49. 3-(Prop-2-enylidene)azetidin-2-one Derivatives: Synthesis, Structure, and Formation of 3-Spiro-β-lactams *via Diels-Alder* Reactions

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Dedicated to Prof. *Fritz Sauter*, Wien, on the occasion of his 65th birthday

(2.XII.94)

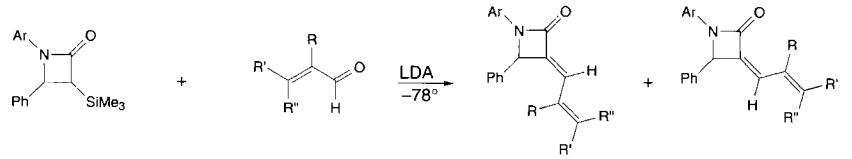
Reactions of 3-silylated β-lactams (**1**) with α,β-unsaturated ketones give the propylidene-β-lactams **3** and the cycloalkenylidene derivatives **5**. Structure and configuration are elucidated by spectroscopic methods, and the reactivity is discussed. While compounds **5** do not react with dienophiles, the (*Z*)-isomers of **3** are the favored substrates for *Diels-Alder* reactions yielding the spiro compounds **6** and 7.

Introduction. – Since not only naturally occurring β-lactam antibiotics like penicillins, cephalosporins, and thienamycins, but even synthetically available derivatives, monobactams, are potent antibiotics [1], the chemistry of monocyclic β-lactam derivatives is studied more and more [2]. The silylation of 1,4-disubstituted β-lactams has already been described [3], and we have converted 3-silylated derivatives into 3-arylidene or 3-alkylidene derivatives, from which substitued 3-(hydroxyalkyl) or 3-(hydroxyaryl) derivatives can be obtained [4]. In this paper, we report on the synthesis, properties, and the synthetic use of 3-propenylidene-β-lactams opening a new way to spiro β-lactams *via Diels-Alder* reactions. Although there are some reports on spiro-β-lactams prepared by ring closure [5] [6b], and we have already described some examples using a β-lactam derivative as a dienophile in a *Diels-Alder* reaction [6], the use of a β-lactam derivative as a diene has not been reported so far.

Results. – 3-Arylidene and 3-alkylidene derivatives are available from a *Peterson* olefination of the 3-silylated compounds **1** [4]. We expected this reaction being useful even for the synthesis of the propenylidene derivatives **3**, and indeed, by reaction of **1** with the α,β-unsaturated carbonyl compounds **2** at −78°, we obtained **3** in yields of >70%. By the analogue reaction of **1a** with the cycloalkenones **4**, cycloalkenylidene derivatives **5** were prepared (*Scheme 1*). As expected, all products were obtained as (*E*)/(*Z*)-mixtures, which were separated by column chromatography and characterized by spectroscopic data. The ratio (*E*)/(*Z*) was *ca.* 1:1, determined by the ^{1}H-NMR spectra of the crude mixtures. The ^{1}H-NMR data (*Table 1* and *Exper. Part*) establish the configuration of the isomers. The signal of the MeO group usually is found between 6.88 and 7.23 ppm (not included in *Table 1*).

The assignment of configuration is confirmed by the NOE in the spectra of the (*Z,E*)-isomers of **3c** and of both isomers of **3d** (*Fig. 1*). The positive NOE between H–C(4) and H–C(1′) in (*Z,E*)-**3c** and (*Z*)-**3d** supports the (*Z*)-configuration, while in

Scheme 1

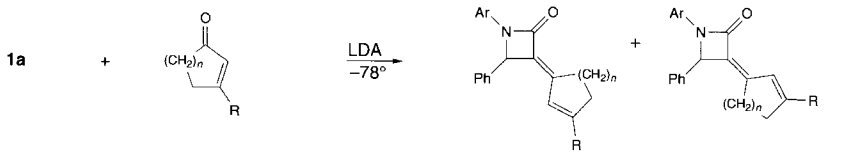


1a Ar = 4-MeO–C_6H_4
b Ar = Ph

2a R = R'' = H, R' = Ph
b R = R'' = H, R' = Me
c R = Me, R' = R'' = H
d R = H, R' = R'' = Me

(*E*)-**3** (*Z*)-**3**

a Ar = Ph, R = H, R' = Ph, R'' = H
b Ar = 4-MeO–C_6H_4, R = H, R' = Ph, R'' = H
c Ar = 4-MeO–C_6H_4, R = H, R' = Me, R'' = H
d Ar = 4-MeO–C_6H_4, R = Me, R' = H, R'' = H
e Ar = 4-MeO–C_6H_4, R = H, R' = Me, R'' = Me



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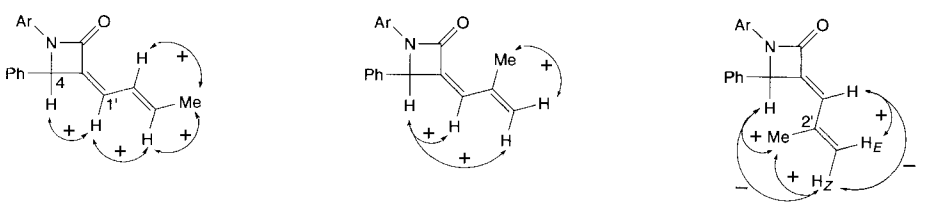
(*E*)-**5** (*Z*)-**5**

a Ar = 4-MeO–C_6H_4, R = Me, n = 1
b Ar = 4-MeO–C_6H_4, R = H, n = 2
c Ar = 4-MeO–C_6H_4, R = H, n = 3

