68. Facile Hetero-*Diels-Alder* Reaction of α,β-Unsaturated Acyl Cyanides and Enol Ethers: Syntheses of 2-Alkoxy-3,4-dihydro-2*H*-Pyran-6-carbonitriles

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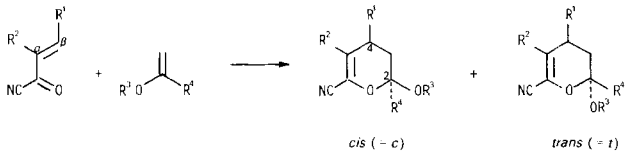
2-Ethoxy-3,4-dihydro-2*H*-pyran-6-carbonitriles are obtained in high yield by stereospecific *endo*-mode cycloadditions of α,β-unsaturated acyl cyanides and ethyl vinyl ether at room temperature. The nitrile group is converted to some other functionalities.

1. Introduction. – The reaction of α,β-unsaturated carbonyl compounds with alkyl vinyl ethers, a classical example of a *Diels-Alder* cycloaddition of inverse electron demand [1], makes available various derivatives of 2-alkoxy-3,4-dihydro-2*H*-pyrans useful in the synthesis of carbohydrates [2], thromboxanes [3], and spiroacetals [4].

When elevated temperature is used for this reaction, the theoretically favoured *'endo'* adducts are not the exclusive products. Attempts to improve the stereospecificity by lowering the reaction temperature led to the use of high pressure [5]. It is also known that electron-attracting groups in α or β position to the carbonyl function permit the reaction temperature to be reduced to ambient [2a] [6]. *Lewis* acids such as $ZnCl_2$ [7a] and soluble lanthanide complexes [7b] have proven efficient catalysts. We now present new findings with α,β-unsaturated acyl cyanides as potent heterodienes in cycloaddition reactions with enol ethers.

2. Results. – 2.1. *Products.* The α,β-unsaturated acyl cyanides listed in *Scheme 1* are readily prepared by treating the parent chlorides with Cu(I)CN in CH_3CN according to

Scheme 1. *Cycloaddition Products of Acryloyl Cyanides with Enol Ethers*



cis (= *c*) *trans* (= *t*)

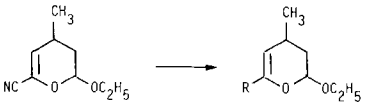
Product	R^1	R^2	R^3	R^4	Yield	*cis*/*trans* Ratio of crude product	*cis*/*trans* Ratio after epimerization
1	H	H	C_2H_5	H	63%		
2	CH_3	H	C_2H_5	H	82%	95:5	22:78
3	C_6H_5	H	C_2H_5	H	85%	93:7	25:75
4	H	CH_3	C_2H_5	H	34%		
5	CH_3	CH_3	C_2H_5	H	60%	96:4	
6	$COOC_2H_5$	H	C_2H_5	H	96%	98:2	
7	CH_3	H	CH_3	CH_3	76%	92:8	

the procedure of [8]; most are known compounds [9]. Acryloyl cyanides with R^1 = H and R^2 = H or CH_3 are generated in solution only.

The acryloyl cyanides react at room temperature with excess enol ether to give the dihydropyrans **1**–**7** mostly in high yields. The above mentioned non-isolated examples can be trapped effectively *in situ* with ethyl vinyl ether. In those cases where the acryloyl cyanide has a substituent in β-position, the corresponding *cis*-dihydro-2*H*-pyrans (*c*) are formed along with only small amounts of their *trans*-epimers (*t*). The acryloyl cyanide bearing an ethoxycarbonyl substituent in β-position condenses within a few min, even at 0°, whereas the β,β-dimethyl-substituted acryloyl cyanide does not react.

The structures of the products were determined by ^{1}H-NMR and mass spectrometry *(vide infra)*. To ensure the configurational assignment of the original adducts as *cis*, advantage was taken of the fact that the pyrans can be *cis*/*trans* isomerized under acidic conditions. In presence of $BF_3 \cdot Et_2O$ at r.t., equilibrium mixtures (1:3) of the *cis*/*trans* isomers of **2** and **3** are obtained. This demonstrates the higher thermodynamical stability of the *trans* isomers. Product analysis is achieved by GC, the *trans* isomers moving slightly faster. In comparison, the spectral data of the *cis* and *trans* epimers could be attributed.

Scheme 2. *Transformation Products of 2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyrane-6-carbonitrile* (**2**)



2

8 R = C(=NH)OCH$_3$
9 R = COOCH$_3$
10 R = CH$_2$OH
11 R = CH$_2$NH$_2$
12 R = CHO

Transformation of the nitrile group can be effected under basic conditions without significant stereoisomerization (see *Scheme 2*). MeOH addition to the nitrile **2** (*c*/*t* 95:5) catalyzed by NaOMe leads to the methyl imidate **8**; this is hydrolyzed by dilute acid in a two-phase system to the methyl ester **9**. The latter is reduced with $LiAlH_4$ to the primary alcohol **10**. Reduction of **2** (*c*/*t* 95:5) with $LiAlH_4$ gives the primary amine **11**. Diisobutylaluminum hydride (DIBAH) reduction followed by acid hydrolysis affords the aldehyde **12** in excellent yield.

