Synthesis and Transformations of Urazoles Derived from 7,7-Dicarboxynorcaradiene: Formation of 2,4-Dioxohexahydro-1,3,5-triazines by an Unusual Base-Catalyzed Rearrangement

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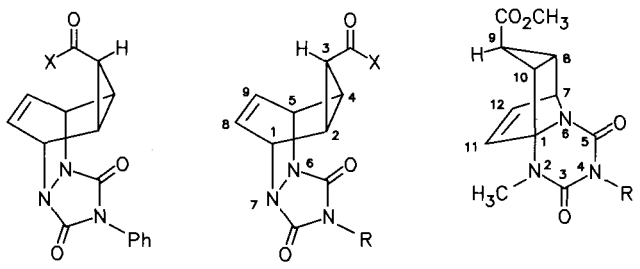
4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) or 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) cycloaddition to the 7-cycloheptatrienecarboxylates gave the *endo*-urazoles **1**. With the 7,7-cycloheptatrienedicarboxylates **5** the urazoles **6** were formed. Decarboxylation of urazole **6c** led to *endo*-**1b**, showing that steric factors prevent formation of the desired *exo*-**1b** isomer. Attempts to isomerize *endo*-**1b** and *endo*-**1c** by base catalysis, afforded after methylation with methyl iodide the 2,4-dioxohexahydro-1,3,5-triazine derivatives **2a,b**. This unusual rearrangement also took place with urazole **3** leading to 1,3,5-triazine **4**, but the urazoles derived from butadiene and cyclopentadiene did not respond. ^{1}H NMR differential NOE and X-ray analysis of **2b** and **6c** were necessary for the structural elucidation of the 1,3,5-triazines **2a,b**.

Synthese und Umwandlung der Urazole des 7,7-Dicarboxynorcaradiens: Bildung von 2,4-Dioxohexahydro-1,3,5-triazinen durch eine ungewöhnliche basenkatalysierte Umlagerung

Cycloaddition von 4-Phenyl-1,2,4-triazolin-3,5-dion (PTAD) oder 4-Methyl-1,2,4-triazolin-3,5-dion (MTAD) an 7-Carboxy- bzw. 7-(Methoxycarbonyl)-1,3,5-cycloheptatrien ergab die *endo*-Urazole **1**. Die 7,7-Cycloheptatriendicarboxylate **5** reagierten mit PTAD unter Bildung der Urazole **6**. Die Decarboxylierung von **6c** ergab aus sterischen Gründen nicht das gewünschte Urazol *exo*-**1b**, sondern das isomere Urazol *endo*-**1b**. Versuche, *endo*-**1b** und *endo*-**1c** durch Basenkatalyse zu isomerisieren, führen nach Reaktion mit Methyliodid zur Bildung der 2,4-Dioxohexahydro-1,3,5-triazine **2a,b**. Diese ungewöhnliche Umlagerung wurde auch im Fall des Urazols **3** beobachtet, wo sie zur Bildung des 1,3,5-Triazins **4** führte. Im Gegensatz dazu reagierten die Urazole des Butadiens und Cyclopentadiens unter diesen Bedingungen nicht. Die Strukturaufklärung der 1,3,5-Triazine **2a,b** erfolgte durch ^{1}H-NMR-NOE-Experimente und Röntgenstrukturanalyse von **2b** und **6c**.

In our synthetic utilization of triazolinedione adducts[1] we required the hitherto unknown urazole **1** with an *exo*-carboxylic acid substituent. However, cycloaddition of 4-phenyl-1,2,4-triazolin-3,5-dione (PTAD) to 7-(methoxycarbonyl)-1,3,5-cycloheptatriene afforded exclusively the urazole *endo*-**1b**[2]. In attempt to equilibrate the ester *endo*-**1b** into its isomer *exo*-**1b** by base-catalyzed reaction with a strong base like lithium diisopropylamide (LDA), the ester *endo*-**1b** was recovered. To test whether deprotonation of the *exo*-cyclopropane hydrogen in the ester *endo*-**1b** had indeed taken place, but reprotonation occurred exclusively from the *exo* side, the LDA treated reaction mixture of ester *endo*-**1b** in THF at −78 °C was allowed to react with methyl iodide under these conditions. Much to our surprise, the unusual rearrangement product **2a** was obtained in 21% yield. The NMR spectral data clearly revealed *N*-methylation, δ_H = 3.25 and δ_C = 31.81. Also, the ^{1}H-differential NOE spectroscopy exhibited enhancements of the *N*-methyl signal when the 11-H and 10-H protons were irradiated and vice versa. The unequivocal structure assignment rests, however, on X-ray analysis. For this purpose the derivative **2b** had to be prepared (isolated in 22% yield), using 4-methyl-1,2,4-triazoline-3,5-dione (MTAD), since the crystals of the PTAD-derived adduct **2a** were too severly disordered to permit structure determination. The X-ray structure of **2b** is exhibited in Figure 1.