Table 1. *^{1}H-NMR Data of 3-Propenylidene-β-lactams* **3** (δ [ppm], J [Hz], 80-MHz spectra, $CDCl_3$)

No.	H–C(4)	H–C(1′)	H–C(2′)	H–C(3′)	Others	J(1′,2′)	J(2′,3′)	Others
(3*E*,2′*E*)-**3a**	5.52	[a])	[a])	[a])	6.3–7.65[b])			
(3*Z*,2′*E*)-**3a**	5.38	6.65	7.70	6.16	6.8–7.55[b])	15	10	
(3*E*,2′*E*)-**3b**	5.45	[a])	[a])	[a])	6.2–7.6[b])			
(3*Z*,2′*E*)-**3b**	5.31	6.58	7.64	6.10	6.6–7.7[b])	15	10	
(3*E*,2′*E*)-**3c**[c])	5.41	6.62	5.81	5.97	1.71[d]), 6.7–7.5[b])			–1.5[e]), 5.5[f])
(3*Z*,2′*E*)-**3c**[g])	5.27	5.95	6.89	5.86	1.82[d]), 6.8–7.4[b])	11.25	15	–1.5[e]), 6.75[f])
(*E*)-**3d**[g])	5.35	6.75		5.12/5.20	1.57[d]), 6.7–7.5[b])			–1.5[h])
(*Z*)-**3d**[g])	5.92	5.14		5.14/5.22	2.24[d]), 6.8–7.5[b])			–1.5[i])
(*E*)-**3e**[c])	5.40	6.91	5.60	1.73[d]/1.79[d])	6.7–7.5[b])	12		–1.5[h])
(*Z*)-**3e**[c])	5.29	6.22	6.74	1.73[d])/1.88[d])	6.8–7.4[b])	13		

[a]) Signals of the proton under aromatic proton signals. [b]) Aromatic protons. [c]) 250-MHz Spectra. [d]) Me group. [e]) H–C(2′)/Me. [f]) H–C(3′)/Me. [g]) 400-MHz Spectra. [h]) H–C(1′)/H–C(4) and H–C(1′)/H_Z–C(3′). H_E–C(3′)/Me.



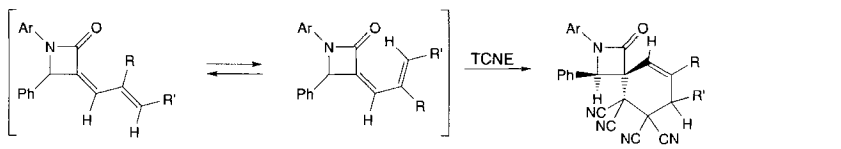
(*Z*,*E*)-**3c** (*Z*)-**3d** (*E*)-**3d**

Figure. *NOE Determined in the ^{1}H-NMR spectra of propylidene-β-lactams (*Z,E*)-***3c*** and (*Z*)- and (*E*)-**3d***

(*E*)-**3d** a positive effect between H–C(4) and the Me group at C(2′) is found. In the spectrum of (*E*)-**3d**, we detected two negative NOE, indicating a quasiplanar multispin system [7]. We found them in the systems H–C(1′)/H_E–C(3′)/H_Z–C(3′) and H–C(4)/Me/H_Z–C(3′).

Diels-Alder reactions of **3** with the highly reactive tetracyanoethylene (TCNE) were performed in THF at 65° (reflux), and were checked by TLC. We obtained the spiro compounds **6** in yields between a few percents and nearly 100% (*Scheme 2*). The reaction time varied between 1 h and 16 days (*Table 2*).

Scheme 2



(*Z*)-**3**

6a Ar = Ph, R = H, R' = Ph
b Ar = 4-MeO–C_6H_4, R = H, R' = Ph
c Ar = 4-MeO–C_6H_4, R = H, R' = Me
d Ar = 4-MeO–C_6H_4, R = Me, R' = H

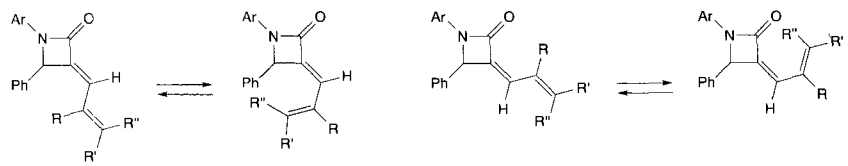
Table 2. *Reaction Time and Yield of* **6** *from the Reactions of* **3** *with TCNE*

	(3*Z*,2′*E*)-**3a**	(3*Z*,2′*E*)-**3b**	(3*E*,2′*E*)-**3b**	(3*Z*,2′*E*)-**3c**	(3*E*,2′*E*)-**3c**	(*Z*)-**3d**	(*E*)-**3d**	(*Z*)-**3e**	(*E*)-**3e**
Time [h]	48	48	384	24	240	1	192	336	336
Yields [%] of **6**	91	78	4	54	0	58	48	0	0

Considering the theory of frontier orbitals [8], the reactivity of a diene can be enhanced by introduction of substituents which are able to hyperconjugate with the diene (Ph, alkyl, vinyl, and similar groups). Accordingly, we expected an increase of the reactivity in the sequence **3d** < **3c** < **3a** ≈ **3b** < **3e**. As can be seen from *Table 2*, we obtained opposite results. Compound **3e**, which was expected to be the most reactive compound, did not undergo any reaction. On the other hand, **3d** with the lowest predicted potency gave the best results, as both isomers led to adducts. Furthermore, only the (*Z*,*E*)- or (*Z*)-isomers gave cycloadducts with the exception of **3d**, from which both isomers yielded adducts. To explain these results, which seem to be opposite to the expected, we calculated the preferred conformations and the minimum energies.

