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Chiral Induction in Photochemical Reactions, XIII[1]

The Paternò-Büchi Reaction of Achiral and Chiral Acyl Cyanides with Furan

Cyrill Žagar and Hans-Dieter Scharf*

Institut für Organische Chemie der Technichen Hochschule Aachen,
Prof.-Pirlet-Straße 1, W-5100 Aachen

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The acyl cyanides **1a–d** are prepared from the corresponding acyl chlorides. The Paternò-Büchi reaction of **1a–f** with furan (**2**) yields the bicyclic oxetanes **3a–f** with an *endo/exo* ratio varying from 3.5:1 (**1a**) to 16:1 (**1d**). However, in the reaction of the chiral acyl cyanides **1b** and **1c**, a low chiral induction is observed (maximum de: 13%).

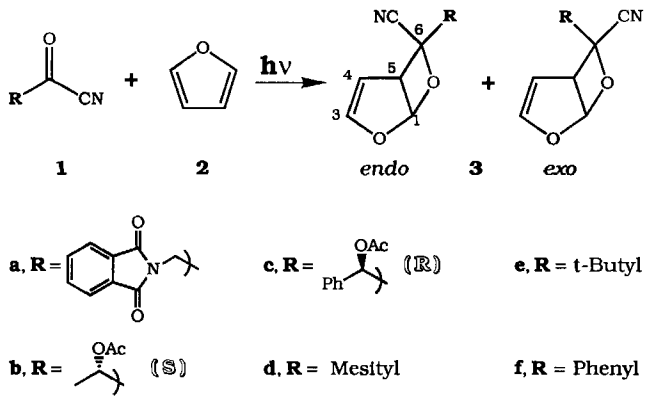
The mechanistic and preparative aspects of the Paternò-Büchi reaction of an excited carbonyl compound with an olefin have extensively been studied[2]. Temperature dependence studies of diastereoselective reactions have led to a more general theory of diastereoselectivity[3].

The diastereomeric excess in the Paternò-Büchi reaction of chiral aldehydes is usually low[4], whereas the application of chiral phenylglyoxylates as carbonyl compounds often leads to a single detectable oxetane diastereomer[5]. Thus, the photoreaction of chiral acyl cyanides (2-oxonitriles, **1b** and **1c**) appears to be mechanistically and preparatively interesting.

The acyl cyanides **1a–d** are prepared from the corresponding acyl chlorides either according to the procedure of Hermann and Simchen[6] by refluxing with cyanotrimethylsilane and a catalytic amount of zinc iodide in benzene or with copper(I) cyanide and acetonitrile in benzene or toluene according to Klenk et al.[7]

Irradiation of the acyl cyanides **1a–f** in furan (**2**) as solvent and reaction partner yields the bicyclic oxetanes **3a–f** (Scheme 1). The reaction proceeds regioselectively, but both diastereomeric *endo*- and *exo*-oxetanes are formed (assignment based on ^{1}H-NMR data). The results are summarized in Table 1.

Scheme 1. Paternò-Büchi reaction of the acyl cyanides **1a–f** with furan (**2**)



In fact, in the reaction of the chiral acyl cyanides **1b** and **1c** a low asymmetric induction is observed. The oxetanes **3b** and **3c** are obtained as mixtures of four diastereomers (two *endo* and two *exo* diastereomers; Table 2).

Table 1. Chemical yields and *endo/exo* ratios of the Paternò-Büchi reaction of the acyl cyanides **1a–f** with furan (**2**)

Acyl cyanide	Temp. [°C]	Chemical yield of oxetane (%)	Chemical yield of *endo*-oxetane by crystallization (%)	*endo/exo*[a]
1a	- 55	30		3.5 : 1
1b	room temp.	25		4.6 : 1
	- 55	61		5.3 : 1
1c	- 55	71		6.2 : 1
1d	- 55	89	67	16 : 1
1e	room temp.	86		8.9 : 1
	- 55	89	63	9.3 : 1
1f	room temp.	77		3.7 : 1
	- 55	95		5.3 : 1

[a] According to ^{13}C-NMR data.

Table 2. Diastereomeric excess of the Paternò-Büchi reaction of the chiral acyl cyanides **1b** and **1c** with furan (**2**), according to ^{13}C-NMR data

Acyl cyanide	Temp. [°C]	*endo* de (%)	*exo* de (%)
1b	room temp.	- 1	- 4
	- 55	+ 4	+ 10
1c	- 55	5	13

Only low chemical yields of oxetanes are obtained in the Paternò-Büchi reaction of acyl cyanides with electron-rich olefins such as 2,2-dimethyl-1,3-dioxole, 2,2-diisopropyl-1,3-dioxole, dihydro-1,4-dioxine, and 1,3-dioxol-2-one.

The photoreactions described here differ markedly from those of chiral phenylglyoxylates with regard to the diastereoselectivity. This may simply be due to the low conformational stability of the excited

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acyl cyanides or a change of the mechanism. Thus, the reaction may proceed only through one selection step[3], or the $S_1(n\pi^*)$ state may be more strongly involved in the process.