	X
exo-1a	OH
exo-1b	OMe

	X	R
endo-1a	OH	Ph
endo-1b	OMe	Ph
endo-1c	OMe	Me

	R
2a	Ph
b	Me

Presumably steric reasons prevent access to the more acidic cyclopropane hydrogen atom adjacent to the meth-

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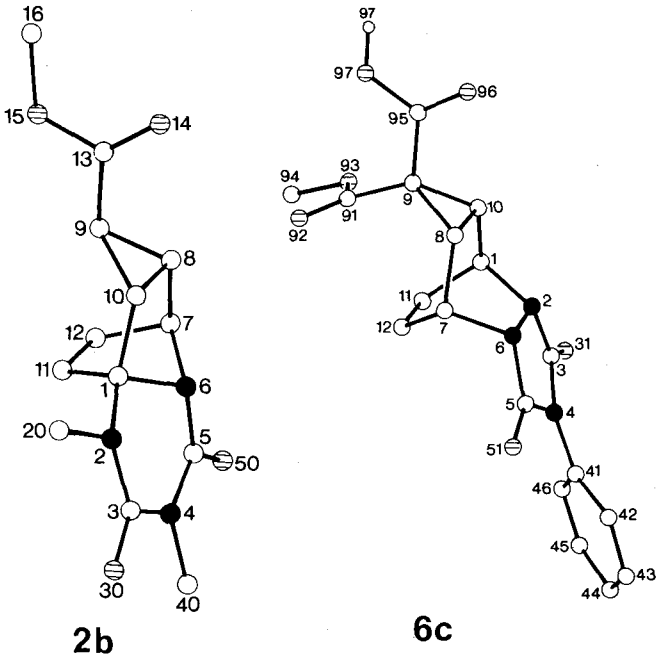
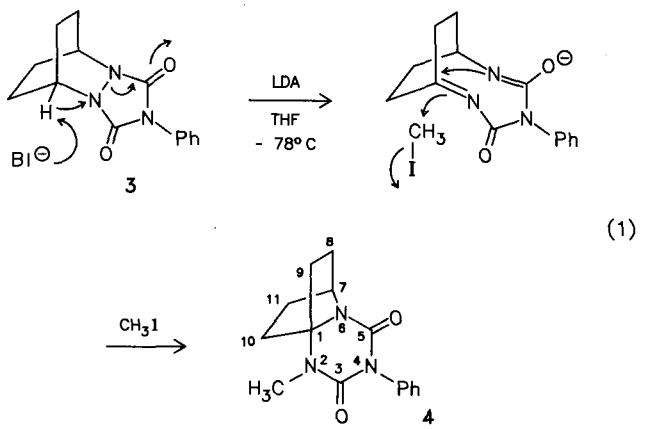


Figure 1. Perspective drawing of **2b** and **6c** with the numbering of the atoms corresponding to Tables 2 and 3; white, hatched, and black spheres represent carbon, oxygen, and nitrogen atoms, respectively

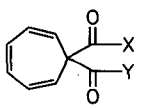
oxycarbonyl group, obliging deprotonation of the bridgehead hydrogen atom next to the urazole moiety with subsequent rearrangement. To test this hypothesis, urazole **3** was submitted to the LDA treatment followed by methylation with methyl iodide. Indeed, the corresponding rearrangement product **4** was obtained in 67% yield. A reasonable mechanism is shown in Eq. (1), in which base-catalyzed cleavage of the urazole ring and reclosure on methylation leads to the complex 2,4-dioxohexahydro-1,3,5-triazine derivative **4**. Since such substances possess antiphytoviral activity[3], an attempt was made to explore the general scope of this novel and expedient synthetic methodology. Unfortunately, the urazoles of cyclopentadiene and of 1,3-butadiene failed to respond to the sequence outlined in Eq. (1).



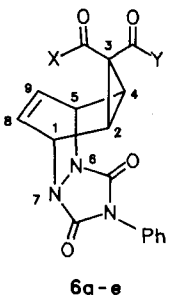
(1)

Since the base-catalyzed equilibration of *endo*-**1b** failed to give the desired *exo*-**1b**, leading instead to the unexpected 2,4-dioxohexahydro-1,3,5-triazine **2a**, an indirect synthetic pathway was sought. For example, lithiation of 7-carboxy-1,3,5-cycloheptatriene with *n*-BuLi and carboxylation gave the 7,7-dicarboxylate **5d**. Urazole **6a** was obtained by cycloadding first PTAD to dicarboxylate **5d** to give urazole **6d** and subsequent protonation, or first protonating dicarboxylate **5d** to give the dicarboxylic acid **5a** and subsequent PTAD cycloaddition to the latter. Treatment of the urazole dicarboxylic acid **6a** with diazomethane led to the urazole diester **6b**. Potassium hydroxide hydrolysis of the diester **6b** gave the half ester **6c**.

