

**New Chiral Auxiliaries and New Optically Pure Ketene Equivalents Derived from Tartaric Acids.  
Improved Synthesis of (-)-7-Oxabicyclo[2.2.1]hept-5-en-2-one.**

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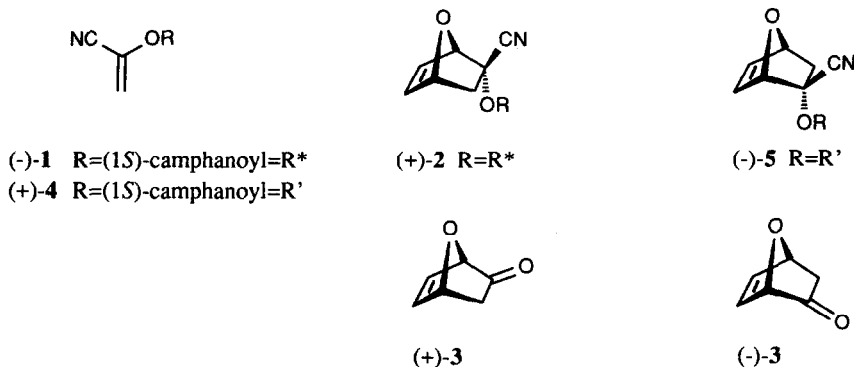
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(Received 22 August 1990)

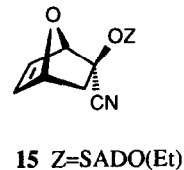
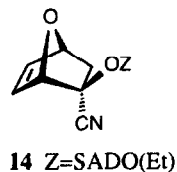
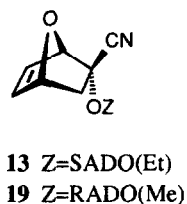
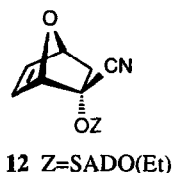
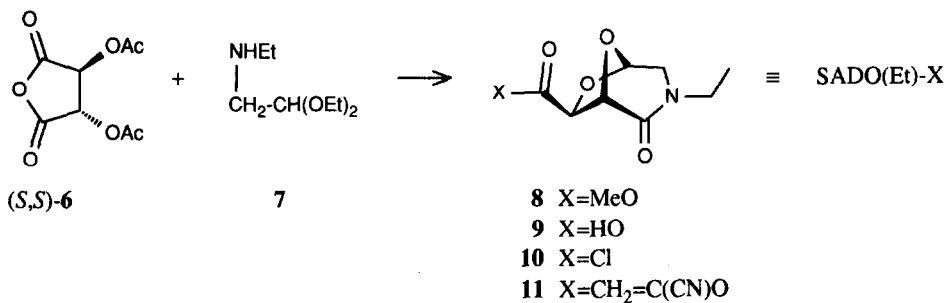
**Abstract:** Condensation of di-O-acetyl (*R,R*)- and (*S,S*)-tartaric anhydride with acetals of *N*-alkylaminoacetaldehyde gave new chiral auxiliaries (1*R*,5*S*,7*R*)- and (1*S*,5*R*,7*S*)-3-alkyl-2-oxo-3-aza-6,8-dioxabicyclo[3.2.1]octane-7-carboxylic (RADO(alkyl)-X and SADO(alkyl)-X) derivatives, respectively. The latter could be used to generate the corresponding 1-cyanovinyl esters that add to furan to give readily crystallizable, optically pure *Diels-Alder* adducts. The method was illustrated by application to the synthesis of (-)-(1*S*,4*S*)-7-oxabicyclo[2.2.1]hept-5-en-2-one.

Since ketenes do not undergo satisfactory [4+2] cycloadditions because the [2+2] mode is preferred [1], several dienophilic equivalents of ketene have been developed such as 1-cyanovinyl esters [2] [3], 2-chloroacrylonitriles [4], 2-chloroacrylyl chloride [5], 2-aminoacrylonitriles [6], 2-methylthioacrylonitriles [7] and vinyl sulfoxides [8] [9]. In 1983 we showed that (-)-1-cyanovinyl (1'*S*)-camphanate ((-)-1) added to furan in the presence of ZnI<sub>2</sub>, leading to optically pure adduct (+)-2 after repetitive recrystallizations; saponification of (+)-2 gave (+)-3 and (1*S*)-camphanic acid (recovery of the chiral auxiliary) [10]. The diastereomeric adduct (-)-5 and the corresponding enone (-)-3 were obtained as readily from (+)-1-cyanovinyl (1'*R*)-camphanate ((+)-4) derived from (1*R*)-camphanic acid. The optically pure 7-oxanorbomenyl derivatives (+)-2, (+)-3 and (-)-5 ("naked sugars" [11]) are useful chirons [12] in the total synthesis of rare carbohydrates [13], C-nucleosides [14], castanospermine [15] and other compounds of biological interest [16]. Since the scaling up of the preparations of (+)-2 and (-)-5 was somewhat troublesome, we have developed a new generation of optically pure 1-cyanovinyl esters derived from inexpensive (*R,R*)- and (*S,S*)-tartaric acids [17].