All dienes **3** exist in solution in equilibria between s-*trans*- and s-*cis*-conformation (*Scheme 3*). Depending on the configuration of the double bond, one conformation seems to be favored. MMX calculations [9] of **3c–e** indicate that the (*Z*,*E*)- or the (*Z*)-isomers are the better dienophils. The s-*cis*-conformation of (*Z*,*E*)-**3c** shows no interaction between the substituent at C(4) (Ph) and the Me group at C(3′), while this interaction in (*E*,*E*)-**3c** makes the s-*trans*-form to the preferred conformation. In **3d**, the Me group at C(2′) exhibits only a weak influence on the preferred conformations. Therefore, both isomers react with TCNE. Finally, the two Me groups at C(3′) in **3e** inhibit the s-*cis*-conformation of the (*E*)- and of the (*Z*)-isomer by a strong interaction with the Ph group ((*E*)) or with the O-atom at C(2) ((*Z*)). This is in aggreement with the experiments.

Scheme 3



The results with TCNE are in accordance with *Diels-Alder* reactions with the less reactive maleic anhydride and with maleinimides. These reactions are performed under similar conditions by refluxing the appropriate mixture of compounds in THF.

When we tried to react **3a**, **3b**, (*E*,*E*)-**3c**, (*E*)-**3d**, or **3e** with one of the maleic-acid derivatives, no reaction was observed even after some days. On the other hand, (*Z*,*E*)-**3c** and (*Z*)-**3d** reacted in times between 2 and 24 h, giving single isomers of the crystalline adducts. The structure of all derivatives of **7** are clearly established by their ^{1}H- and ^{13}C-NMR data (see *Exper. Part*) and by measuring the NOE of **7a** (*Table 3*). Furthermore, **7a** is partially converted into the diester **8b** by refluxing with MeOH in the presence of conc. H_2SO_4, while hydrolysis of **7a** with aqueous MeOH results in the formation of the acid **8a** (*Scheme 4*).

Scheme 4

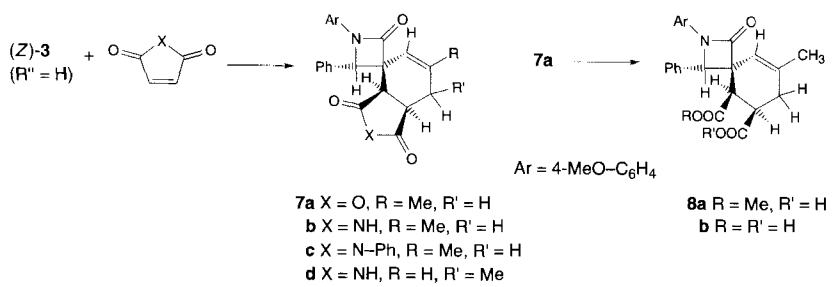


Table 3. *NOE Experiment with 2-(4-Methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,6-dicarboximide* (**7a**)[a])

Irradiation at	H–C(3)	H–C(5)	H–C(6)	H_t–C(7)	H_c–C(7)	H–C(9)	A,A′	B,B′	C,C′
H–C(3)		++	–			+	++	–	++
H–C(5)	++		++			+	–		–
H–C(6)	–	++			+				
H_t–C(7)					++				
H_c–C(7)		–	++	++					

[a]) +: Positive NOE, ++: very strong NOE, –: negative NOE.

Financial support provided by the *Fond der Chemischen Industrie*, Frankfurt, is greatfully appreciated. We thank *Farbwerke Hoechst SA*, Paris, for the supply of chemicals, and Dr. *D. Hunkler*, Chemisches Laboratorium der Universität Freiburg, for recording some NMR spectra.

Experimental Part

General. See [6b].

1-(4-Methoxyphenyl)-4-phenyl-3-(trimethylsilyl)azetidin-2-one (**1a**) *and 1,4-Diphenyl-3-(trimethylsilyl)azetidin-2-one* (1b). See [3].

Synthesis of 3-(Prop-2-enylidene)-β-lactams. – General Procedure. At −78°, a soln. of **1** in 50 ml of THF is added dropwise to a soln. of LDA in 20 ml of THF. After 15 min stirring, the freshly distilled carbonyl compound is slowly added. The mixture is slowly warmed to r.t. (*ca.* 45 min). Then, it is hydrolyzed with a NH_4Cl soln. (60 g/l), the org. layer is separated, the aq. layer is 2 to 3 times extracted with an appropriate amount of $CHCl_3$, all org. extracts are combined, dried ($MgSO_4$), and evaporated. The residue is purified by column chromatography (CC) with $CHCl_3$ or by recrystallization.