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Experimental

Melting points: Büchi m.p. apparatus. – Specific optical rotations: Perkin-Elmer polarimeter 241. – NMR: Varian VXR 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), TMS internal standard. – IR: Perkin-Elmer FT-IR 1250. – Preparative HPLC: Abimed-Gilson, pump 303, modul 803, Dynamax Macro column (silica; LiChrosorb Si 60, 7 μ), and RI detector 131.

2-Oxo-3-(phthalimido)propanenitrile (**1a**)[8]: 6.7 g (30 mmol) of phthalimidoacetyl chloride, 3.0 g of cyanotrimethylsilane, 0.1 g of zinc iodide, and 4 ml of benzene are refluxed and stirred for 3 h. The cold suspension is filtered and the solvent removed from the combined filtrate. Yield of **1a** 5.6 g (87%), m.p. 143–145°C (ref.[8] 140–143°C).

(S)-(–)-3-Acetoxy-2-oxobutanenitrile (**1b**): 60.0 g (0.40 mol) of (*S*)-(–)-2-acetoxypropionyl chloride is refluxed with 53.7 g of copper(I) cyanide, 32.8 g of acetonitrile, and 80 ml of benzene for 3 h. The cold suspension is filtered and the solvent removed from the filtrate by evaporation. Distillation (b.p. 61°C/12 Torr) of the residue yields 37.1 g (66%) of **1b**, $[\alpha]_D^{22} = -56.0$ (c = 1 in $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 2225 cm^{-1}, 1750, 1450, 1375, 1225, 1070, 1025, 935. – ^{1}H NMR ($CDCl_3$): δ = 1.54 (d, J = 7.2 Hz, 3H, CH_3), 2.22 (s, 3H, $COCH_3$), 5.15 (q, 1H, CH). – ^{13}C NMR ($CDCl_3$): δ = 15.0 (CH_3), 20.3 ($COCH_3$), 74.2 (CH), 111.6 (CN), 170.3 (CO_2), 175.3 (COCN).

$C_6H_7NO_3$ (141.1) Calcd. C 51.1 H 5.0 N 9.9
Found C 51.4 H 4.7 N 9.6

(R)-(–)-β-Acetoxy-α-oxobenzenepropanenitrile (**1c**)[9]: 15.2 g (0.10 mol) of (*R*)-(–)-mandelic acid is converted to (*R*)-α-acetoxybenzeneacetyl chloride[10]. Without purification, 13.4 g of copper(I) cyanide, 8.2 g of acetonitrile, and 20 ml of benzene are added and treated as described above for **1b**. Distillation yields 8.4 g (overall yield 41%) of **1c**, b.p. 101–103°C/150 Pa (ref.[9] 150–151°C/10 Torr for the racemic compound). $[\alpha]_D^{22} = -153.9$ (c = 0.9 in cyclohexane).

2,4,6-Trimethyl-α-oxobenzeneacetonitrile (**1d**)[11]: 18.3 g (0.10 mol) of mesitoyl chloride, 13.4 g of copper(I) cyanide, 8.2 g of acetonitrile, and 20 ml of toluene are treated as described above for **1b**. Distillation (b.p. 118°C/12 Torr) yields 14.7 g (85%) of **1d**, m.p. 37–39°C.

General Procedure for the Photoreactions: The acyl cyanide is dissolved in 200 ml of furan (or, in the case of **1a**: 200 ml of 15% acetonitrile in furan) within a pyrex flask (vacuum cavity with Philips HPK 125 W lamp), and flushed with nitrogen. After 0.5 h, the stream of nitrogen is reduced, and the solution irradiated. Afterwards, the solution is evaporated to dryness, and polymeric byproducts are removed by chromatography on a few grams of silica (ethyl acetate/cyclohexane). The NMR data of the oxetanes are summarized in Table 3.

Table 3. Selected NMR data of the oxetanes **3a–f**. Only values of *endo*-oxetanes are presented, and in the case of **3b** and **3c** only of the major *endo* isomer ($CDCl_3$; δ values)

Oxetane	1-H	3-H	4-H	5-H	C-1	C-3	C-4	C-5	C-6	CN
3a	6.23	6.74	5.45	4.36	106.4	150.7	102.0	53.1	85.2	115.8
3b	6.25	6.78	5.46	3.87	106.5	150.8	101.6	51.1	87.7	115.4
3c	6.00	6.71	5.36	3.93	106.3	150.7	101.7	51.1	87.4	115.4
3d	6.14	6.83	5.56	4.17	105.9	151.3	101.7	57.2	89.9	116.9
3e	6.14	6.76	5.42	3.89	106.3	150.4	102.7	49.5	94.3	117.1
3f	6.43	6.83	5.60	4.01	106.6	150.8	102.3	57.7	87.4	117.2

6-(Phthalimidomethyl)-2,7-dioxabicyclo[3.2.0]hept-3-ene-6-carbonitrile (**3a**): 1.30 g (6.07 mmol) of **1a** is irradiated at –55°C for 24 h. Purification by preparative HPLC (1% triethylamine, 35% ethyl acetate in cyclohexane) yields 0.39 g (30%) of **3a**.