Only one of the two carboxylic groups of tartaric acid is needed to generate the corresponding 1-cyanovinyl ester. The protection of the other carboxylic group and of the two alcoholic functions should resist the highly acidic conditions of the formation of the corresponding acyl chloride required in its condensation with pyruvonnitrile into the corresponding ketene equivalent, and of the Lewis acid induced



Diels-Alder additions to furan. Furthermore it should allow one to carry out all these transformations, and also the saponification of the adducts into the corresponding enones with recovery of the chiral auxiliary without epimerization at the carbon centres  $\alpha$  to the carboxylic groups. These requirements were met for (1*R*,5*S*,7*R*) and (1*S*,5*R*,7*S*)-3-alkyl-2-oxo-3-aza-6,8-dioxabicyclo[3.2.1]octane-7-*exo*-carboxylic (RADO(alkyl)-X and SADO(alkyl)-X) derivatives obtained by condensation of di-*O*-acetyl-(*R,R*)- and -(*S,S*)-tartaric anhydride, respectively, with an acetal of *N*-alkylaminoacetaldehyde. The bicyclic structure prohibits enolization at the bridgehead centre C(1); epimerization at C(7) can occur but the *exo* stereomers are thermodynamically favoured. The alkyl group at N(3) can be adapted for optimal applications of these new chiral auxiliaries. In the case of the preparation of 7-oxanorbomenyl derivatives ("naked sugars"), adducts derived from RADO(Et)-OH or SADO(Et)-OH were found to have better crystallizability than those derived from RADO(Me)-OH or SADO(Me)-OH. As an illustration, we report here a new synthesis of (-)-3.





## Experimental Part.

General. See [19].

*N*-Ethylaminoethanol ethyl acetal (**7**). A mixture of  $\text{BrCH}_2\text{CH}(\text{OEt})_2$  (350 ml),  $\text{EtNH}_2$  (70% aq, 1 l) MeOH (750 ml) was heated under reflux for 24 h. After addition of NaOH (90 g), the solvent was led off (Vigreux column). Ice (100 g) was added and the mixture extracted with ether (400 ml, 3 times). Extracts were combined and washed with brine (400 ml, twice) and the solvent distilled off (Widmerman) and the residue distilled and redistilled on  $\text{CaH}_2$ : 270 g (74.3%), B.p.  $85^\circ\text{C}/20$  Torr,  $n_{\text{D}}^{20} = 1.40$ .