1,4-Diphenyl-3-(3-phenylprop-2-enylidene)azetidin-2-one (**3a**). From **1b** (1.48 g, 5 mmol), LDA (10 mmol), and **2a** (6.9 ml, 50 mmol): 850 mg (50%) of **3a** (mixture of isomers). IR: 3060, 3030 (CH), 1740 (CO), 1685 (C=C). Anal. calc. for $C_{24}H_{19}NO$ (337.43): C 85.43, H 5.68, N 4.15; found: C 85.16, H 5.38, N 4.33. Separation by CC.

(3E,2'E)-**3a**: R_f 0.69: 250 mg (15%). Light-yellow crystals. M.p. 217–218° (MeOH). ^{1}H-NMR: 5.52 (*s*, H–C(4)); 6.30–7.65 (*m*, 15 arom. H, H–C(1'), H–C(2'), H–C(3')).

(3Z,2'E)-**3a**: R_f 0.78: 500 mg (30%). Light-yellow crystals. M.p. 225° (NeOH). ^{1}H-NMR: 5.38 (*s*, H–C(4)); 6.16 (*d*, J = 10, H–C(3')); 6.65 (*d*, J = 15, H–C(1')); 6.80–7.55 (*m*, 15 arom. H); 7.70 (*dd*, J = 15, 10, H–C(2')).

1-(4-Methoxyphenyl)-4-phenyl-3-(3-phenylprop-2-enylidene)azetidin-2-one (**3b**). From **1a** (1.63 g, 5 mmol), LDA (10 mmol), and **2a** (6.9 ml, 50 mmol): 800 mg (43%) of **3b** (mixture of isomers). Separation by CC.

(3E,2'E)-**3b**: R_f 0.63: 300 mg (16%). Yellow crystals. M.p. 226° (MeOH). IR: 3060, 3030, 3010, 2960, 2930, 2910, 2840 (CH), 1730 (CO), 1675, 1625 (C=C). ^{1}H-NMR: 3.66 (*s*, MeO); 5.45 (*s*, H–C(4)); 6.20–7.58 (*m*, 14 arom. H, H–C(1'), H–C(2'), H–C(3')). Anal. calc. for $C_{25}H_{21}NO_2$ (367.45): C 81.72, H 5.76, N 3.81; found: C 81.50, H 5.83, N 3.89.

(3Z,2'E)-**3b**: R_f 0.72: 400 mg (21%). Light-yellow crystals. M.p. 235° (MeOH). IR: 3090, 3060, 3035, 3000, 2950, 2930, 2910, 2840 (CH), 1720 (CO), 1680, 1620 (C=C). ^{1}H-NMR: 3.70 (*s*, MeO); 5.31 (*s*, H–C(4)); 6.10 (*d*, J = 10, H–C(3')); 6.58 (*d*, J = 15, H–C(1')); 6.58–7.69 (*m*, 14 arom. H); 7.64 (*dd*, J = 15, 10, H–C(2')). Anal. calc. for $C_{25}H_{21}NO_2$ (367.45): C 81.72, H 5.76, N 3.81; found: C 81.51, H 5.74, N 3.70.

3-(But-2-enylidene)-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (**3c**). From **1a** (9.75 g, 30 mmol), LDA (60 mmol), and **2b** (12.4 ml, 150 mmol) in 150 ml of THF: 7.0 g (77%) of **3c** (mixture of isomers). Separation by CC.

(3E,2'E)-**3c**: R_f 0.48: 2.7 g (29%). Yellow crystals. M.p. 158–159° (MeOH). IR: 3090, 3060, 3030, 3015, 2960, 2940, 2910, 2840 (CH), 1735 (CO), 1690, 1635 (C=C). ^{1}H-NMR (250 MHz): 1.71 (*dd*, J = 5.5, −1.5, Me); 3.73 (*s*, MeO); (*d*, J = −1.5, H–C(4)); 5.81 (*m*, H–C(2')); 5.97 (*m*, H–C(3')); 6.62 (*d*, H–C(1')); 6.73–7.48 (*m*, 9 arom. H). Anal. calc. for $C_{20}H_{19}NO_2$ (305.38): C 78.66, H 6.27, N 4.59; found: C 78.86, H 6.18, N 4.51.

(3Z,2'E)-**3c**: R_f 0.70: 3.2 g (35%). Yellow crystals. M.p. 169–170° (MeOH). IR: 3060, 3037, 3010, 2960, 2940, 2910, 2840 (CH), 1725 (CO), 1690, 1685, 1635 (C=C). ^{1}H-NMR (400 MHz): 1.82 (*dd*, J = 6.75, −1.5, Me); 3.72 (*s*, MeO); 5.27 (*s*, H–C(4)); 5.86 (*dq*, J = 15, 6.75, H–C(3')); 5.95 (*d*, J = 11.25, H–C(1')); 6.89 (*m*, J = 15, 11.25, −1.5, H–C(2')); 6.75–7.37 (*m*, 9 arom. H). Anal. calc. for $C_{20}H_{19}NO_2$ (305.38): C 78.66, H 6.27, N 4.59; found: C 78.76, H 6.22, N 4.50.

1-(4-Methoxyphenyl)-3-(2-methylprop-2-enylidene)-4-phenylazetidin-2-one (**3d**). From **1a** (9.75 g, 30 mmol), LDA (60 mmol), and **2c** (17.9 ml, 300 mmol) in 150 ml of THF: 6.6 g (72%) of **3d** (mixture of isomers). Separation by CC.