	X	Y
a	OH	OH
b	OMe	OMe
c	OMe	OH
d	$O^{\ominus}$	$O^{\ominus}$
e	$O^{\ominus}$	OMe



5a-e



6a-e

Although spectral evidence suggested that in **6c** the carboxylic acid group should be in the *endo* position and on steric grounds hydrolysis should be preferred at the *endo*-methoxycarbonyl group, thermal decarboxylation with cuprous oxide gave the *endo*-**1b** ester. Either the stereochemical assignment of the half ester **6c** was wrong, or isomerization took place during the decarboxylation. For this reason an X-ray determination was performed on the half ester **6c** to be absolutely sure of its stereochemistry. As revealed in Figure 1, the stereochemistry of the half ester **6c** was exactly as assigned. Unquestionably, inversion at the cyclopropane carbon atom bearing the carboxylic acid group took place during decarboxylation[4].

Quite analogous observations were made with 7-(methoxycarbonyl)-1,3,5-cycloheptatriene. Thus, its anion, generated with LDA, followed by carboxylation afforded the carboxylate **5e**. Protonation of **5e** led to the half ester **5c**, which on treatment with diazomethane gave 7,7-bis-(methoxycarbonyl)-1,3,5-cycloheptatriene (**5b**). Cycloaddition of the half ester **5c** with PTAD resulted in the half ester **6c**, indicating again that the carboxylic acid group preferred the *endo* position during the PTAD cycloaddition. The half ester **6c** was also obtained when the carboxylate **5e** was first allowed to react with PTAD to give the urazole **6e** which was subsequently protonated.

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Experimental

Boiling points: Uncorrected. – Melting points: Uncorrected, Reichert Thermovar apparatus. – Infrared spectra: Beckman Acculab 4. – ^{1}H NMR: Hitachi-Perkin-Elmer R-24 B (60 MHz), Var-

ian EM 390 spectrometer (90 MHz). – ^{13}C NMR: AC 200 spectrometer (200 and 50.32 MHz), Bruker WM 400 spectrometer (400 and 100.61 MHz). – Mass spectra: Varian MAT CH 7. – Elemental analyses were kindly run for us either in-house or by Professor G. Maier's staff of the University of Gießen. – Thin-layer chromatography (TLC): Polygram SIL/UV (40 × 80 mm), Machery & Nagel Co. – Column chromatography: Silica gel 70–230 mesh ASTM (activity III). – Solvents were purified according to standard literature procedures. – Known compounds were either purchased from commercial suppliers or prepared according to published methods and purified to match reported physical data. 7-(Methoxycarbonyl)-1,3,5-cycloheptatriene, 7-carboxy-1,3,5-cycloheptatriene[5], the urazoles *endo*-**1b**[2] and **3**[6] were prepared according to literature procedures.

Nuclear Overhauser Spectroscopy of 1,3,5-Triazine **2a**: The NOE experiments were carried out on a Bruker WP 200 SY instrument. The samples (in $CDCl_3$) were freed from oxygen through sonication under N_2 purging. The usual procedure for gated irradiation experiments was modified and the selected resonance was saturated by a 8-s cyclic perturbation of all lines with a 38–40 dB attenuation of a nominal 0.2 W decoupling power. The enhancements (in %) were obtained from the multiplier of the reference spectrum by bringing the observed multiplet to exact matching with the corresponding multiplet in the perturbed spectrum. Errors are ca. 3%. By careful choice of the multiplier, in most cases it was possible in the differential mode to single out a pure multiplet from a bunch of overlapping signals.

X-Ray Crystallography of the 1,3,5-Triazine **2b** *and the Urazole* **6c**: The special operations and results are listed in Table 1, the positional and thermal parameters in Table 2. The structures are exhibited in Figure 1.

Further details of the structure determination are deposited at the Fachinformationszentrum Energie Physik Mathematik, D-7514 Eggenstein-Leopoldshafen 2 (West-Germany). These data are available with quotation of the registry number CSD 52480, the authors and the reference to this publication.