2.2. *Spectroscopy and Structure.* Completely resolved ^{1}H-NMR signals (360 MHz) of the initial adducts, the mixtures obtained by anomerisation, and some of their transformation products are given in the *Table*. The relative configuration of the initial adducts could not have been inferred solely from their ^{1}H-NMR spectra. Thus, we first analysed the configuration of the anomerised adducts and then compared them with the initial ones.

In the ^{1}H-NMR spectrum of the anomerised dihydropyrans *t*-**2** and *t*-**3**, 2 small *J* (2.5 Hz each) between H–C(2) and the 2 H–C(3) are seen. This indicates a large preference of the conformation with an axial EtO group (α in the *Fig.*, *trans*) in the rapidly interconverting equilibrium of half chairs, a constraint well known as anomeric effect [10] and explained by stereoelectronic factors. A large coupling (*J* = 11.1 and 11.7 Hz, resp.) involving H–C(4) (α-axial) and one of the ^{2}H–C(3) (β-axial) identifies an antiperiplanar H,H arrangement between these H-atoms. Thus, the substituent R at C(4) in both *t*-**2** and *t*-**3** has to be β-equatorial in this preferred conformation and, therefore, *trans* to the α-axial EtO group at C(2).

Whereas steric and anomeric effects cooperate in the aforementioned anomerised *trans*-configurated adducts to favor strongly one conformation, this is not the case in the initial *cis* isomers *c*-**2** and *c*-**3**, since the stereoelectronic preference for an axial EtO group is counteracted by a 1,3 steric repulsion of that group with the substituent

Table. *^{1}H-NMR Chemical Shifts and Coupling Constants*

	1	*c*-**2**	*t*-**2**	*c*-**3**	*t*-**3**	**4**	*c*-**6**	*c*-**9**	*c*-**12**
H_α–C(2)	–	5.03	–	5.14	–	–	5.16	5.08	5.10
H_β–C(2)	5.13	–	5.12	–	5.18	5.05	–	–	–
H_α–C(3)	1.91	2.06	1.96	2.33	2.17	1.89	2.53	2.04	2.04
H_β–C(3)	1.80	1.60	1.45	1.97	1.85	1.79	2.03	1.59	1.64
H_α–C(4)	2.31	2.50	2.57	3.71	3.73	2.27	3.12	2.50	2.60
H_β–C(4)	2.08	–	–	–	–	1.97	–	–	–
H–C(5)	5.75	5.56	5.60	5.74	5.81	–	5.91	6.00	5.77
CH_3CH_2O	1.22	1.23	1.21	1.20	1.24	1.20	1.26	1.23	1.18
CH_3CH_2O, H_A	3.86	3.92	3.85	3.98	3.92	3.82	3.79	3.98	3.93
H_B	3.63	3.58	3.60	3.71	3.65	3.58	3.54	3.60	3.57
CH_3–C(4)	–	1.12	1.07	–	–	–	–	1.14	1.19
Others				7.4–7.8 (C_6H_5)	7.1–7.4 (C_6H_5)	1.88 (CH_3–C(5))	1.15 (*t*) CH_3CH_2OCO 4.16 (*q*, CH_3CH_2OCO)	3.80 (CH_3OCO)	9.10 (CHO)
$^2J(3\alpha,3\beta)$	13.7	13.8	13.6	13.8	13.6	14	14.1	14.0	13.8
$^2J(4\alpha,4\beta)$	18.7	–	–	–	–	18	–	–	–
$^3J(2\alpha,3\alpha)$	–	2.3	–	2.1		–	2.2	2.4	2.5
$^3J(2\alpha,3\beta)$	–	7.1	–	8.2	–	–	3.5	6.8	6.7
$^3J(2\beta,3\alpha)$	2.8	–	2.5		2.5	2.5	–	–	–
$^3J(2\beta,3\beta)$	2.8	–	2.5	–	2.5	2.5	–	–	–
$^3J(3\alpha,4\alpha)$	6.6	6.7	6.1	6.9	6.3	6.5	3.5	6.6	6.6
$^3J(3\alpha,4\beta)$	3.1	–	–	–	–	2.7	–	–	–
$^3J(3\beta,4\alpha)$	11.0	6.9	11.1	9.7	11.7	11	7.4	7.3	6.8
$^3J(3\beta,4\beta)$	6.3	–	–	–	–	6.3	–	–	–
$^3J(4\alpha,5)$	2.9	3.5	2.4	2.9	2.6	–	4.9	3.3	3.5
$^3J(4\beta,5)$	5.0	–	–	–	–	–	–	–	–
$^4J(3\alpha,5)$	0.9	0.9	1.5	1.2	1.5	–	1.1	1	–
$J(CH_3$–C(4),$4\alpha)$	–	7.1	7.1	–	–	–	–	7.2	7.3
$J(CH_3$–C(5),$4\beta)$	–	–	–	–	–	1.4	–	–	–
J of CH_3CH_2O	9.7				10.5	10	9.5		9.5
$ABJ(CH_3CH_2O,CH_3CH_2O)$	7.2				7.2	7	7.2		6.9