(E)-**3d**: R_f 0.46: 1.2 g (24%). Yellow crystals. M.p. 156–157° (MeOH). IR: 3080, 3055, 3030, 3005, 2970, 2930, 2835 (CH), 1730 (CO), 1680 (C=C). ^{1}H-NMR (400 MHz): 1.57 (*s*, Me); 3.70 (*s*, MeO); 5.12 (*d*, J = −1.5, $=CH_Z$); 5.20 (br. *s*, $=CH_E$); 5.35 (*d*, J = −1.5, H–C(4)); 6.75 (*d*, J = −1.5, H–C(1')); 6.7–7.5 (*m*, 9 arom. H). Anal. calc. for $C_{20}H_{19}NO_2$ (305.38): C 78.66, H 6.27, N 4.59; found: C 78.62, H 6.20, N 4.50.

(Z)-**3d**: R_f 0.63: 3.0 g (33%). Yellowish crystals. M.p. 147–148° (MeOH). IR: 3070, 3015, 2970, 2950, 2930, 2840 (CH), 1720 (CO). ^{1}H-NMR (400 MHz): 2.24 (*t*, J = −1.5, Me); 3.72 (*s*, MeO); 5.14 (*m*, H_Z–C(3'), H–C(1')); 5.22 (*d*, J = −1.5, H_E–C(3')); 5.92 (*t*, J = −1.5, H–C(4)); 6.77–7.47 (*m*, 9 arom. H). Anal. calc. for $C_{20}H_{19}NO_2$ (305.38): C 78.66, H 6.27, N 4.59; found: C 78.94, H 6.27, N 4.47.

1-(4-Methoxyphenyl)-3-(3-methylbut-2-enylidene)-4-phenylazetidin-2-one (**3e**). From **1a** (3.25 g, 10 mmol), LDA (20 mmol), and **2d** (5.95 ml, 100 mmol): 2.41 g (76%) of **3e** (mixture of isomers). Separation by CC.

(E)-**3e**: R_f 0.62: 810 mg (25%). Light-yellow crystals. M.p. 199° (MeOH). IR: 3070, 3040, 3000, 2970, 2940, 2910, 2840 (CH), 1725 (CO), 1675, 1635 (C=C). ^{1}H-NMR (250 MHz): 1,73, 1.79 (2*s*, 2 Me); 3.73 (*s*, MeO); 5.40 (*d*, J = −1.5, H–C(4)); 5.60 (*dd*, J = 12, −1.5, H–C(2')); 6.91 (*dd*, J = 12, −1.5, H–C(1')); 6.7–7.5 (*m*, 9 arom. H). Anal. calc. for $C_{21}H_{21}NO_2$ (319.41): C 78.97, H 6.63, N 4.39; found: C 78.74, H 6.55, N 4.48.

(Z)-**3e**: R_f 0.70: 1.3 g (41%). Yellow crystals. M.p. 173° (MeOH). IR: 3080, 3040, 3005, 2965, 2935, 2910, 2840 (CH), 1720 (CO), 1675, 1635 (C=C). ^{1}H-NMR (250 MHz): 1.73, 1.88 (2*s*, 2 Me); 3.73 (*s*, MeO); 5.29 (*s*,

H–C(4)); 6.22 (*d*, *J* = 13, H–C(1′)); 6.74 (*d*, *J* = 13, H–C(2′)); 6.8–7.4 (*m*, 9 arom. H). Anal. calc. for $C_{21}H_{21}NO_2$ (319.41): C 78.97, H 6.63, N 4.39; found: C 78.90, H 6.67, N 4.47.

1-(4-Methoxyphenyl)-3-(3-methylcyclopent-2-enylidene)-4-phenylazetidin-2-one (**5a**). From **1a** (3.25 g, 10 mmol), LDA (20 mmol), and 3-methylcyclopent-2-en-1-one (10 g, 100 mmol): 1.38 g (42%) of **5a** (mixture of isomers). Yellowish crystals. Anal. calc. for $C_{22}H_{21}NO_2$ (331.42): C 79.73, H 6.39, N 4.23; found: C 79.54, H 6.36, N 4.34. MS (70 eV): 333 (1, $[M+2]^+$), 332 (17, $[M+1]^+$), 331 (64, M^+), 181 (100). Separation by CC.

(E)-**5a**: R_f 0.73: 250 mg (8%). Light-yellow crystals. M.p. 216° (MeOH). IR: 3090, 3010, 2980, 2945, 2920, 2850 (CH), 1715 (CO), 1680 (C=C). ^{1}H-NMR (400 MHz): 1.84 (*m*, *J* = –1.5, Me); 2.45 (*m*, CH_2); 2.95 (*m*, CH_2); 3.71 (*s*, MeO); 5.78 (*s*, H–C(4)); 5.65 (*q*, *J* = –1.5, H–C(1′)); 6.7–7.45 (*m*, 9 arom. H).

(Z)-**5a**: R_f 0.77: 600 mg (18%). Light-yellow crystals. M.p. 193° (MeOH). IR: 3080, 3050, 3005, 2970, 2950, 2930, 2910, 2840 (CH), 1715 (CO). ^{1}H-NMR (400 MHz): 1.90 (*d*, *J* = –1.5, Me); 2.07, 2.35 (*m*, CH_2CH_2); 3.71 (*s*, MeO); 5.25 (*s*, H–C(4)); 6.62 (*q*, *J* = –1.5, H–C(1′)); 6.7–7.4 (*m*, 9 arom. H).