endo-3-(Methoxycarbonyl)-N-methyl-6,7-diazatricyclo[3.2.2.0^{2,4}]-non-8-ene-6,7-dicarboximide (*endo*-**1c**): To a magnetically stirred solution of 1.31 g (8.72 mmol) of 7-(methoxycarbonyl)-1,3,5-cycloheptatriene in 20 ml of methylene chloride cooled by means of an ice bath, 0.986 g (8.72 mmol) of 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) was added in small portions. The reaction mixture was allowed to warm up to ca. 20°C and the solvent was rotary-evaporated. Flash chromatography on silica gel (adsorbent-substrate ratio 30:1) of the pale yellow residue eluting with methylene chloride/ethyl acetate (10:1) (R_f = 0.34) and rotary-evaporation of the solvent gave 1.96 g of a colorless powder which was recrystallized from ethanol affording 1.64 g (72%) of colorless needles, m.p. 172–173°C. – IR (KBr): 3080 cm^{-1}, 3010, 2960, 1770 (C=O), 1740–1690 (C=O), 1450, 1435, 1395, 1370, 1325, 1250, 1185, 1050, 1045, 945, 920, 895, 848, 782, 778, 762, 748, 730, 720, 705, 685, 645, 621. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.43 (t, $J_{2,3} = J_{3,4}$ = 3.1 Hz, 1H, 3-H), 2.18 (br. dd, $J_{1,2} = J_{4,5}$ = 5.0, $J_{2,3} = J_{3,4}$ = 3.1 Hz, 2H, 2,4-H), 3.02 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3), 5.16 (mc, 2H, 1,5-H), 6.11 (mc, 2H, 8,9-H). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 15.3 (d, C-2,4), 23.1 (d, C-3), 25.1 (q, NCH_3), 51.9 (d, C-1,5), 52.0 (q, OCH_3), 125.7 (d, C-8,9), 158.1 (s, imide C=O), 170.7 (s, ester C=O). – MS (70 eV): *m/z* (%) = 263 (5, M^+), 232 (1, M – OCH_3), 150 (24, M – MTAD), 118 (19), 92 (8), 91 (100, $C_7H_7^+$), 90 (9), 65 (12), 59 (5, $C_2H_3O_2^+$).

$C_{12}H_{13}N_3O_4$ (263.2) Calcd. C 54.75 H 4.96 N 15.96
Found C 55.16 H 5.11 N 16.32

Table 1. X-ray operations and results for **2b** and **6c**

crystallographic section		
compound	**2b**	**6c**
empirical formula	$C_{13}H_{15}N_3O_4$	$C_{18}H_{15}N_3O_6$
molecular mass	277.28	369.33
a [pm]	825.7(3)	1244.4(8)
b [pm]	2726.0(9)	1383.3(9)
c [pm]	630.0(2)	1100.7(9)
β [deg]	108.61(3)	92.53(6)
z	4	4
V [$pm^3 \cdot 10^{-6}$]	1343.9(8)	1892(2)
d(calcd.)	1.370	1.296
crystal system	monoclinic	
space group	$P2_1/a$	$P2_1/c$
data collection		
diffractometer	Syntex P3	
radiation	MoKα	
monochromator	graphite	
crystal size [mm]	0.7 x 1.0 x 0.45	0.85 x 0.85 x 0.1
data collect. mode	ω-scan	
theta range [deg]	1.75 - 27.5	
recip. latt. segment	h = 0 - 10	h = 0 - 16
	k = 0 - 35	k = 0 - 17
	l = $\bar{8}$ - 8	l = $\overline{14}$ - 14
no. refl. measd.	2917	1740
no. unique refl.	2700	1733
no. refl. F>3σ(F)	2649	1648
lin. absorp. coeff.	0.97	0.93
absorp. correction	ψ-scan	
structural analysis and refinement		
method of solution	direct phase determination	
method of refinement	anisotropic block diagonal matrix least squares; hydrogen positions were calculated and considered isotropically	
parameter/F_o ratio	0.068	0.159
R, R_w	0.062, 0.068	0.058, 0.072
program used	SHELXTL [7]	

Table 2. Positional (× 10^4) and thermal (× 10^3) [$Å^2$] of **2b** and **6c**. The standard deviations are given in parentheses