*Methyl (1S,5R,7S)-3-ethyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylate (SADO)-Me: 8*. To a stirred suspension of di-*O*-acetyl (*S,S*)-tartaric anhydride ((*S,S*)-**6**) (100 g, 0.463 mol) in  $\text{CH}_2\text{Cl}_2$  (400 ml), **7** (86 ml, 0.463 mol) was added dropwise in 20 min. The mixture was stirred at  $20^\circ\text{C}$  for 2 h and the solvent evaporated. The residue was dissolved in MeOH (1 l) and  $\text{SOCl}_2$  (20 ml) was added with stirring at  $20^\circ\text{C}$ . After 24 h at  $20^\circ\text{C}$ , the solvent was evaporated, the residue dried *in vacuo* and redissolved in toluene (2 l). After addition of acidic  $\text{SiO}_2$  (prepared by dropwise addition of conc.  $\text{H}_2\text{SO}_4$  (20 g) to 40 g of silica gel stirred in 500 ml of  $\text{CH}_2\text{Cl}_2$ , and then solvent evaporation), the mixture was heated with stirring (oil bath  $160^\circ\text{C}$ ). Solvents distilling between  $85$ - $108^\circ\text{C}$  were distilled off (20 min). After cooling to  $20^\circ\text{C}$ , the solution was filtered through  $\text{NaHCO}_3$  (rinsing with  $\text{CH}_2\text{Cl}_2$ ) and the solvent evaporated to dryness. The residue was taken with  $\text{AcOEt}$ /petroleum ether 3:1 (250 ml) and filtered through silica gel (200 g; elution with same solvent (1.5 L)). After solvent evaporation, the residue was crystallized from  $\text{Et}_2\text{O}$  (400 ml): 54 g (54%), colourless crystals, m.p.  $75$ - $78^\circ\text{C}$ .  $[\alpha]_{\text{D}}^{20} = +52.5$ ,  $[\alpha]_{578}^{20} = +61.2$ ,  $[\alpha]_{546}^{20} = +61.2$ ,  $[\alpha]_{436}^{20} = +97.0$ ,  $[\alpha]_{365}^{20} = +133.3$  ( $c = 10$  g/dm<sup>3</sup>,  $\text{CH}_2\text{Cl}_2$ ). IR (KBr): 2970, 1750, 1490, 1455, 1435, 1365, 1345, 1330, 1300, 1280, 1210, 1145, 1105, 1080, 1050, 1010, 980, 945, 925, 865, 825, 795, 720, 670.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 360 MHz): 5.93 (*d*,  $^3J = 2.5$ , H-C(5)); 4.89 (*s*, H-C(1)); 4.71 (*d*, H-C(7)); 3.79 (*s*, MeO); 3.50 (*dd*,  $^2J = 12$ ,  $^3J = 3.5$  H-*exo*-C(4)) & 3.22 (*d*,  $^2J = 12$ , H-*endo*-C(4)); 3.46-3.32 (*m*,  $^3J = 7$ , Et).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 90.55 MHz): 169.2, 165.0 (2*s*), 100.0 (*d*,  $^1J(\text{C,H}) = 175$ , C(5)); 77.5 (*d*,  $^1J(\text{C,H}) = 160$ , C(7)); 52.7 (*q*,  $^1J(\text{C,H}) = 150$ , MeO); 50.9 (*t*,  $^1J(\text{C,H}) = 140$ , C(4)); 40.0 (*t*,  $^1J(\text{C,H}) = 140$ ); 11.7 (*q*, Et). MS (70 eV): 216 (8), 215 (72,  $M^+$ ), 170 (15), 156 (20), 144 (16), 114 (12), 113 (12), 99 (15), 86 (16), 85 (13), 71 (32), 59 (18), 58 (100), 57 (30), 56 (15). Anal. for  $\text{C}_9\text{H}_{13}\text{NO}_5$  (215.20): C 50.23, H 6.09, N 6.51; found: C 50.30, H 6.01, N 6.43.

*1'-Cyanovinyl ((1S,5R,7S)-3-ethyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylate* **8**). A soln. of **8** (30 g, 0.14 mol) in  $\text{H}_2\text{O}$  (60 ml) and conc. HCl (3 ml) was heated to  $75^\circ\text{C}$  for 3 h. After solvent evaporation to dryness ( $\text{P}_2\text{O}_{10}$ ), acid **9** (28 g, 100%) was heated under reflux in  $\text{SOCl}_2$  (20 ml) until end of gas evolution.  $\text{SOCl}_2$  was distilled off *in vacuo* and the residue recrystallized from  $\text{Et}_2\text{O}$  (100 ml) and petroleum ether (300 ml): 28 g (92%) of **10**. **10** was dissolved in anh.  $\text{CH}_2\text{Cl}_2$  (120 ml) and pyruvonnitrile (10.5 ml, 0.128 mol). Freshly distilled (over  $\text{CaH}_2$ ) pyridine (10.5 ml) in solution in anh.  $\text{CH}_2\text{Cl}_2$  (50 ml) was added slowly with stirring at  $0^\circ\text{C}$ . The temperature was allowed to reach  $20^\circ\text{C}$  in 4 h and the mixture

was stirred at 20°C for 20 h. The solvent was evaporated and the residue dissolved in AcOEt (250 ml) and the solution decolourized with active charcoal. After filtration on silica gel (150 g, elution with 600 ml of AcOEt), the solvent was evaporated and the residue recrystallized from AcOEt/Et<sub>2</sub>O : 27.7 g (86.3%), colourless crystals, m.p. 90-91.5°C.  $[\alpha]_{\text{D}}^{20} = +53.9$ ,  $[\alpha]_{578}^{20} = +135.2$ , ( $c = 10 \text{ g/dm}^3$ , CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3120, 3035, 2970, 2925, 2865, 2235, 1780, 1660; <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 360 MHz): 5.97 (*d*, <sup>3</sup>*J* = 2.5); 5.88 & 5.82 (*2d*, <sup>2</sup>*J* = 3.2, H<sub>2</sub>C(2')); 4.96, 4.86 (*2s*), 3.54 (*dd*, <sup>2</sup>*J* = 12.5, <sup>3</sup>*J* = 3.5); 3.25 (*d*, <sup>2</sup>*J* = 12.5, H<sub>2</sub>C(4)); 3.49-3.35 (*m*); 1.15 (*t*, Et). <sup>13</sup>C-NMR (90.55 MHz, CDCl<sub>3</sub>): 165.4 (*s*, CO); 164.2 (*s*, C(2)); 127.0 (*s*, C(1')); 120.1 (*t*, <sup>1</sup>*J*(C,H) = 170, C(2')); 100.4 (*d*, <sup>1</sup>*J*(C,H) = 175, C(5)); 77.3 (*2d*, <sup>1</sup>*J*(C,H) = 165, C(1), C(7)); 50.7 (*t*, <sup>1</sup>*J*(C,H) = 140, C(4)); 40.1 (*t*, <sup>1</sup>*J*(C,H) = 140, Et); 11.67 (*q*, <sup>1</sup>*J*(C,H) = 130, Et). CI-MS (NH<sub>3</sub>): 253 (14), 252 (*M*<sup>+</sup>, 9), 207 (17), 156 (97), 149 (7), 114 (13), 98 (19), 86 (45), 85 (58), 72 (13), 71 (53), 70 (40), 69 (9), 58 (100), 57 (78), 56 (27), 54 (11), 52 (20). Anal. calc. for C<sub>11</sub>H<sub>12</sub>N<sub>2</sub>O<sub>5</sub> (252.22): C 52.38, H 4.80, N 11.11; found: C 52.44, H 4.77, N 11.12.