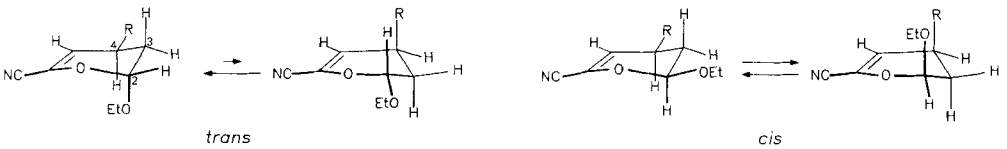


Figure. *Half-chair conformations of the* cis*-configurated adducts and their* trans *epimers*

at C(4). Thus, the equilibrium of half-chair conformations tends to a rather equal population of 1,3-diaxial and 1,3-diequatorial substituents (see *Fig.*), an effect which had been noted earlier [10] [11]. Accordingly, we find a big and a small J between H–C(2) and the 2 H–C(3) (7.1 and 2.3 Hz in *c*-**2**, 8.2 and 2.1 Hz in *c*-**3**) for the *trans* and the *cis* arrangement of these H-atoms, respectively.

The ^{1}H-NMR spectrum of the unsubstituted dihydropyran **1** strongly confirms the large preference for the conformation with an axial EtO group (see *Fig.*, *trans*, R = H). Note *(Table)* the close resemblance of coupling constants between corresponding proton pairs in **1**, *t*-**2** and *t*-**3**, namely the small couplings between H–C(2) and the 2 H–C(3) (J=2.8 Hz each), the only large coupling (J = Hz) between the antiperiplanar H–C(3) and H–C(4), and a small long-range coupling between the equatorial H_α–C(3) and H–C(5).

Routine mass spectra of the 2-ethoxy-3,4-dihydro-2*H*-pyrans show only a weak molecular-mass ion. The major peaks result from a *retro-Diels-Alder* fragmentation: the parent peak is due to the enol ether fragment (*m/z* 72 in most cases); the acyl-cyanide fragment immediately looses cyanide to give the acyl fragment. Other notable masses are ethoxy *m/z* and the corresponding dihydropyranyl fragments. The IR spectra contain the stretching-mode bands of the nitrile (2230–2240 cm^{-1}) and of the double bond (1630–1640 cm^{-1}).

3. Discussion. – The rather reactive α,β-unsaturated acyl cyanides have aroused interest only recently. *Jellal* and *Santelli et al.* reported that ethylenic acyl cyanides undergo $TiCl_4$-catalyzed nucleophilic conjugate additions with allylsilanes [12a], alkynylsilanes [12b], and trimethylsilyl enol ethers [12c] which lead to δ,ε-ethylenic and δ,ε-acetylenic acyl cyanides or δ-keto acyl cyanides, respectively. In the latter case, some pyran formation was noticed as well and attributed to the particular reaction conditions. The same authors reported the easy dimerization of ethylenic acyl cyanides under basic conditions [12d]. A dihydropyran as cycloaddition product was obtained earlier, unexpectedly, by heating cinnamoyl cyanide and tetraethoxy- or tetramethoxyethene to 100° [13]. *Hoffmann et al.* have successfully employed α,β-unsaturated acyl cyanides as dienes in *Lewis*-acid-catalyzed condensation with unreactive olefins [9a]; one case of successful cycloaddition of isopropyl vinyl ether to 2-oxo-3-pentenenitrile without catalyst at 160°/10 h is reported, however [9c].

The reaction of α,β-unsaturated acyl cyanides with enol ethers is new, and its ease is surprising. Neither elevated temperature nor catalysts are necessary, and the hitherto unknown 2-alkoxy-3,4-dihydro-2*H*-pyran-6-carbonitriles are formed with high stereospecificity in good yields.

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Experimental Part

(In collaboration with *Markus Zutter* and *Selim Dusi*)

General. All starting materials were purchased from *Fluka AG*. IR spectra (cm^{-1}): *Beckmann IR-20A*. NMR spectra ($CDCl_3$): *Bruker WP 80, WH 360* and *AM 400*. Mass spectra (*m/z* (intensities in % of base peak)): *Finnigan 1020*. GC: capillary column *HP ultra No. I* (methylsilicone); all runs were programmed as follows: 4 min at initial temp. 100° (unless indicated otherwise), linear gradient 16°/min, final temp. 200°; retention time R_t in min.