$C_{15}H_{10}N_2O_4$ (282.3) Calcd. C 63.8 H 3.6 N 9.9
Found C 63.7 H 3.5 N 10.0

6-[(1S)-1-Acetoxyethyl]-2,7-dioxabicyclo[3.2.0]hept-3-ene-6-carbonitrile (**3b**): 4.00 g (28.3 mmol) of **1b** is irradiated at room temp. for 16 h, or 10.0 g (70.9 mmol) is irradiated at –55°C for 48 h. Purification by preparative HPLC (1% triethylamine, 30% ethyl acetate in cyclohexane) yields 1.47 g (25%) or 9.10 g (61%) of **3b**.

$C_{10}H_{11}NO_4$ (209.2) Calcd. C 57.4 H 5.3 N 6.7
Found C 57.5 H 5.5 N 6.6

6-[(R)-Acetoxyphenylmethyl]-2,7-dioxabicyclo[3.2.0]hept-3-ene-6-carbonitrile (**3c**): 2.14 g (10.5 mmol) of **1c** is irradiated at –55°C for 24 h. Purification by preparative HPLC (1% triethylamine, 30% ethyl acetate in cyclohexane) yields 2.02 g (71%) of **3c**.

$C_{15}H_{13}NO_4$ (271.3) Calcd. C 66.4 H 4.8 N 5.2
Found C 66.2 H 5.2 N 5.7

(±)-6-(2,4,6-Trimethylphenyl)-2,7-dioxabicyclo[3.2.0]hept-3-ene-endo-6-carbonitrile (*endo*-**3d**): 10.0 g (53.7 mmol) of **1d** is irradiated at –55°C for 48 h. Oxetane yield: 12.4 g (89%). Crystallization yields 9.3 g (67%) of racemic *endo*-**3d**, m.p. 112°C (cyclohexane). –IR (KBr): $\tilde{\nu}$ = 1605 cm^{-1}, 1450, 1050, 1000, 955, 865, 725.

$C_{15}H_{15}NO_2$ (241.3) Calcd. C 74.7 H 6.3 N 5.8
Found C 74.6 H 6.3 N 6.0

(±)-6-tert-Butyl-2,7-dioxabicyclo[3.2.0]hept-3-ene-endo-6-carbonitrile (*endo*-**3e**): 4.00 g of pivalyl cyanide (**1e**)[7] (36.0 mmol) is irradiated at room temp. for 16 h, or 1.0 g (90.0 mmol) at –55°C for 48 h. Oxetane yield: 5.55 g (86%) or 14.4 g (89%). Crystallization of the latter yields 10.2 g (63%) of racemic *endo*-**3e**, m.p. 51°C (*n*-hexane). – IR ($CHCl_3$): $\tilde{\nu}$ = 1610 cm^{-1}, 1470, 1045, 985, 960.

$C_{10}H_{13}NO_2$ (179.2) Calcd. C 67.0 H 7.3 N 7.8
Found C 66.9 H 7.4 N 7.8

6-Phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene-6-carbonitrile (**3f**): 4.00 g of benzoyl cyanide (**1f**) (30.5 mmol) is irradiated at room temp. for 16 h, or 10.0 g (76.3 mmol) at –55°C for 48 h. Yield: 5.23 g (86%) or 14.4 g (95%) of **3f**.

$C_{12}H_9NO_2$ (199.2) Calcd. C 72.4 H 4.6 N 7.0
Found C 72.1 H 4.6 N 7.0

CAS Registry Numbers

1a: 3313-29-9 / **1b**: 131635-46-6 / **1c**: 131635-47-7 / **1d**: 55878-82-5 / **1e**: 42867-40-3 / **1f**: 613-90-1 / (*endo*)-**3a**: 131365-48-8 / (*exo*)-**3a**: 131722-70-8 / (*endo*)-**3b** (Isomer 1): 131724-02-2 / (*endo*)-**3b** (Isomer 2): 131722-74-3 / (*exo*)-**3b** (Isomer 1): 131635-53-5 / (*exo*)-**3b** (Isomer 2): 131722-46-4 / (*endo*)-**3c** (Isomer 1): 131635-49-9 / (*endo*)-**3c** (Isomer 2): 131722-77-5 / (*exo*)-**3c** (Isomer 1): 131722-71-9 / (*exo*)-**3c** (Isomer 2): 131722-78-6 / (*endo*)-**3d**: 131635-50-2 / (*exo*)-**3d**: 131722-72-0 / (*endo*)-**3e**: 131635-51-3 / (*exo*)-**3e**: 131722-73-1 / (*endo*)-**3f**: 131635-52-4 / (*exo*)-**3f**: 131722-74-2 / phthalimidoacetyl chloride: 6780-38-7 / (*S*)-(–)-2-acetoxypropionyl chloride: 36394-75-9 / (*R*)-α-acetoxybenzeneacetyl chloride: 49845-69-4 / mesitoyl chloride: 938-18-1

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