(1'S,2'R,4'S)-2'-exo-Cyano-7'-oxabicyclo[2.2.1]hept-5'-en-2'-endo-yl (1S,5R,7S)-3-ethyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-exo-carboxylate (**12**). A mixture of finely ground 4 Å molecular sieves (10 g, dried in a flame under N<sub>2</sub> flow), anh. ZnBr<sub>2</sub> (20 g, 89 mmol, finely ground and dried over P<sub>4</sub>O<sub>10</sub>), **11** (20 g, 79.4 mmol) and furan (200 ml) was stirred in the dark at 20°C for 7 d. After distilling off the excess of furan, the residue was taken with CH<sub>2</sub>Cl<sub>2</sub> (200 ml), filtered through Celite and washed with H<sub>2</sub>O (300 ml, twice). The aq. layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml, 5 times). The org. extracts were dried (MgSO<sub>4</sub>) and the solvent evaporated to dryness. The residue was dissolved in boiling AcOEt (150 ml) and the solution was allowed to reach 20°C in 15 h. It was then cooled to 4°C (1 d), and then to -20°C (3 d). The precipitate was washed with Et<sub>2</sub>O and recrystallized as above from AcOEt (130 ml) : 8.9 g (35%), colourless crystals, m.p. 147-8°C (dec.).  $[\alpha]_{\text{D}}^{20} = -38$ ,  $[\alpha]_{578}^{20} = -39.5$ ,  $[\alpha]_{546}^{20} = -47.3$ ,  $[\alpha]_{436}^{20} = -97.5$ ,  $[\alpha]_{365}^{20} = -190.6$  ( $c = 10 \text{ g/dm}^3$ , CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 2980, 2930, 1770, 1660, 1485, 1430, 1350, 1325, 1300, 1275, 1215, 1195, 1170, 1135, 1105, 1065, 1015, 920, 900, 870, 750, 725, 705. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 360 MHz): 6.69 (*dd*, <sup>3</sup>*J* = 6.0, 2.0, H-C(5')); 6.19 (*dd*, <sup>3</sup>*J* = 6.0, 2.0, H-C(6')); 5.93 (*d*, <sup>3</sup>*J* = 2.5, H-C(5)); 5.67 (*dd*, <sup>3</sup>*J* = 2.0, <sup>4</sup>*J* = 1.0, H-C(1')); 5.18 (*ddd*, <sup>3</sup>*J* = 5.0, 2.0, <sup>4</sup>*J* = 1.0, H-C(4')); 4.72 (*s*, H-C(1)); 4.68 (*s*, H-C(7)); 3.50 (*dd*, <sup>2</sup>*J* = 12.5, <sup>3</sup>*J* = 2.5, H<sub>exo</sub>-C(4)); 3.22 (*d*, <sup>2</sup>*J* = 12.5, H<sub>endo</sub>-C(4)); 3.44-3.33 (*m*, 2 H); 1.14 (*t*, <sup>3</sup>*J* = 7.0, Et); 2.78 (*dd*, <sup>2</sup>*J* = 13.0, <sup>3</sup>*J* = 5.0, H<sub>exo</sub>-C(3')); 1.85 (*d*, <sup>2</sup>*J* = 13.0, H<sub>endo</sub>-C(3')). <sup>13</sup>C-NMR (90.55 MHz, CDCl<sub>3</sub>): 167.0 (*s*, CO); 164.3 (*s*, C(2)); 140.1 (*d*, <sup>1</sup>*J*(C,H) = 180, C(5')); 130.4 (*d*, <sup>1</sup>*J*(C,H) = 175, C(6')); 118.3 (*s*, CN); 100.2 (*d*, <sup>1</sup>*J*(C,H) = 175, C(5)); 83.4 (*d*, <sup>1</sup>*J*(C,H) = 175, C(1')); 78.7 (*d*, <sup>1</sup>*J*(C,H) = 170, C(4')); 77.2 (*d*, C(1)); 77.1 (*d*, C(7)); 72.9 (*s*, C(2')); 50.7 (*t*, <sup>1</sup>*J*(C,H) = 145, C(4)); 41.0 (*t*, <sup>1</sup>*J*(C,H) = 145, C(3')); 40.1 (*t*, <sup>1</sup>*J*(C,H) = 145, Et); 11.6 (*q*, <sup>1</sup>*J*(C,H) = 130, Et). MS (70 eV): 320 (*M*<sup>+</sup>, 4), 207 (15), 179 (7), 157 (8), 156 (45), 114 (8), 99 (6), 98 (8), 92 (5), 86 (26), 81 (7), 71 (34), 70 (7), 69 (12), 68 (100), 65 (8), 58 (54), 57 (40), 56 (16), 54 (9), 53 (7), 52 (15). Anal. calc. for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub> (320.29): C 56.25, H 5.04, N 8.75; found: C 56.20, H 5.15, N 8.74.