Acyl Cyanides (= *2-Oxonitriles*). The acyl cyanides were prepared from the corresponding chlorides by treatment with Cu(I)CN in OH_3CN following known methods [8] [9]; 2-oxo-3-pentenenitrile, 3-methyl-2-oxo-3-pentenenitrile, and 2-oxo-4-phenyl-3-butenenitrile were already characterized by *Hoffmann et al.* [9]; 2-oxo-3-butenenitrile and 3-methyl-2-oxo-3-butenenitrile, obviously never isolated, were prepared in solution and directly reacted with enol ether to give the dihydropyrans **1** and **4**, respectively. The preparation of 4-ethoxy carbonyl-substituted 2-oxonitrile is described below.

Ethyl 4-Cyano-4-oxo-2-butenoate. Ethyl 4-chloro-4-oxo-2-butenoate [14] was obtained from ethyl hydrogen fumarate (50 g) and $SOCl_2$ (32 ml) after refluxing for 5 h, and the product was distilled (63°/14 Torr) to give a colorless oil (34 g, 68%). ^{1}H-NMR ($CDCl_3$, 60 MHz): 6.95 (*s*, H–C(2), H–C(3)); 4.30 (*q*, CH_3CH_2O); 1.35 (*t*, CH_3CH_2O).

Ethyl 4-chloro-4-oxo-2-butenoate (20 g, 0.12 mol) and CuCN (11 g, 0.12 mol) in CH_3CN (49 ml) were heated to reflux for 30 min. After cooling, the mixture was distilled (97°/14 Torr) to give a colorless oil (10 g, 53%). GC: R_t 5.0. IR (film): 2232*s*, 1790*w*, 1775*w*, 1740v*s* (sh), 1740v*s*, 1735v*s*, 1700–1690v*s*, 1645*w*, 1630*w*, 1478–70*w*, 1450*w*, 1398*w*, 1372*s*, 1319v*s*, 1310 (sh), 1285*s*, 1260v*s*, 1210–1190v*s* (br.), 1100*m*, 1030*s* (br.), 975*s*, 890*w*, 865*w*, 755*w*, 720*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 7.08 (*s*, H–C(2), H–C(3)); 4.32 (*q*, CH_3CH_2O); 1.35 (*t*, CH_3CH_2O).

*2-Ethoxy-3,4-dihydro-2*H*-pyran-6-carbonitrile* (**1**). CH_3CN (100 ml), NaI (11.5 g, 75 mmol), and CuCN (3.6 g, 40 mmol) were stirred until complete dissolution of the salts. Acryloyl chloride (3.62 g, 40 mmol) was added

(→precipitation bright-orange mixture) and stirring continued for 30 min. The flask was then connected *via* a bridge to a second round-bottom flask and cooled with liq. N_2; this system was evacuated to 0.02 Torr, and by cooling the second flask and heating the reaction mixture to r.t. the solvent and 2-oxo-3-butenenitrile was distilled. Ethyl vinyl ether (15 ml, 11.3 g, 157 mmol) was added to the frozen distillate, and this was allowed to warm to r.t. The excess liquid was removed by distillation in a rotatory evaporator, and the residue was bulb-to-bulb distilled (100°/0.05 Torr); 3.89 g (63%) of **1** $n_D^{20} = 1.458$. IR (film): 3090*w*, 3000*m*, 2955*m*, 2240*m*, 1650*s*, 1447*m*, 1380*m*, 1360*m*, 1330*m*, 1298*s*, 1241*s*, 1198*s*, 1165*s*, 1125*s* (br.), 1070*m*, 1055*m*, 1030*s* (br.), 986*m*, 960*m*, 910*s*, 847*s*, 787*m*. MS: 153 (18, $M^{+\cdot}$), 124 (4), 109 (8), 108 (21), 97 (9), 96 (7), 85 (7), 82 (7), 81 (15), 80 (14), 72 (100), 70 (19), 69 (30), 68 (16), 57 (9), 56 (9), 55 (45), 54 (22), 53 (41), 52 (26), 53 (41), 51 (25), 50 (6), 46 (6), 45 (23). ^{1}H-NMR: *Table*.

