1649, 1618. Uv: 283 (26200). ^{1}H-Nmr: 6.82 (2H, s), 7.5-7.9 (10H, m). ^{13}C-Nmr: 111.4 (sx2), 125.9 (dx4), 129.1 (dx4), 131.4 (sx2, dx2), 163.3 (sx2), 180.1 (s). HRms Calcd for $C_{17}H_{12}O_2$ (M^+): 248.0834. Found: 248.0832.

6a: 35 mg (5%). Yellow plates from ether, mp 103-106°C [lit.,[13,17,18] mp 105-109°C]. Ir: 1601, 1570. Uv: 382 (30800). HRms Calcd for $C_{17}H_{14}O_3$ (M^+): 266.0942. Found: 266.0957.

2) Reaction with 3b.

6c: 15 mg (2%). Yellow needles from ether-hexane, mp 80-81°C. Ir: 1593, 1562, 1512, 1493. Uv: 386 (26400). HRms Calcd for $C_{18}H_{16}O_3$ (M^+): 280.1054. Found: 280.1104.

3) Reaction with 3c.

5e: 150 mg (19%). Colorless needles from CH_2Cl_2, mp 158-160°C [lit.,[13,19,20] mp 160-161°C]. Ir: 1644, 1601, 1570, 1512. Uv: 266 (25700), 297 (26000). ^{1}H-Nmr: 3.89 (3H, s), 6.78 (1H, d, J=2 Hz), 6.83 (1H, d, J=2 Hz), 7.0-7.1 (2H, m), 7.5-7.6 (2H, m), 7.8-8.0 (5H, m). ^{13}C-Nmr: 55.5 (q), 109.8 (d), 111.1 (d), 114.5 (dx2), 123.6 (s), 125.8 (dx2), 127.5 (d), 129.0 (dx3), 131.2 (s), 131.5 (d), 162.2 (s), 162.9 (s), 163.2 (s), 180.1 (s). HRms Calcd for $C_{18}H_{14}O_3$ (M^+): 278.0942. Found: 278.0942.

6e: 70 mg (8%). Yellow needles from ether, mp 79-81°C [lit.,[13] recrystallized from benzene, mp 121-122°C]. Ir: 1595, 1564, 1512, 1493. Uv: 384 (31100).

4) Reaction with 3d.

5g: 278 mg (37%). Pale brown needles from $CHCl_3$-MeOH, mp 260-262°C. Ir: 1647, 1615, 1582, 1572, 1547, 1516. Uv: 265 (25400), 297 (24600). ^{1}H-Nmr (acetone-d_6): 6.68 (1H, d, J=2 Hz), 6.78 (1H, d, J=2 Hz), 7.6-7.7 (4H, m) , 7.9-8.1 (5H, m). ^{13}C-Nmr (acetone-d_6): 109.9 (d), 111.6 (d), 116.9 (dx2), 123.7 (s), 126.8 (dx2), 128.8 (d), 130.0 (dx3), 132.1 (d), 132.7 (s), 161.4 (s), 163.4 (s), 164.1 (s), 179.7 (s). HRms Calcd for $C_{17}H_{12}O_3$ (M^+): 264.0784. Found: 264.0799.

5) Reaction with 3e.

6i: 200 mg (23%). Yellow needles from CH_2Cl_2-ether, mp 104-105°C [lit.,[13] mp 106-107.5°C]. Ir: 1605, 1562, 1493. Uv: 384 (33400). HRms Calcd for $C_{17}H_{13}O_3Cl$ (M^+): 300.0550. Found: 300.0537.

6) Reaction with 3f.

6k: 23 mg (3%). Yellow prisms from ether, mp 100-102°C. Ir: 1597, 1562, 1510, 1493. HRms Calcd for $C_{17}H_{13}NO_5$ (M^+): 311.0791. Found: 311.0776.

General Procedure for Thermal Cycloaddition of *p*-Nitrobenzoylketene (2b) to 1-Aryl-1-trimethylsilyloxyethylene (3).

A mixture of **1b** (500 mg, 2.28 mmol) and **3** (2 mol eq.) in toluene (10 ml) was heated at 100°C for 1 h in a sealed tube. After the reaction mixture was concentrated to dryness *in vacuo*, the residue was purified by recrystallizations from appropriate solvents to afford the pyran-4-one (**5**). The mother liquor was chromatographed on SiO_2 and elution with benzene:hexane (1:1) gave the triketone (**6**).

1) Reaction with 3a.

5b: 340 mg (51%). Pale brown needles from CH_2Cl_2-benzene, mp 235-236°C. Ir: 1667, 1552. Uv: 301 (18500). ^{1}H-Nmr: 6.68 (1H, d, *J*=2 Hz), 6.92 (1H, d, *J*=2 Hz), 7.5-7.6 (3H, m), 7.8-8.1 (4H, m), 8.4-8.5 (2H, m). ^{13}C-Nmr: 111.6 (d), 113.3 (d), 124.5 (dx2), 126.2 (dx2), 127.2 (d), 129.5 (dx3), 130.9 (s), 132.1 (d), 137.1 (s), 149.5 (s), 161.3 (s), 164.5 (s), 180.4 (s). HRms Calcd for $C_{17}H_{11}NO_4$ (M^+): 293.0687. Found: 293.0547.

6b: 34 mg (5%). This was identical with the triketone (**6k**) described above.

2) Reaction with 3b.