(1'R,2'S,4'R)-2'-exo-Cyano-7'-oxabicyclo[2.2.1]hept-5'-en-2'-endo-yl (1S,5R,7S)-3-ethyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-exo-carboxylate (**13**). The mother-liquor of the first crystallization of

**12** was evaporated to dryness and the residue recrystallized from 20 ml, and then from 14 ml of AcOEt : 4.35 g (17%), colourless crystals, m.p. 139-141°C (dec).  $[\alpha]_{\text{D}}^{20} = +127.5$ ,  $[\alpha]_{578}^{20} = +133.1$ ,  $[\alpha]_{546}^{20} = +152.1$ ,  $[\alpha]_{436}^{20} = +264.2$ ,  $[\alpha]_{365}^{20} = +128.1$  ( $c = 10 \text{ g/dm}^3$ ,  $\text{CH}_2\text{Cl}_2$ ). IR (KBr): 3090, 2980, 2940, 2880, 2245, 1770, 1670, 1570, 1490, 1445, 1365, 1325, 1295, 1235, 1205, 1175, 1150, 1110, 1095, 1065, 1045, 1030, 980, 920, 900, 865, 850, 835, 815, 790, 755, 725, 660.  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ): 6.67 (*dd*, 1 H,  $^3J = 5.9$ , 1.8, H-C(5'')); 6.23 (*dd*, 1 H,  $^3J = 5.9$ , 1.8, H-C(6'')); 5.91 (*d*, 1 H,  $^3J = 2.2$ , H-C(5)); 5.63 (*dd*, 1 H,  $^3J = 1.8$ ,  $^5J(1'-4') = 1.0$ , H-C(1'')); 5.17 (*ddd*, 1 H,  $^3J = 4.7$ , 1.8,  $^5J(1'-4') = 1.0$ , H-C(4'')); 4.79 (*s*, 1 H, H-C(1)); 4.66 (*s*, 1 H, H-C(7)); 3.50 (*dd*, 1 H,  $^2J = 12.3$ ,  $^3J = 2.3$ ,  $\text{H}_{\text{exo}}\text{-C}(4)$ ); 3.37 (*q*, 2 H,  $^3J = 7.2$ , Et); 3.20 (*d*, 1 H,  $^2J = 12.3$ ,  $\text{H}_{\text{endo}}\text{-C}(4)$ ); 2.78 (*dd*, 1 H,  $^2J = 12.8$ ,  $^3J = 4.7$ ,  $\text{H}_{\text{exo}}\text{-C}(3')$ ); 1.79 (*d*, 1 H,  $^2J = 12.8$ ,  $\text{H}_{\text{endo}}\text{-C}(3')$ ); 1.13 (*t*, 3 H,  $^3J = 7.0$ , Et).  $^{13}\text{C-NMR}$  (90.55 MHz,  $\text{CDCl}_3$ ): 167.1 (*s*, CO); 164.4 (*s*, C(2)); 140.0 (*d*,  $^1J(\text{C,H}) = 180$ , C(5'')); 130.6 (*d*,  $^1J(\text{C,H}) = 180$ , C(6'')); 118.4 (*s*, CN); 100.2 (*d*,  $^1J(\text{C,H}) = 175$ , C(5)); 83.3 (*d*,  $^1J(\text{C,H}) = 175$ , C(1'')); 78.8 (*d*,  $^1J(\text{C,H}) = 170$ , C(4'')); 77.2 (*d*,  $^1J(\text{C,H}) = 170$ , C(1), C(7)); 73.0 (*s*, C(2'')); 50.7 (*t*,  $^1J(\text{C,H}) = 140$ , C(4)); 41.1 (*t*,  $^1J(\text{C,H}) = 145$ , C(3'')); 40.1 (*t*,  $^1J(\text{C,H}) = 145$ , Et); 11.7 (*q*,  $^1J(\text{C,H}) = 130$ , Et). MS (70 eV): 320 ( $M^+$ , 3), 209 (6), 207 (13), 206 (3), 179 (5), 157 (6), 156 (50), 114 (6), 98 (10), 86 (25), 85 (29), 72 (11), 71 (29), 69 (9), 68 (100), 58 (61), 57 (34), 56 (13), 54 (9), 52 (12). Anal. calc. for  $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_6$  (320.29): C 56.25, H 5.04, N 8.75; found: C 56.27, H 5.06, N 8.70.