2b	x	y	z	U_{EQU}	6c	x	y	z	U_{EQU}
C(1)	3076(2)	1142(1)	1762(3)	41(1)	C(1)	4525(4)	1104(4)	3866(4)	41(2)
N(2)	1344(2)	1225(1)	1741(3)	50(1)	N(2)	3443(3)	629(3)	3782(3)	42(1)
C(3)	68(2)	946(1)	381(4)	52(1)	C(3)	2676(4)	869(4)	4611(4)	42(2)
N(4)	453(2)	671(1)	-1227(4)	51(1)	N(4)	1703(3)	1015(3)	3931(3)	41(1)
C(5)	1994(2)	692(1)	-1729(3)	43(1)	C(5)	1890(4)	1030(4)	2696(4)	47(2)
N(6)	3098(2)	1051(1)	-545(3)	44(1)	N(6)	2949(3)	746(3)	2563(3)	44(1)
C(7)	4977(2)	951(1)	143(4)	48(1)	C(7)	3644(4)	1336(4)	1768(4)	45(2)
C(8)	5590(2)	1459(1)	1223(4)	50(1)	C(8)	4637(4)	703(4)	1688(4)	47(2)
C(9)	6145(2)	1522(1)	3726(4)	52(1)	C(9)	5785(4)	1044(4)	1943(4)	42(2)
C(10)	4280(2)	1594(1)	2303(3)	47(1)	C(10)	5154(4)	554(4)	2928(4)	43(2)
C(11)	4024(2)	687(1)	2964(3)	47(1)	C(11)	4332(4)	2147(4)	3536(5)	44(2)
C(12)	5165(2)	576(1)	1971(4)	49(1)	C(12)	3868(4)	2267(4)	2430(5)	49(2)
C(13)	7132(3)	1970(1)	4611(4)	63(1)	O(31)	2820(3)	909(3)	5705(3)	53(1)
O(14)	7100(3)	2343(1)	3600(4)	93(1)	C(41)	671(4)	1226(4)	4408(5)	44(2)
O(15)	8127(3)	1905(1)	6721(3)	91(1)	C(42)	-248(5)	870(5)	3821(5)	56(2)
O(16)	9184(5)	2310(2)	7803(7)	126(2)	C(43)	-1240(5)	1119(5)	4233(6)	66(3)
C(20)	1057(3)	1475(1)	3630(4)	60(1)	C(44)	-1321(5)	1715(6)	5224(6)	75(3)
O(30)	-1355(2)	934(1)	546(3)	78(1)	C(45)	-397(5)	2052(5)	5826(6)	69(3)
C(40)	-875(3)	352(1)	-2705(4)	71(1)	C(46)	609(4)	1821(5)	5417(5)	53(2)
O(50)	2274(2)	438(1)	-3155(2)	58(1)	O(51)	1255(3)	1224(3)	1864(3)	61(1)
					C(91)	6083(4)	2093(4)	1952(5)	47(2)
					O(92)	5938(3)	2641(3)	1106(3)	63(2)
					O(93)	6612(3)	2328(3)	3001(3)	52(1)
					C(94)	6954(6)	3330(5)	3127(6)	74(3)
					C(95)	6586(5)	392(5)	1411(4)	51(2)
					O(96)	6417(3)	-459(3)	1184(4)	68(2)
					O(97)	7510(4)	828(4)	1231(4)	67(2)
					H(97)	8010(70)	430(66)	880(77)	162(40)
					O	1057(5)	412(5)	-546(5)	115(3)
					C	8/1(9)	1152(7)	-1390(8)	137(5)

General Procedure for the Synthesis of 1,3,5-Triazines **2a**, **2b** *and* **4**: A flame-dried three-necked flask, provided with a magnetic spinbar, rubber septum, and dropping funnel, was charged with dry THF (ca. 20 ml per mmol urazole) and dry diisopropylamine (1.5 mmol per mmol urazole) and under nitrogen cooled to −78°C. While stirring, an *n*-BuLi solution (1.2 mmol per mmol urazole) in hexane was added dropwise with a syringe. The reaction mixture was allowed to warm up to ca. 20°C, stirred 30 min at this temperature and cooled again under nitrogen to −78°C. A solution of 1 mmol urazole *endo*-**1b** (*endo*-**1c** or **3**) in ca. 15−20 ml of dry THF was added dropwise to the LDA solution at −78°C. On adding the urazole, the color of the reaction mixture changed from pale yellow to orange finally red. After 90 min stirring at −78°C, a solution of methyl iodide (ca. 6 mmol per mmol urazole) in ca. 15 ml of dry THF was added dropwise at −78°C. After 1 h additional stirring at −78°C, the solution was allowed to warm up to room temp. and stirred for about 12 h. The precipitate that formed was removed by filtration and ether (ca. 20 ml) and water (ca. 20 ml) were added to the filtrate. The organic layer was separated and the aqueous layer was extracted with ether (ca. 2 × 15 ml). The combined organic layers were washed with saturated sodium hydrogen sulfite solution (2 × 15 ml) and water (2 × 5 ml) and dried with magnesium sulfate. Rotary-evaporation of the solvent afforded the crude reaction mixtures which were worked up as described below.