5d: 180 mg (26%). Pale brown needles from CH_2Cl_2, mp 275-277°C. Ir: 1642, 1613, 1520. Uv: 278 (22900), 304 (22600). ^{1}H-Nmr: 2.47 (3H, s), 6.90 (1H, d, *J*=2 Hz), 7.00 (1H, d, *J* =2 Hz), 7.3-7.4 (2H, m), 7.8-7.9 (2H, m), 8.1-8.2 (2H, m), 8.4-8.5 (2H, m). HRms Calcd for $C_{18}H_{13}NO_4$ (M^+): 307.0845. Found: 307.0870.

6d: 75 mg (10%). Yellow needles from CH_2Cl_2-ether, mp 168°C. Ir: 1599, 1522. Uv: 398 (32500). HRms Calcd for $C_{18}H_{15}NO_5$ (M^+): 325.0950. Found: 325.0965.

3) Reaction with 3c.

5f: 450 mg (61%). Pale yellow needles from CH_2Cl_2, mp 257-258°C. Ir: 1649, 1605, 1514. Uv: 290 (32600). ^{1}H-Nmr (acetone-d_6): 3.92 (3H, s), 6.78 (1H, d, *J* =2 Hz), 6.98 (1H, d, *J* =2 Hz), 7.1-7.2 (2H, m), 8.0-8.4 (6H, m). HRms Calcd for $C_{18}H_{13}NO_5$ (M^+) : 323.0791. Found: 323.0780.

6f: 39 mg (5%). Yellow needles from AcOEt-hexane, mp 178-180°C. Ir: 1609, 1572, 1514. Uv: 407 (26800). HRms Calcd for $C_{18}H_{15}NO_6$ (M^+) : 341.0897. Found: 341.0890.

4) Reaction with 3d.

5h: 463 mg (63%). Orange needles from $CHCl_3$-MeOH, mp > 300°C. Ir: 1638, 1615, 1551, 1516. Uv: 291 (12600). HRms Calcd for $C_{17}H_{11}NO_5$ (M^+): 309.0635. Found: 309.0624.

5) Reaction with 3e.

5j: 56 mg (7%). Colorless needles from CH_2Cl_2, mp 236-239°C. Ir: 1649, 1591, 1491. Uv: 263 (29300). ^{1}H-Nmr: 6.81 (1H, s), 6.83 (1H, s), 7.4-7.9 (8H, m). LRms : 316, 318 (peak, M-11) .

6j: 156 mg (20%). Yellow needles from benzene, mp 149-150°C. Ir: 1603, 1562, 1491. Uv: 386 (35600). LRms (CI): 335 (peak, M-12).

6) Reaction with 3f.

6l : 21 mg (3%). Orange needles from CH_2Cl_2, mp 233-236°C. Ir: 1624, 1589, 1516. Uv: 400 (35300). HRms Calcd for $C_{17}H_{12}N_2O_7$ (M^+): 356.0624. Found: 356.0639.

REFERENCES AND NOTES

1. M. Sato, *Yuki Gousei Kagaku Kyokaishi*, 1988, **46**, 596.
2. E. Ziegler, C. Kollenz, C. Kriwetz, and W. Ott, *Liebigs Ann. Chem.*, 1976, 2071.
3. L. Capuano, H. R. Kirn, and R. Zander, *Chem. Ber.*, 1976, **109**, 2456.
4. a) Y. S. Andreichikov and D. D. Nekrasov, *Zh. Org. Kim.*, 1984, **20**, 1775; b) Y. S. Andreichikov, D. D. Nekrasov, M. A. Rudenko, and O. V. Vinokurova, *Kim. Geterotsikl Soedin SSSR*, 1989, 1265.
5. J. A. Hyatt, P. L. Feldman, and R. J. Clemens, *J. Org. Chem.*, 1984, **49**, 5105.
6. Y. S. Andreichikov, V. L. Gein, A. P. Kozlov, and O. V. Vinokurova, *Zh. Org. Khim.*, 1988, **24**, 210.
7. L. Capuano, G. Bolz, R. Burger, V. Burkhardt, and V. Huch, *Liebigs Ann. Chem.*, 1990, 239.
8. M. Sato, N. Katagiri, K. Takayama, M. Hirose, and C. Kaneko, *Chem. Pharm. Bull.*, 1989, **37**, 665.
9. M. Sato, H. Ogasawara, K. Kato, M. Sakai, and T. Kato, *Chem. Pharm. Bull.*, 1983, **31**, 4300.
10. R. S. Coleman and E. B. Grant, *Tetrahedron Lett.*, 1990, **30**, 3677.
11. E. Wenkert, T. P. Ananthanarayan, V. F. Ferreira, M. G. Hoffmann, and H. S. Kim, *J. Org. Chem.*, 1990, **55**, 4975.
12. S. Murai, K. Hasegawa, and N. Sonoda, *Angew. Chem., Int. Ed. Engl.*, 1979, **14**, 639.
13. R. J. Light and C. R. Hauser, *J. Org. Chem.*, 1960, **25**, 538.
14. Treatment of **6a** with diazomethane in Et_2O gave **5a** in 54% yield.
15. P. Cazeau, F. Duboudin, F. Moulines, O. Babot, and J. Dunogues, *Tetrahedron*, 1987, **43**, 2075.
16. S. Ruhemann, *J. Chem. Soc.*, 1908, **93**, 434.
17. K. Balenovic and R. Munk, *Archiv. Kem.*, 1946, **18**, 41.
18. C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, 1958, **80**, 6360.
19. G. Soliman and I. E-S. El-Kholy, *J. Chem. Soc.*, 1954, 1755.
20. G. W. Perold, A. P. Steyn, and F. V. K. von Reiche, *J. Am. Chem. Soc.*, 1957, **79**, 462.

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