3-(Cyclohex-2-enylidene)-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (**5b**). From **1a** (3.25 g, 10 mmol), LDA (20 mmol), and cyclohex-2-enone (9.61 g, 100 mmol): 2.22 g (67%) of **5b** (mixture of isomers). Light-yellow crystals. M.p. 170° (MeOH). R_f 0.69. IR: 3070, 3030, 2995, 2930, 2830 (CH), 1720 (CO). ^{1}H-NMR (400 MHz): 1.52–2.96 (*m*, *J* = 9.75, 4.05, –1.8, 3 CH_2); 3.71 (*s*, MeO); 5.30 (*Z*), 5.32 (*E*) (2*s*, H–C(4)); 5.85 (*E*), 7.08 (*Z*) (2*dt*, *J* = 9.75, –1.8, H–C(1′)); 6.05 (*E*), 6.11 (*Z*) (2*dt*, *J* = 9.75, 4.05, H–C(2′)); 6.75–7.45 (*m*, 9 arom. H). Anal. calc. for $C_{22}H_{21}NO_2$ (331.42): C 79.73, H 6.39, N 4.23; found: C 79.44, H 6.38, N 4.12.

3-(Cyclohept-2-enylidene)-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (**5c**). From **1a** (3.25 g, 10 mmol), LDA (20 mmol), and cyclohept-2-enone (5.5 g, 50 mmol): 1.58 g (45%) of **5c** (mixture of isomers). Light-yellow crystals. M.p. 157° (MeOH). R_f 0.71. IR: 3080, 3060, 3020, 2930, 2855, 2830 (CH), 1720 (CO), 1685 (C=C). ^{1}H-NMR: 1.50, 2.17 (*m*, 4 CH_2); 3.67 (*s*, MeO); 5.25 (*s*, H–C(4)); 5.92 (*m*, H_Z–C(1′), H_Z–C(2′), H_E–C(2′)); 6.6–7.55 (*m*, H_E–C(1′), 9 arom. H). $C_{23}H_{23}NO_2$ (345.44). MS (70 eV): 347 (1, $[M+2]^+$), 346 (26, $[M+1]^+$), 345 (100, M^+), 344 (16, $[M-1]^+$).

Diels-Alder *Reaction. General Procedure.* The β-lactam **3** and an excess (10–50%) of the dienophile are dissolved in an appropriate amount of THF and refluxed for the time indicated. The solvent is evaporated, and the residue is recrystallized or purified as noted.

1-Oxo-2,3,7-triphenyl-2-azaspiro[3.5]non-8-ene-5,5,6,6-tetracarbonitrile (**6a**). From (3*Z*,2′*E*)-**3a** (300 mg, 1 mmol) and tetracyanoethylene (TCNE; 300 mg, 2.34 mmol), 3 d: 420 mg (91%) of **6a**. Colorless crystals. M.p. 197° (dec., MeOH). IR: 3070, 3030 (CH), 2255 (CN), 1760 (CO), 1600, 1490 (Ar). ^{1}H-NMR: 4.28 (*s*, H–C(7)); 5.76 (*s*, H–C(3)); 5.91 (*s*, H–C(9), H–C(8)); 6.99–7.70 (*m*, 15 arom. H). ^{13}C-NMR: 45.30 (C(4)); 46.89 (C(5), C(6)); 61.30 (C(7)); 64.83 (C(3)); 108.11, 109.24, 109.86, 110.71 (4 CN); 118.36, 122.23, 125.97, 128.48, 129.08, 129.40, 129.46, 129.54, 129.69, 130.22, 130.27, 130.60, 131.69, 132.26, 135.52 (arom. C); 158.79 (CO). Anal. calc. for $C_{30}H_{19}N_5O$ (465.52): C 77.40, H 4.11, N 15.04; found: C 77.66, H 4.25, N 15.00.

2-(4-Methoxyphenyl)-1-oxo-3,7-diphenyl-2-azaspiro[3.5]non-8-ene-5,5,6,6-tetracarbonitrile (**6b**). *a*) From (3*Z*,2′*E*)-**3b** (300 mg, 0.8 mmol) and TCNE (300 mg, 2.34 mmol), 3 d. *b*) From: (3*E*,2′*E*)-**3b** (300 mg, 0.8 mmol) and TCNE (300 mg, 2.34 mmol), 16 d; purification by CC ($CHCl_3$): *a*) 310 mg (78%), *b*) 15 mg (4%) of **6b**. Yellowish crystals. M.p. 201° (dec., MeOH). IR: 3070, 3040, 3010, 2940, 2840 (CH), 2260 (CN), 1765 (CO), 1510 (Ar). ^{1}H-NMR: 3.75 (*s*, MeO); 4.38 (*s*, H–C(7)); 5.68 (*s*, H–C(3)); 5.90 (*s*, H–C(9), H–C(8)); 6.70–7.58 (*m*, 14 arom. H). Anal. calc. for $C_{31}H_{21}N_5O_2$ (495.55): C 75.14, H 4.27, N 14.13; found: C 75.00, H 4.37, N 14.08.