Methyl (1R,7S*,8R*,9S*,10S*)-2-Methyl-3,5-dioxo-4-phenyl-2,4,6-triazatetracyclo[5.3.2.0^{1,6}.0^{8,10}]dodec-11-ene-9-carboxylate* (**2a**): Reaction of 9.00 g (27.7 mmol) of *endo*-**1b** according to the general procedure afforded 8.00 g of a dark brown solid which was allowed to pass through a short silica gel (ca. 20 g) column, eluting with ca. 500 ml of methylene chloride/ethyl acetate (10:1). Rotary-evaporation of the solvent gave 6.51 g of a brown residue which was flash-chromatographed on silica gel (adsorbent-substrate ratio 50:1) eluting with methylene chloride/ethyl acetate (4:1). The first fraction that was collected (R_f = 0.66) consisted of 2.79 g (8.58 mmol) of unreacted *endo*-**1b**. As a second fraction (R_f = 0.51), 2.42 g of a pale yellow granular solid was eluted. Recrystallization from ethanol afforded 1.96 g (5.77 mmol, 21%) of **2a** as colorless needles, m.p. 186−187°C. − IR (KBr): 3180 cm^{-1}, 2955, 1730, 1675, 1562, 1493, 1435, 1415, 1398, 1350, 1300, 1278, 1245, 1212, 1170, 1110, 1095, 885, 740. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.86 (dd, $J_{9,10}$ = $J_{8,9}$ = 2.6 Hz, 1H, 9-H), 2.57 (B part of split AB system, J_{AB} = $J_{8,10}$ = 8.7, $J_{7,8}$ = 4.8 Hz, 1H, 8-H), 2.59 (A part of split AB system, $J_{7,10}$ = −0.20 Hz, 1H, 10-H), 3.25 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3), 5.06 (mc, 1H, 7-H), 6.29 (B part of split AB system, J_{AB} = $J_{11,12}$ = 5.6, $J_{7,11}$ = 0.9 Hz, 1H, 11-H), 6.35 (A part of split AB system, $J_{7,12}$ = 2.5 Hz, 1H, 12-H), 7.10−7.38 (m, 5H, aromatic H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.1 and 25.8 (two d, C-8,10), 31.8 (q, NCH_3), 34.0 (d, C-9), 52.0 (q, OCH_3), 60.4 (d, C-7), 83.4 (s, C-1), 127.4 (d), 128.2 (d), 129.0 (d), 130.7 (d), 133.3 (d), 135.5 (s), 152.0 (s, C=O), 152.3 (s, C=O), 169.1 (s, ester C=O). − MS (70 eV): *m/z* (%) = 339 (27, M^+), 324 (64, M − CH_3), 308 (10, M − OCH_3), 307 (42, M − CH_3OH), 280 (99, M − $C_2H_3O_2$), 279 (12), 241 (100).

$C_{18}H_{17}N_3O_4$ (339.4) Calcd. C 63.71 H 5.05 N 12.38
Found C 63.71 H 4.93 N 12.27

Methyl (1R,7S*,8R*,9S*,10S*)-2,4-Dimethyl-3,5-dioxo-2,4,6-triazatetracyclo[5.3.2.0^{1,6}.0^{8,10}]dodec-11-ene-9-carboxylate* (**2b**): Reaction of 1.18 g (4.5 mmol) of *endo*-**1c** according to the general procedure gave 940 mg of a brown oil, which was flash-chromatographed on silica gel (adsorbent-substrate ratio 50:1) eluting with methylene chloride/ethyl acetate (4:1) (R_f = 0.48), affording 396 mg of a colorless, sticky oil. The oil was crystallized twice from ethanol, yielding 279 mg (22%) of **2b** as colorless needles, m.p. 149−151°C. − IR (KBr): 3130 cm^{-1}, 3075, 2950, 1735, 1712, 1670, 1560, 1470, 1443, 1420, 1390, 1360, 1295, 1280, 1247, 1210, 1200, 1272, 1065, 960, 847, 790, 755, 687. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.79 (dd, $J_{8,9}$ = $J_{9,10}$ = 2.6 Hz, 1H, 9-H), 2.45−2.56 (m, 2H, 8,10-H), 3.13 (s, 3H, NCH_3), 3.20 (s, 3H, NCH_3), 3.67 (s, 3H, OCH_3), 4.98−5.04 (m, 1H, 7-H), 6.18 (B part of split AB system, J_{AB} = $J_{11,12}$ = 5.6, $J_{7,11}$ = 0.7 Hz, 1H, 11-H), 6.28 (A part of split AB system, $J_{7,12}$ = 2.4 Hz, 1H, 12-H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.1 and 25.8 (two d, C-8,10), 28.5 (q, NCH_3), 31.9 (q, NCH_3), 34.0 (d, C-9), 52.2 (q, OCH_3), 60.3 (d, C-7), 83.2 (s, C-1), 130.9 and 133.0 (two d, C-11,12). − MS (70 eV): *m/z* (%) = 277 (3, M^+), 262 (54, M − CH_3), 245 (28, M − CH_3OH), 218 (100, M − $C_2H_3O_2$), 217 (20, M − $C_2H_4O_2$).