Recovery of **11**. The mother-liquors of the crystallization of **12** were evaporated to dryness, mixed with activated and ground 4 Å molecular sieves and heated under reflux in PhMe (200 ml). After solvent evaporation, the residue was taken with AcOEt, filtered on silica gel. The solvent was evaporated and the residue recrystallized from  $\text{Et}_2\text{O}$  : 6.5 g (32.6%).

(-)-(1*S*,4*S*)-7-Oxabicyclo[2.2.1]hept-5-en-2-one ((-)-**3**). A mixture of **12** (10 g, 31.3 mmol), 1*N* NaOH (40 ml), 40% aq.  $\text{CH}_2\text{O}$  (15 ml, 0.2 mol) was stirred at 20°C for 4 h. Extraction with  $\text{CH}_2\text{Cl}_2$  (30 ml, 8 times), washing (brine: 70 ml, twice), drying ( $\text{MgSO}_4$ ) and distillation gave 3.25 g (95%), oil, b.p. 120°C/20 Torr.<sup>[10]</sup>

Recovery of (1*S*,5*R*,7*S*)-3-ethyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylic acid (SADO(Et)-OH, **9**). Acidification of the aq. layer obtained above with conc. HCl (3.5 ml) gave a precipitate : 4.9 g (78%) of **9**, colourless crystals, m.p. 225-227°C (dec.). IR (KBr): 3200-2500, 1740, 1640, 1500, 1455, 1435, 1330, 1280, 1250, 1205, 1150, 1100, 1050, 1020, 930, 905, 870, 825, 765, 710, 665. MS (70 eV): 201 ( $M^+$ , 10), 156 (13), 112 (11), 86 (11), 71 (35), 70 (14), 58 (100), 57 (41), 56 (23), 55 (12). Anal. calc. for  $\text{C}_8\text{H}_{11}\text{NO}_5$  (201.18): C 47.76, H 5.51, N 6.96; found: C 47.77, H 5.52, N 6.99.

*Methyl* (1*R*,5*S*,7*R*)-3-methyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylate (RADO(Me)-OMe, **17**). *N*-methylaminoethanal dimethylacetal (5 ml, 39 mmol) was added slowly to a soln. of di-*O*-acetyl (*R,R*)-tartaric anhydride ((*R,R*)-**6**, 8.4 g, 39 mmol) in anh.  $\text{CH}_2\text{Cl}_2$  (100 ml). After solvent evaporation, MeOH (135 ml) and  $\text{SOCl}_2$  (2.7 ml) were added. After heating to 50°C for 2 h, the solvent was evaporated and the residue recrystallized from  $\text{CHCl}_3/\text{Et}_2\text{O}$ /petroleum ether at 20°C. The crystalline product (9.0 g) was dissolved in toluene (180 ml) and acidic silica gel (prepared by slow addition of conc.  $\text{H}_2\text{SO}_4$