2-(4-Methoxyphenyl)-7-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,5,6,6-tetracarbonitrile (**6c**). From (3*Z*,2′*E*)-**3c** (500 mg, 1.67 mmol) and TCNE (500 mg, 3.9 mmol), 24 h: 388 mg (54%) of **6c**. Colorless crystals. M.p. 198° (dec., MeOH). IR: 3060, 3010, 2980, 2930, 2830 (CH), 2255 (CN), 1750 (CO), 1590 (Ar). ^{1}H-NMR: 1.48 (*d*, *J* = 7, Me); 3.31 (*q*, *J* = 7, H–C(7)); 3.71 (*s*, MeO); 5.60 (*s*, H–C(3)); 5.66 (*s*, H–C(9), H–C(8)); 6.68–7.48 (*m*, 9 arom. H). Anal. calc. for $C_{26}H_{19}N_5O_2$ (433.47): C 72.04, H 4.42, N 16.16; found: C 71.94, H 4.49, N 16.05.

2-(4-Methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,5,6,6-tetracarbonitrile (**6d**). *a*) From (*Z*)-**3d** (500 mg, 1.67 mmol) and TCNE (500 mg, 3.9 mmol), 1 h. *b*) From: (*E*)-**3d** (500 mg, 1.67 mmol) and TCNE (500 mg, 3.9 mmol), 8 d: *a*) 420 mg (58%), *b*) 350 mg (48%) of **6d**. Colorless crystals. M.p. 198–199° (dec., MeOH). IR: 3070, 3010, 2950, 2930, 2830 (CH), 2250 (CN), 1765–1750 (CO), 1585, 1510 (Ar). ^{1}H-NMR (400 MHz): 1.70 (*s*, MeO); 2.97, 3.10 (2*d*, each *J* = –18.75, 2 H–C(7)); 3.76 (*s*, MeO); 5.39 (*q*, *J* = –1.5, H–C(9)); 5.58 (*s*, H–C(3)); 6.79–7.44 (*m*, 9 arom. H). ^{13}C-NMR: 23.14 (Me); 36.25 (C(5), C(6)); 37.69 (CH_2); 55.51 (MeO); 62.58 (C(4)); 64.49 (C(3)); 108.5, 110.05, 110.15, 112.0 (4 CN); 114.71, 115.17, 119.70, 128.15, 128.50, 128.75, 128.93, 129.33, 129.98 (olefin. and arom. C), 131.46, 134.27, 157.41 (quart. arom. C), 159.00 (CO). Anal. calc. for $C_{26}H_{19}N_5O_2$ (433.47): C 72.04, H 4.42, N 16.16; found: C 72.16, H 4.48, N 16.00.

2-(4-Methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,6 dicarboxylic Acid 5,6-Anhydride (**7a**). From (*Z*)-**3d** (1.0 g, 3.34 mmol) and maleic anhydride (1.2 g, 12.2 mmol), 24 h: 935 mg (69%) of **7a**. Colorless crystals. M.p. 193° (MeOH). IR: 3070, 3040, 3010, 2960, 2940, 2010, 2840 (CH), 1860, 1780, 1735 (CO), 1510 (Ar).

^{1}H-NMR (400 MHz): 1.67 (*s*, Me); 2.46 (*d*, $J = -15, -1.5$, H_{cis}–C(7)); 3.23 (*ddd*, $J = -15, 7.5, -1.5$, H_{trans}–C(7)); 3.73 (*dt*, $J = 9.75, 7.5, -1.5$, H–C(6)); 3.75 (*s*, MeO); 3.82 (*d*, $J = 9.75$, H–C(5)); 4.96 (*s*, H–C(9)); 5.82 (*s*, H–C(3)); 6.78–7.41 (*m*, 9 arom. H). ^{13}C-NMR: 24.59 (Me); 30.89 (CH_2); 40.48, 46.84 (C(5), C(6)); 56.03 (MeO); 60.73 (C(4)); 62.49 (C(3)); 114.69, 117.22, 119.12, 127.19, 127.77, 128.93, 129.25, 130.62, 133.86, 141.41, 156.68 (olefin. and arom. C); 165.71, 173.64, 177.74 (3 CO). Anal. calc. for $C_{24}H_{21}NO_5$ (403.44): C 71.45, H 5.25, N 3.47; found: C 71.18, H 5.33, N 3.42.

2-(4-Methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,6-dicarboximide (**7b**). From (*Z*)-**3d** (1.0 g, 3.34 mmol) and maleimide (1.0 g, 10.33 mmol), 4 h: 784 mg (59%) of **7b**. Yellow crystals. M.p. 247–248° (MeOH). IR: 3190 (NH), 3090, 3050, 2950, 2860 (CH), 1775, 1710, 1745 (CO), 1510 (Ar). ^{1}H-NMR (400 MHz): 1.63 (*s*, Me); 2.42 (*dd*, $J = -15, -1.5$, H_{cis}–C(7)); 3.16 (*ddd*, $J = 15, 7.5, -1.5$, H_{trans}–C(7)); 3.43 (*dt*, $J = 9.75, 7.5, -1.5$, H–C(6)); 3.62 (*d*, $J = 9.75$, H–C(5)); 3.71 (*s*, MeO); 4.90 (*s*, H–C(9)); 5.96 (*s*, H–C(3)); 6.78–7.40 (*m*, 9 arom. H); 8.08 (br. *s*, NH). Anal. calc. for $C_{24}H_{22}N_2O_4$ (402.45): C 71.63, H 5.51, N 6.96; found: C 71.46, H 5.59, N 6.88.