cis-*2-Ethoxy-3,4-dihydro-4-methyl-2*H-*pyran-6-carbonitrile* (*c*-**2**). At r.t. 2-oxo-3-pentenenitrile (9.6 g, 0.1 mol) [9] and freshly distilled ethyl vinyl ether (21.6 g, 0.3 mol) were mixed. After 2 h (monitoring by GC), evaporation followed by bulb-to-bulb distillation (150°/0.01 Torr) gave a clear colorless oil (13.5 g, 80%). GC (initial temp. 50°): **2c**, R_t 16.4 (95%); **2t**, R_t 15.7 (5%). IR (film): 2230*m*, 1638*s*, 1390*m*, 1378*s*, 1322*m*, 1282*s*, 1125v*s*, 1045v*s*, 1020*m*, 972*s*, 910*w*, 848*s*. GC/MS: 167, 122, 95, 72 (100), 69. ^{1}H-NMR: *Table*. ^{13}C-NMR ($CDCl_3$): 126.3 (C(6)); 122.5 (C(5)); 114.5 (CN); 100.0 (C(2)); 64.9 (CH_3CH_2O); 34.7 (C(3)); 26.4 (C(4)); 20.2 (CH_3–C(4)); 15.0 (CH_3CH_2O).

Epimerization of c-**2** *to* t-**2**. To *c*-**2**/*t*-**2** (95:5; 0.5 g) and 5 ml of Et_2O 10 drops of $BF_3 \cdot Et_2O$ were added. After standing at r.t. (or refluxing), 5 ml of brine were added, the Et_2O layer was dried (Na_2SO_4) and evaporated and the residue bulb-to-bulb distilled: 80% (0.4 g) of compound were recovered. GC: *c*-**2**/*t*-**2**/21.5:78.2 before and 29:71% after bulb-to-bulb distillation (*c*-**2**, R_t 7.90; *t*-**2**, R_t 7.66). ^{1}H-NMR of *t*-**2**: *Table*.

*6-Cyano-2-ethoxy-3,4-dihydro-4-phenyl-2*H-*pyran* (*c*-**3**). Ethyl vinyl ether (10 ml, 7.5 g, 0.1 mol) was added to 2-oxo-4-phenyl-3-butenenitrile (1.5 g, 9.5 mmol). The mixture was left it r.t. until nearly all nitrile had reacted (*ca.* 10 h (GC control); product formation progressing nearly linear). The ether was removed and the product bulb-to-bulb distilled (150°/0.05 Torr). Product composition before and after distillation, 93% *c*-**3** and 7% *t*-**3** (R_t 13.6 and 13.0, resp.). ^{1}H-NMR: *Table*. IR (film): 2220*s*, 1648v*s*, 1610*m*, 1505*s*, 1490*w*, 1460*s*, 1450*m*, 1390*s*, 1380*m*, 1365 (sh), 1350*w*, 1315*s*, 1300*m*, 1280*s*, 1255*w*, 1230*w*, 1200 (sb), 1185*s*, 1145*s*, 1125v*s*, 1075*w*, 1065*m*, 1035v*s*, 1025v*s*, 1005*w*, 980*m*, 945*s*, 915*m*, 880*m*, 850*s* (br.), 770*s*, 705v*s*.

Epimerization of c-**3**. To *c*-**3** and 2 ml of Et_2O were added 2 drops of $BF_3 \cdot Et_2O$. GC after 8 min: *t*-**3**/*c*-**3** 72:25, which did not vary on further standing for 2 days at r.t. Then, the soln. was extracted with sat. $NaHCO_3$ soln., evaporated, and the residue distilled. ^{1}H-NMR of *t*-**3** (in the mixture with *c*-**3**): *Table*.

*2-Ethoxy-3,4-dihydro-5-methyl-2*H-*pyran-6-carbonitrile* (**4**). A mixture of methacryloyl chloride (8.6 g, 82 mmol) and CuCN (7.1 g, 79 mmol) in CH_3CN (200 ml) was refluxed for 15 min. To the black soln., a 4-fold excess of ethyl vinyl ether (23.2 g, 322 mmol) was added and left at r.t. overnight. After distillation of the solvents, the residue was distilled at 140° (bath temp.)/0.01 Torr: 4.93 g (34%) of **4** as a yellow oil. GC: R_t 8.6. ^{1}H-NMR ($CDCl_3$, 80 MHz): 5.03 (*m*, H–C(2)); 3.85, 3.55 (2 *dq*, CH_3CH_2O); 1.85 (*s*, CH_3–C(5)); 1.2 (*t*, CH_3CH_2O). EI-MS: 167 (7, $M^{+\cdot}$), 122 (11), 106 (7), 94 (9), 83 (12), 82 (12), 72 (100), 69 (23), 67 (23); 55 (32), 54 (31), 53 (37), 45 (14).