(0.8 g) to stirred silica gel (2.2 g) in  $\text{CH}_2\text{Cl}_2$ , and then solvent evaporation) was added. The mixture was stirred at 160 °C and the vapors were distilled off for 15 min. After cooling to 20 °C, the mixture was filtered through  $\text{NaHCO}_3$  and the solvent evaporated. The residue was recrystallized from  $\text{Et}_2\text{O}$  at 20 °C, yielding 5.9 g (78%), colourless crystals, m.p. 106 °C.  $[\alpha]_{589}^{20} = -53.6$ ,  $[\alpha]_{578}^{20} = -55.3$ ,  $[\alpha]_{546}^{20} = -62.0$ ,  $[\alpha]_{436}^{20} = -97.6$ ,  $[\alpha]_{365}^{20} = -134$  ( $c = 10 \text{ g/dm}^3$ ,  $\text{CH}_2\text{Cl}_2$ ). IR (KBr): 3020, 2945, 1750, 1660, 1455, 1430, 1400, 1340, 1285, 1215, 1150, 1100, 1060, 1015, 905, 870, 830, 730, 700, 670.  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ): 5.89 (*d*, 1 H,  $^3J = 2.3$ , H-C(5)); 4.90 (*s*, 1 H, H-C(1)); 4.71 (*s*, 1 H, H-C(7)); 3.79 (*s*, 3 H, MeO); 3.49 (*dd*, 1 H,  $^2J = 12.2$ ,  $^3J = 2.3$ ,  $\text{H}_{\text{exo}}$ -C(4)); 3.22 (*d*, 1 H,  $^2J = 12.2$ ,  $\text{H}_{\text{endo}}$ -C(4)); 2.91 (*s*, 3 H, Me).  $^{13}\text{C-NMR}$  (90.55 MHz,  $\text{CDCl}_3$ ): 169.1 (*s*, CO); 165.5 (*s*, C(2)); 99.8 (*d*,  $^1J(\text{C,H}) = 175$ , C(5)); 77.6 (*d*,  $^1J(\text{C,H}) = 160$ , C(1)); 77.4 (*d*,  $^1J(\text{C,H}) = 165$ , C(7)); 53.7 (*t*,  $^1J(\text{C,H}) = 140$ , C(4)); 52.7 (*q*,  $^1J(\text{C,H}) = 150$ , OMe); 32.5 (*q*,  $^1J(\text{C,H}) = 140$ , Me). MS (70 eV): 202 (3), 201 ( $M^+$ , 28), 142 (22), 128 (25), 113 (22), 99 (20), 85 (38), 84 (24), 72 (44), 71 (100), 58 (59). Anal. calc. for  $\text{C}_8\text{H}_{11}\text{NO}_5$  (201.18): C 47.76, H 5.51, N 6.96; found: C 47.62, H 5.47, N 6.93.

*1'-Cyanovinyl ((1R,5S,7R)-3-methyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylate)* (**18**). 1N NaOH (12 ml) was added in 20 min to a stirred soln. of **17** (2.0 g, 11.3 mmol) in  $\text{H}_2\text{O}$  (10 ml) to 20 °C. After acidification with 2N HCl (6 ml), the solvent was evaporated.  $\text{SOCl}_2$  (16 ml) was added and the mixture heated under reflux for 1 h. The excess of  $\text{SOCl}_2$  was distilled off and the residue taken with anh.  $\text{CH}_2\text{Cl}_2$ . The precipitate (NaCl) was filtered off and the solvent evaporated. The residue was recrystallized from  $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ /petroleum ether at 20 °C, yielding 1.5 g (73%) of the corresponding acyl chloride. After dissolution in anh.  $\text{CH}_2\text{Cl}_2$  (10 ml), pyruvonnitrile (0.5 ml, 8.3 mmol) was added and the mixture cooled to 0 °C. A soln. of anh. pyridine (0.75 ml) in anh.  $\text{CH}_2\text{Cl}_2$  (5 ml) was added dropwise under stirring at 0 °C. After stirring at 20 °C for 24 h, the mixture was filtered through a short column of silica gel (EtOAc), yielding 1.15 g (62%), colorless crystals, m.p. 116-117°C after crystallization from  $\text{Et}_2\text{O}$ /petroleum ether (20 °C).  $[\alpha]_{589}^{20} = -56.6$ ,  $[\alpha]_{578}^{20} = -58.6$ ,  $[\alpha]_{546}^{20} = -66.1$ ,  $[\alpha]_{436}^{20} = -105$ ,  $[\alpha]_{365}^{20} = -145$  ( $c = 10 \text{ g/dm}^3$ ,  $\text{CH}_2\text{Cl}_2$ ). IR (KBr): 3120, 3010, 2950, 2930, 1775, 1675, 1630, 1500, 1450, 1405, 1330, 1285, 1230, 1175, 1145, 1100, 1040, 1010, 940, 905, 865.  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ): 5.95 (*d*, 1 H,  $^3J = 2.3$ , H-C(5)); 5.86 & 5.81 (*2d*, 2x1 H,  $^2J = 3.2$ ,  $\text{H}_2$ -C(2')); 4.97 (*s*, 1 H, H-C(1)); 4.85 (*s*, 1 H, H-C(7)); 3.55 (*dd*, 1 H,  $^2J = 12.0$ ,  $^3J = 2.3$ ,  $\text{H}_{\text{exo}}$ -C(4)); 3.26 (*d*, 1 H,  $^2J = 12.0$ ,  $\text{H}_{\text{endo}}$ -C(4)); 2.95 (*s*, 3 H, Me).  $^{13}\text{C-NMR}$  (90.55 MHz,  $\text{CDCl}_3$ ): 165.4 (*s*, CO); 164.6 (*s*, C(2)); 127.0 (*s*, C(1')); 120.1 (*t*,  $^1J(\text{C,H}) = 165$ , C(2')); 112.4 (*s*, CN); 100.3 (*d*,  $^1J(\text{C,H}) = 180$ , C(5)); 77.2 (*d*,  $^1J(\text{C,H}) = 165$ , C(1)); 77.1 (*d*,  $^1J(\text{C,H}) = 160$ , C(7)); 53.5 (*t*,  $^1J(\text{C,H}) = 145$ , C(4)); 32.26 (*q*,  $^1J(\text{C,H}) = 140$ , Me). MS (70 eV): 238 ( $M^+$ , 7), 193 (14), 142 (88), 137 (10), 99 (7), 91 (16), 86 (14), 85 (77), 84 (27), 72 (75), 71 (100), 69 (18), 58 (85), 52 (53). Anal. calc. for  $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_5$  (238.19): C 50.42, H 4.23, N 11.76; found: C 50.52, H 4.20, N 11.73.