$C_{13}H_{15}N_3O_4$ (277.3) Calcd. C 56.31 H 5.43 N 15.15
Found C 56.50 H 5.56 N 15.28

The X-ray structure of **2b** is displayed in Figure 1, and the data are summarized in Tables 1 and 2.

(1S,7R*)-2-Methyl-4-phenyl-2,4,6-triazatricyclo[5.2.2.0^{1,6}]undecane-3,5-dione* (**4**): Reaction of 771 mg (3.0 mmol) of **3** according to the general procedure afforded after recrystallization from ethyl acetate 545 mg (67%) of **4** as colorless needles, m.p. 180−182°C. − IR (KBr): 3020 cm^{-1}, 2960, 2920, 1710, 1675, 1490, 1475, 1445, 1420, 1360, 1330, 1315, 1245, 1185, 760, 740, 690. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.58−2.48 (m, 8H), 3.08 (s, 3H, CH_3), 4.55 (ps-t, *J* = 4.7 Hz, 1H, 7-H), 7.18−7.44 (m, 5H, aromatic H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.9 (t), 30.7 (q, CH_3), 34.2 (t), 55.6 (d, C-7), 78.4 (s, C-1), 128.0 (d), 128.8 (d), 129.2 (d), 135.0 (s), 152.0 (s, C=O), 152.1 (s, C=O). − MS (70 eV): *m/z* (%) = 271 (89, M^+), 243 (100, M − CO), 123 (25), 119 (48), 96 (63).

$C_{15}H_{17}N_3O_2$ (271.3) Calcd. C 66.40 H 6.32 N 15.49
Found C 66.69 H 6.42 N 15.73

3,3-Bis(methoxycarbonyl)-N-phenyl-6,7-diazatricyclo[3.2.2.0^{2,4}]non-8-ene-6,7-dicarboximide (**6b**) *via 3,3-Dicarboxy-N-phenyl-6,7-diazatricyclo[3.2.2.0^{2,4}]non-8-ene-6,7-dicarboximide* (**6a**): A 100-ml three-necked flask, provided with a magnetic spinbar, nitrogen inlet and outlet tubes, and rubber septum, was charged with 500 mg (3.70 mmol) of 1,3,5-cycloheptatriene-7-carboxylic acid in 60 ml of dry THF and cooled to −78°C under nitrogen. While stirring, 4.8 ml of a 1.7 N *n*-BuLi solution in hexane was added dropwise with a syringe. After 30 min stirring at −78°C, a stream of dry carbon dioxide was bubbled through the dark blue colored dianion solution, until complete decoloration (ca. 3−5 min), leading to a pale yellow reaction mixture. The mixture was allowed to warm up to ca. 20°C and while stirring was added 500 mg (4.40 mmol) of PTAD. After 30 min the resulting mixture was acidified with 6 N HCl until pH ca. 3, extracted with ether (3 × 15 ml), the combined ether extracts were dried with magnesium sulfate, the solvent was rotary-evaporated and the residue recrystallized from THF/hexane, affording 810 mg (75%) of white powder, m.p. 173−175°C (with gas evolution). Final characterization was achieved by treatment of the carboxylic acid **6a** with excess diazomethane in ether at 0°C, resulting after recrystallization from methylene chloride/hexane 769 mg (88%) of **6b** as colorless granular solid, m.p. 180−182°C. − IR (KBr): 3050 cm^{-1}, 3000, 1775, 1715, 1600, 1500, 1455, 1435, 1402, 1325, 1235, 1200, 1160, 1140, 1100, 1050, 1020, 953, 900. − ^{1}H NMR ($CDCl_3$, 90 MHz): δ = 2.50 (ps-t, *J* = 3.0 Hz, 2H, 2,4-H), 3.69 (s, 3H, *exo*-CH_3), 3.74 (s, 3H, *endo*-CH_3), 5.45 (m, 2H, 1,5-H), 6.10 (ps-t, *J* = 3.8 Hz, 2H, 8,9-H), 7.5 (m, 5H, aromatic H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.6 (d, C-2,4), 38.1 (s, C-3), 51.7 (d, C-1,5), 52.4 (q, CH_3), 53.3 (q, CH_3), 125.5 (d, C-8,9), 126.8, 128.3, 129.1, 131.5, 156.7 (s), 166.4 (s), 168.3 (s). − MS (70 eV): *m/z*

(%) = 384 (2, M^+), 324 (7, M − $C_2H_3O_2$), 232 (6, M − PTAD), 176 (74), 149 (100), 90 (55), 59 (18, $C_2H_3O_2^+$).