2-Ethoxy-3,4-dihydro-4,5-dimethyl-pyran-6-carbonitrile (**5**). A mixture of 3-methyl-2-oxo-3-pentenenitrile [9] (0.4 g, 3.6 mmol) and ethyl vinyl ether was allowed to stand at r.t. for 3 h until no more nitrile could be detected (GC). Evaporation followed by bulb-to-bulb distillation (0.01 Torr) gave a colorless oil (0.4 g (61%) of **5**). GC: R_t 9. IR (film): 2230*s*, 1695*s*, 1677*m*, 1645*s*, 1441*s*, 1380*s*, 1345*w*, 1325*w*, 1305*m*, 1255*s*, 1225*w*, 1175 (sh), 1160v*s*, 1145–1135*s*, 1095v*s*, 1055v*s*, 903v*s*, 940*m*, 915*w*, 886*s*, 813*s*. ^{1}H-NMR (80MHz, $CDCl_3$): 5.0 (*dd*, $J = 2.6$, $J = 5.2$, H–C(2)); 3.9, 3.5 (2 *dq*, $J = 9.8$, 7, CH_3CH_2O); 2.32 (*m*, H–C(4)); 1.5–2.2 (*m*, 2 H–C(3)); 1.88 (*s*, CH_3–C(5)); 1.21 (*t*, CH_3CH_2O); 1.16 (*d*, $J = 7$, CH_3–C(4)). ^{13}C-NMR: 130.5 (C(6)); 121.7 (C(5)); 114.3 (CN); 98.2 (C(2)); 64.4 (CH_3CH_2O); 34.4 (C(3)); 30.0 (C(4)); 18.7 (CH_3–C(4)); 16.7 (CH_3–C(5)); 14.9 (CH_3CH_2O).

*Ethyl 6-Cyano-2-ethoxy-3,4-dihydro-2*H-*pyran-4-carboxylate* (**6**). Ethyl 4-cyano-4-oxo-2-butenoate (5 g, 32 mmol) and ethyl vinyl ether (6.9 g, 96 mmol) were mixed at 0°. The reaction was complete within 5 min (GC, R_t 11.7); if the reactants were mixed at r.t. the mixture heated up considerably. Evaporation of excess ether gave 7 g (95%) of **6** as a colorless oil which could be bulb-to-bulb distilled (140°/0.01 Torr). IR(film): 2240*m*, 1790*w*, 1742v*s* (br.), 1655*s*, 1482*w*, 1465*w*, 1450*m*, 1378*s*, 1375*s*, 1350*m*, 1300*s*, 1268*s*, 1236*s*, 1205v*s*, 1170*s*, 1120v*s*, 1097*w*, 1052v*s*, 1020*s*, 982*s*, 950*s*, 905*w*. ^{1}H-NMR: *Table*. ^{13}C-NMR ($CDCl_3$): 170.4 (CO); 136.6 (C(6)); 126.4 (C(5)); 114.7 (CN); 97.0 (C(2)); 64.2 (CH_3CH_2O); 61.2 (CH_3CH_2OCO); 34.5 (C(4)); 28.2 (C(3)); 14.7 (CH_3CH_2O); 14.0 (CH_3CH_2OCO).

*3,4-Dihydro-2-methoxy-2,4-dimethyl-2*H-*pyran-6-carbonitrile* (*c*-**7**/*t*-**7**). 2-Methoxypropene (16 g, 222 mmol) was added to 2-oxo-3-pentenenitrile (4 g, 42 mmol) and the mixture allowed to stand for 2 h at r.t. After evaporation, the residue was bulb-to-bulb distilled (90°/0.02 Torr): 5.4 g (77%) of *c*-**7**/*t*-**7** as a colorless liquid, ratio 92:8 (GC: (R_t 7.6 and 7.2, resp.); on heating above 90°, the ratio changed in favor of *t*-**7**. IR (film): 2240*m*, 1648*s*,

1460*m*, 1440*w*, 1390*s*, 1360*w*, 1343*s*, 1309*s*, 1270*w*, 1260*m*, 1232*m*, 1202*s* (br.), 1085 (sh), 1156*w*, 1132*s*, 1100 (sh), 1086*s*, 1060*s*, 1042*m*, 1010*w*, 980*w*, 955*m*, 935*w*, 845*s*, 830 (sh), 780*w*. MS: 167 ($M^{+\cdot}$), 152, 136, 120, 72, 69, 65, 54.

c-**7**: ^{1}H-NMR ($CDCl_3$, 80 MHz): 5.60 (*d*, *J* = 3.3, H–C(5)); 3.30 (*s*, CH_3O); 2.5 (*m*, H–C(4)); 1.6–2.2 (*m*, 2 H–C(3)); 1.43 (*s*, CH_3–C(2)); 1.18 (*d*, *J* = 7.2, CH_3–C(4)). ^{13}C-NMR ($CDCl_3$): 125.8 (C(6)); 122.3 (C(5)); 114.7 (CN); 101.4 (C(2)); 49.1 (CH_3O); 37.8 (C(3)); 26.2 (C(4)); 22.0 (CH_3–C(2)); 20.1 (CH_3–C(4)).