*2-(4-Methoxyphenyl)-8-methyl-1-oxo-3,*N*-diphenyl-2-azaspiro[3.5]non-8-ene-5,6-dicarboximide* (**7c**). From (*Z*)-**3d** (1.0 g, 3.34 mmol) and *N*-phenylmaleimide (1.16 g, 6.68 mmol), 2.5 h: 540 mg (34%) of **7c**. Colorless crystals. M.p. 161° (dec., MeOH). IR: 3100, 3070, 3040, 3000, 2965, 2930, 2840 (CH), 1740, 1710 (CO), 1600, 1510 (Ar). ^{1}H-NMR (400 MHz): 1.67 (*s*, Me); 2.55 (*dd*, $J = -15, -1.5$, H_{cis}–C(7)); 3.29 (*ddd*, $J = 15, 7.5, -1.5$, H_{trans}–C(7)); 3.55 (*dt*, $J = 9.75, 7.5, -1.5$, H–C(6)); 3.72 (*d*, $J = 9.75$, H–C(5)); 3.75 (*s*, MeO); 4.96 (*s*, H–C(9)); 6.02 (*s*, H–C(3)); 6.78–7.50 (*m*, 14 arom. H). Anal. calc. for $C_{30}H_{26}N_2O_4$ (478.55): C 75.30, H 5.48, N 5.85; found: C 75.48, H 5.42, N 5.89.

2-(4-Methoxyphenyl)-7-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,6-dicarboximide (**7d**). From (3*Z*,2′*E*)-**3c** (530 mg, 1.74 mmol) and maleimide (600 mg, 6.2 mmol), 6.5 h: 350 mg (50%) of **7d**. Colorless crystals. M.p. 234° (dec., MeOH). IR: 3190 (NH), 3080, 3040, 2980, 2940, 2880, 2840 (CH), 1780, 1745, 1715 (CO), 1595, 1515 (Ar). ^{1}H-NMR (250 MHz): 1.35 (*d*, $J = 9$, Me); 3.36 (*t*, $J = 9$, H–C(6)); 3.56 (*m*, H–C(7)); 3.70 (*d*, $J = 9$, H–C(5)); 3.75 (*s*, MeO); 5.21, 5.72 (2*d*, $J = 10, -1.5$, H–C(9), H–C(8)); 5.93 (*s*, H–C(3)); 6.75–7.43 (*m*, 9 arom. H); 8.48 (br. *s*, NH). Anal. calc. for $C_{24}H_{22}N_2O_4$ (402.45): C 71.63, H 5.51, N 6.96; found: C 71.04, H 5.62, N 6.89.

5-(Methoxycarbonyl)-2-(4-methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-6-carboxylic Acid (**8a**). Compound **7a** (500 mg, 1.2 mmol) is refluxed in MeOH (50 ml) for 1 h. After cooling to r.t., the solvent is evaporated: 480 mg (92%) of **8a**. Colorless crystals. M.p. 203° (MeOH). IR: 3200 (OH), 3060, 3030, 3010, 2960, 2930, 2830 (CH), 1750–1720 (CO), 1695 (CO(OH)), 1585, 1510, 1495 (Ar). ^{1}H-NMR (400 MHz): 1.59 (*s*, Me); 2.42 (*m*, CH_2); 3.74 (*s*, 2 MeO); 3.76 (*m*, H–C(5), H–C(6)); 4.96 (*s*, H–C(9)); 5.55 (*s*, H–C(3)); 6.76–7.38 (*m*, 9 arom. H); 7.75 (br. *s*, COOH). ^{13}C-NMR: 23.55 (*Me*–C(8)); 29.49 (CH_2); 38.84, 45.50 (C(5), C(6)); 52.15 (COO*Me*); 55.42 (MeO); 61.57 (C(4)); 65.02 (C(3)); 114.42, 114.97, 118.96, 127.16, 127.72, 128.34, 128.72, 130.83, 134.42, 139.30, 156.29, (olefin. and arom. C), 167.19, 173.73, 175.79 (3 CO). Anal. calc. for $C_{25}H_{25}NO_6$ (435.48): C 68.95, H 5.79, N 3.22; found: C 68.88, H 5.75, N 3.11.

Dimethyl 2-(4-Methoxyphenyl)-8-methyl-1-oxo-3-phenyl-2-azaspiro[3.5]non-8-ene-5,6-dicarboxylate (**8b**). Compound **7a** (1.11 g, 2.75 mmol) is refluxed with abs. MeOH (200 ml) and conc. H_2SO_4 (5 ml) for 8 h. After cooling to r.t., the solvent is evaporated and the crystalline residue, 860 mg of a mixture **8a**/**8b**, is separated by CC with $CHCl_3$: 53 mg (4.3%) of **8b**, R_f 0.42. Colorless crystals. M.p. 130° (MeOH). IR: 3070, 3040, 3005, 2960, 2910, 2840 (CH), 1750–1740 (CO), 1590, 1515 (Ar). ^{1}H-NMR (90 MHz): 1.65 (*s*, Me); 2.34 (*m*, 2 H–C(7)); 3.75 (*m*, C(5), C(6), 2 COO*Me*, MeO); 4.90 (*s*, H–C(9)); 5.50 (*s*, H–C(3)); 6.73–7.51 (*m*, 9 arom. H). $C_{26}H_{27}NO_6$ (449.51). MS: 449 (30 M^+), 182 (100).

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