$C_{19}H_{17}N_3O_6$ (383.3) Calcd. C 59.53 H 4.47 N 10.96
Found C 59.43 H 4.37 N 10.78

exo-3-(Methoxycarbonyl)-endo-3-carboxy-N-phenyl-6,7-diazatricyclo[3.2.2.0^{2,4}]non-8-ene-6,7-dicarboximide (**6c**): A 100-ml three-necked flask, provided with a magnetic spinbar, nitrogen inlet and outlet, and a rubber septum, was charged with 1.01 g (10.0 mmol) of freshly destilled diisopropylamine and 60 ml of dry THF. Under nitrogen the contents were cooled to −60°C and while stirring was added dropwise 7.0 ml of a 1.7 N *n*-BuLi solution in hexane by a syringe. The mixture was allowed to warm up to ca. 20°C, after 30 min was cooled to −78°C, and while stirring and under nitrogen was added dropwise 1.35 g (8.96 mmol) of 7-(methoxycarbonyl)-1,3,5-cycloheptatriene in ca. 3 ml of dry THF by a syringe, forming the characteristic deep blue colored solution of the dianion. After 30 min stirring at −78°C, a stream of dry carbon dioxide was passed through the solution until complete decoloration (ca. 5 min), leading to a clear yellow solution. After ca. 30 min stirring, the reaction mixture was allowed to warm up to ca. 20°C and a solution of 1.00 g (8.80 mmol) of PTAD in 10 ml of dry THF was added dropwise by a syringe. After 30 min additional stirring, the reaction mixture was neutralized to pH ca. 3 with 6 N HCl, diluted with ca. 100 ml of water, extracted with ether (3 × 50 ml), the combined ether extracts were dried with magnesium sulfate and after rotary-evaporation of the solvent the residue was recrystallized from methylene chloride/hexane/THF affording 2.67 g (80%) of **6c** as colorless granular solid, m.p. 116−118°C. − IR (KBr): 3600−3100 cm^{-1}, 2975, 1715, 1500, 1460, 1445, 1415, 1330, 1250, 1204, 1175, 1100, 1025, 1010. − ^1H NMR ($CDCl_3$, 90 MHz): δ = 2.60 (ps-t, *J* = 2.7 Hz, 2H, 2,4-H), 3.70 (s, 3H, CH_3), 5.40 (s, 1H, OH), 5.5 (m, 2H, 1,5-H), 6.20 (ps-t, *J* = 3.9 Hz, 2H, 8,9-H), 7.45 (br. s, 5H, aromatic H). − MS (70 eV): *m/z* (%) = 369 (0.1, M^+), 325 (3, M − CO_2H), 266 (2), 150 (31, $PTAD^+$), 119 (27), 118 (26), 91 (100, C_7H_7), 59 (6).

$C_{18}H_{15}N_3O_6$ (369.1) Calcd. C 58.52 H 4.09 N 11.37
Found C 58.87 H 4.23 N 10.56

The X-ray structure of **6c** is displayed in Figure 1, and the data are summarized in Tables 1 and 2.

6b *from* **6c**: To a solution of 700 mg (2.12 mmol) of **6c** in 20 ml of ether was added dropwise while stirring magnetically a solution of diazomethane in ether until persistence of the yellow color. After stirring for an additional 15 min, a few drops of acetic acid was added for destruction of the excess diazomethane, the solvent rotary-evaporated and the residue recrystallized from methylene chloride/hexane, resulting in 620 mg (88%) of a colorless granular solid, m.p. 180−182°C. The spectral data were identical to that described above in the conversion of **6a** into **6b**.

endo-3-(Methoxycarbonyl)-N-phenyl-6,7-diazatricyclo[3.2.2.0^{2,4}]-non-8-ene-6,7-dicarboximide (*endo*-**1b**) *from Half Ester* **6c**: A 100-ml flask, provided with a magnetic spinbar and a reflux condenser, was charged with 500 mg (1.35 mmol) of **6c** in 20 ml of DMF/toluene (9:1) and ca. 700 mg of copper(I) oxide. The mixture was heated at ca. 130°C for 2 h while stirring, the solids were removed by filtration and the solvent was rotary-evaporated (ca. 70°C/15 Torr). The residue was chromatographied on silica gel (substrate-adsorbent ratio ca. 1:50) eluting with dichloromethane/ether (9:1). Recrystallization from dichloromethane/hexane afforded 286 mg (65%) of a colorless solid, m.p. 186−188°C (ref.[2a] m.p. 187°C).

CAS Registry Numbers

1b: 65138-04-7 / **1c**: 109746-62-5 / **2a**: 109746-63-6 / **2b**: 109746-67-0 / **3**: 30169-55-2 / **4**: 109746-64-7 / **6a**: 109764-59-2 / **6b**: 109746-65-8 / **6c**: 109746-66-9 / MTAD: 13274-43-6 / PTAD: 4233-33-4 / 7-(methoxycarbonyl)-1,3,5-cycloheptatriene: 32399-46-5 / 1,3,5-cycloheptatriene-7-carboxylic acid: 4440-40-8

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