t-**7**: IR (film): 2240*m*, 1648*s*, 1460*m* (br.), 1440*w*, 1390*s*, 1360 (sh), 1343*s*, 1309*s*, 1270 (sh), 1260*s*, 1232*s*, 1202*s* (br.), 1085 (sh), 1156*m*, 1132*s*, 1100 (sh), 1086*s*, 1060*s*, 1042*s*, 1010*w*, 980*w*, 955*m*, 935*w*, 845*s*, 830 (sh), 780*m*. ^{1}H-NMR ($CDCl_3$, 80 MHz): 5.55 (*m*, H–C(5)); 3.28 (*s*, CH_3O); 2.6 (*m*, H–C(4)); 1.6–2.2 (*m*, 2 H–C(3)); 1.45 (*s*, CH_3–C(2)); 1.05 (*d*, *J* = 7.2, CH_3–C(4)). ^{13}C-NMR ($CDCl_3$): 125.7 (C(6)); 123.7 (C(5)); 114.7 (CN); 100.3 (C(2)); 49.1 (CH_3O); 39.9 (C(3)); 24.1 (C(4)); 22.3 (CH_3–C(2)); 19.0 (CH_3–C(4)). GC/MS (*c*-**7**): 167 ($M^{+\cdot}$), 152, 136, 120, 72, 69, 65, 54.

*Methyl 2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyran-6-carboximidate* (**8**). At r.t. 1M NaOMe (2.4 ml) in MeOH was added to a soln. of **2** (*c*/*t* 95:5, 4 g, 23.9 mmol) in dry MeOH (26 ml). Small samples were extracted with H_2O and Et_2O and the Et_2O extracts examined by GC (R_t: *t*-**2** 7.6, *c*-**2** 8.0, *t*-**8** 9.4, and *c*-**8** 9.7). Conversion was 6.1 (after 0.5 h), 30.4 (2.16 h), 48 (3.25 h), 54.5 (3.83 h), 65 (4.83 h) and 74.1 % (5.91 h). The reaction was completed after standing overnight. Brine was added (50 ml), the mixture extracted 3 times with Et_2O, and the combined extract dried ($MgSO_4$) and evaporated: 4.41 g (92%) of **8**. IR (film): 3340*m*, 1670*m*, 1628*vs*, 1449*s*, 1391*s*, 1379*s*, 1356*s*, 1323*s*, 1285*s*, 1265*m*, 1235*m*, 1220*m*, 1190*s*, 1175 (sh), 1160 (sh), 1128*s*, 1120 (sh), 1084*vs*, 1025*m*, 990*s*, 961*m*, 951*m*, 934*w*, 917*m*, 891*w*, 860 (sh), 855*s*, 825 (sh), 815*m*, 733*m*. ^{1}H-NMR ($CDCl_3$, 80 MHz): 7.95 (br. *s*, variable, NH); 5.63 (*d*, *J* = 3, H–C(5)); 5.08 (*dd*, *J* = 7.5, 2, H–C(2)); 3.84 (*s*, CH_3O); 4.0, 3.64 (2 *dq*, *J* = 9.5, 7, CH_3CH_2O); 2.54 (*m*, H–C(4)); 2.06 (*ddd*, *J* = 13.6, 6.5, 2.5, H–C(3)); 1.59 (*ddd*, *J* = 13.6, 8, 1, H–C(3)); 1.26 (*t*, *J* = 7, CH_3CH_2O); 1.12 (*d*, *J* = 7, CH_3–C(4)).

*Methyl 2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyran-6-carboxylate* (**9**). A soln. of **8** (1.0 g, 5 mmol) in Et_2O (10 ml) was stirred rapidly with 1M HCl (5 ml) for 2 h at r.t. The Et_2O layer was washed with sat. $NaHCO_3$ soln. dried ($MgSO_4$), and evaporated to give **9** (0.8 g, 80%) as colorless oil. GC: R_t 10.6 (*cis*), 10.0 (*trans*). IR (film): 1740*vs* (br.), 1648*s*, 1623*m*, 1455 (sh), 1440*s*, 1378*s*, 1358*w*, 1325*s*, 1310 (sh), 1300*vs*, 1270*s*, 1258*s*, 1226*s*, 1209*s*, 1189*s*, 1171*s*, 1123*s*, 1100*s*, 1085*vs*, 1051*vs*, 1022*m*, 1005*w*, 990*m*, 965*m*, 913*m*, 865*m*, 800*m*, 765*m*. EI-MS: no $M^{+\cdot}$, 111 (5), 95 (16), 83 (9), 72 (7), 69 (100), 59 (34), 55 (29), 53 (26), 45 (16).