*(1'R,2'S,4'R)-2'-exo-Cyano-7'-oxabicyclo[2.2.1]hept-5'-en-2'-endo-yl ((1R,5S,7R)-3-methyl-2-oxo-6,8-dioxo-3-azabicyclo[3.2.1]octane-7-exo-carboxylate)* (**19**). A mixture of finely ground 4 Å molecular sieves (6 g, dried in a flame under  $\text{N}_2$ ), anh.  $\text{ZnBr}_2$  (3.0 g, 13 mmol), **18** (3.0 g, 12.6 mmol),  $\text{CH}_2\text{Cl}_2$  (3 ml) and furan (30 ml) was stirred at 20 °C in the dark for 7 days. The mixture was filtered through a short

column of silica gel (150 g, AcOEt). The main fraction was recrystallized from AcOEt (200 ml): 1.24 g (32%). A second recrystallization from AcOEt (100 ml) gave 0.8 g (20.6%) pure **19**, colourless crystals, m.p. 175°C (dec.). IR (KBr): 1765, 1665, 1500, 1440, 1400, 1325, 1280, 1215, 1170, 1150, 1105, 1065, 865. <sup>1</sup>H-NMR (360 MHz, CDCl<sub>3</sub>): 6.71 (dd, 1 H, <sup>3</sup>J = 6.0, 2.0, H-C(5')); 6.19 (dd, 1 H, <sup>3</sup>J = 6.0, 1.5, H-C(6')); 5.92 (d, 1 H, <sup>3</sup>J = 2.5, H-C(5)); 5.68 (dd, 1 H, <sup>3</sup>J = 2.0, <sup>4</sup>J(H1'-H4') = 1.0, H-C(1')); 5.18 (ddd, 1 H, <sup>3</sup>J = 4.5, 1.5, <sup>4</sup>J(H1'-H4') = 1.0, H-C(4')); 4.75 (s, 1 H, H-C(1)); 4.71 (s, 1 H, H-C(7)); 3.52 (dd, 1 H, <sup>2</sup>J = 12.5, <sup>3</sup>J = 2.5, H<sub>exo</sub>-C(4)); 3.24 (d, 1 H, <sup>2</sup>J = 12.5, H<sub>endo</sub>-C(4)); 2.94 (s, 3 H, Me); 2.79 (dd, 1 H, <sup>2</sup>J = 13.0, <sup>3</sup>J = 4.5, H<sub>exo</sub>-C(3')); 1.86 (d, 1 H, <sup>2</sup>J = 13.0, H<sub>endo</sub>-C(3')). <sup>13</sup>C-NMR (90.55 MHz, CDCl<sub>3</sub>): 167.0 (s, CO); 164.8 (s, C(2)); 140.1 (d, <sup>1</sup>J(C,H) = 180, C(5')); 130.4 (d, <sup>1</sup>J(C,H) = 180, C(6')); 118.3 (s, CN); 100.1 (d, <sup>1</sup>J(C,H) = 175, C(5)); 83.4 (d, <sup>1</sup>J(C,H) = 175, C(1')); 78.8 (d, <sup>1</sup>J(C,H) = 170, C(4')); 77.2 (d, <sup>1</sup>J(C,H) = 155, C(1), C(7)); 73.0 (s, C(2')); 53.6 (t, <sup>1</sup>J(C,H) = 140, C(4)); 41.1 (t, <sup>1</sup>J(C,H) = 145, C(3')); 32.6 (q, <sup>1</sup>J(C,H) = 140, Me). CI-MS (NH<sub>3</sub>): 325 (15), 324 (M<sup>+</sup>+18, 100), 307 (17), 256 (16), 239 (19), 144 (15), 142 (12), 141 (4), 91 (11). Anal. calc. for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>6</sub> (306.27): C 54.90, H 4.61, N 9.15; found: C 55.19, H 4.56, N 8.85.

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