*2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyran-6-methanol* (**10**). $LiAlH_4$ (71 mg, 1.9 mmol) was suspended in 2 ml of abs. Et_2O and **9** (0.5 g, 2.5 mmol) in little Et_2O added dropwise with strirring. After refluxing gently for 2 h, H_2O (71 mg) and 15% NaOH soln. (71 mg) were added. Finally, 240 mg of H_2O and Et_2O were added. The white suspension was filtered, the Et_2O phase dried ($NaSO_4$) and evaporated, and the pale yellow oil bulb-to-bulb distilled (89°/0.15 Torr): 0.24 g (56%) of **10**. GC: R_t 11.6. IR (film): 3420*s* (v br.), 1685*s* (br.), 1485*w*, 1455*s* (br.), 1380*vs*, 1360*m*, 1330*m*, 1296*s*, 1275 (sh), 1262*m*, 1230 (br.), 1191*s*, 1165*m*, 1140*vs* (br.), 1080 (sh), 1058*vs*, 1020*s*, 987*s*, 968 (sh), 945*w*, 920*m*, 906*s*, 870*s*, 855 (sh), 790*m* (br). ^{1}H-NMR ($CDCl_3$, 80 MHz): 4.91 (*dd*, *J* = 5, 2, H–C(2)); 4.63 (br. *s*, H–C(5)); 3.90 (*s*, CH_2OH); 3.9, 3.5 (2*dq*, CH_3CH_2O); 2.82 (*s*, OH, exchanging with D_2O); 2.38 (*m*, H–C(4)); 1.96 (*ddm*, H–C(3)); 1.44 (*dd*, H–C(3)); 1.21 (*t*, *J* = 7, CH_3CH_2O); 1.03 (*d*, *J* = 7, CH_3–C(4)). EI-MS: no $M^{+\cdot}$, 131 (29), 119 (11), 100 (19), 73 (100), 69 (55), 59 (10), 50 (11), 45 (15).

*2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyran-6-methylamine* (**11**). $LiAlH_4$ (0.29 g, 7.6 mmol) was added to a soln. of **2** (*c*/*t* 95:5; 0.83 g, 5 mmol) in Et_2O (25 ml) and the mixture gently refluxed for 2 h. H_2O was added dropwise carefully, followed by 2M NaOH. The mixture was extracted with Et_2O, the Et_2O phase dried (Na_2SO_4) and evaporated, and the clear colorless oil bulb-to-bulb distilled to yield 0.7 g (82%) of **11**. GC: R_t 8.0. IR (film): 3400*w*, 1688*s*, 1600*w* (br.), 1478 (sh), 1450*m* (br.), 1380*s*, 1360*w*, 1325*m*, 1290*m*, 1260*w*, 1222*w*, 1190*s*, 1178 (sh), 1133*vs*, 1092*s*, 1058*vs*, 1025*m*, 978*s*, 942*w*, 908*s*, 865*s*, 833*m*, 780*m*. ^{1}H-NMR ($CDCl_3$, 80 MHz): 4.92 (*dd*, *J*(2,3) = 2.5, *J*(2,3) = 8.2, H–C(2)); 4.50 (br. *s*, H–C(5)); 3.92, 3.55 (2*dq*, ^2J = 9, ^3J = 7, CH_3CH_2O); 3.14 (*s*, CH_2NH_2); 2.40 (*m*, H–C(4)); 1.98 (*ddm*, ^2J = 12.9, ^3J(3,4) = 6.8, H–C(3)); 1.46 (*dd*, ^2J = 12.9, ^3J = 8.2, H–C(3)); 1.34 (*s*, NH_2, exchanged with D_2O); 1.24 (*t*, *J* = 7, CH_3CH_2O); 1.02 (*d*, *J* = 7, CH_3–C(4)).

*2-Ethoxy-3,4-dihydro-4-methyl-2*H*-pyran-6-carbaldehyde* (**12**). DIBAH (1M in hexane; 3 ml) was added to a stirred soln. of **2** (*c*/*t* 95:5; 0.34 g, 2 mmol) in 4 ml of dry hexane under N_2 at −5°. The mixture was brought to r.t. and left for 2½ h. H_2SO_4 soln. (5 ml, 5%) was added carefully with cooling followed by 15 ml of Et_2O. The Et_2O layer was separated, the aq. layer washed with 15 ml of Et_2O, and the combined Et_2O extract dried (Na_2SO_4) and evaporated: 0.34 g (> 95%) of **12** as a clear pale yellow oil. GC: R_t 8.1 (*cis*), 7.8 (*trans*). IR (film): 1700*vs* (br.), 1640 (sh), 1636*s*, 1450*m* (br.), 1403*m*, 1381*s*, 1360*w*, 1332*m*, 1298*m*, 1240*w*, 1222*w*, 1190*s*, 1155*s*, 1145*s*, 1090*w*, 1052*vs*, 1025*vs*, 1005*w*, 981*vs*, 940*w*, 915 (sh), 905*s*, 888*s*, 855*w*, 810*w*, 730*m*.

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