3-Hydroxy-2-cyanoalk-2-enamides, and 2-Cyano-2-(tetrahydrofuran-2-ylidene)- and 2-Cyano-2-(tetrahydropyran-2-ylidene)acetamides: Synthesis, Structure, and Solvent-Dependent (*Z*)/(*E*)-Isomerism

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Dedicated to Professor *D. Seebach* on the occasion of his 60th birthday

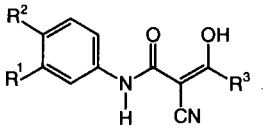
3-Hydroxy-2-cyanoalk-2-enamides, and 2-cyano-2-(tetrahydrofuran-2-ylidene)- and 2-cyano-2-(tetrahydropyran-2-ylidene)acetamides with *N*-alkyl and *N*-aryl substituents have been synthesized in three steps from cyanoacetic acid. Their conformations were investigated by X-ray crystallography and ^{1}H-NMR ROESY spectroscopy at room temperature. The enolic compounds **1**–**3** adopt an extended conformation stabilized by a strong intramolecular O–H ··· O=C bond both in the solid state and in (D_6)DMSO solution. In contrast, the structure of the cyclic derivatives **5a**,**b**–**8a**,**b** is solvent-dependent. In the solid state and in $CDCl_3$ solution, the compounds adopt an extended conformation of type **I** or **III**, while, in (D_6)DMSO solution, their structures undergo time-dependent (*Z*)/(*E*)-isomerization structures (of type **II** or **IV**). This observation is compatible with a dipolar transition state of rotation. The kinetics of the isomerization are controlled by the *N*-substituent, the *N*-(*t*-Bu) derivatives **7a** and **7b** having the highest barrier of rotation around the C=C bond. The whole body of experimental evidence together with the results of molecular-mechanics calculations with **I**–**IV**, indicate that, in DMSO, two (*E*)/(*Z*)-isomers with two conformations are present, and that they undergo interconversion at room temperature with four different constants. The very fast exchange rates $k_{I,II}$ and $k_{III,IV}$ in the NMR time-scale might be responsible for the detection of only two isomers.

Introduction. – *N*-Aryl-cyanopropenamides represent a class of substances of potential interest for the treatment of autoimmune diseases. Starting from compounds **1** and **2**, which are currently undergoing clinical evaluation for the indication of rheumatoid arthritis[1]) [1][2], the synthesis of five- and six-membered ring derivatives, namely 2-tetrahydrofuran-2-ylidene and 2-tetrahydropyran-2-ylidene derivatives, was undertaken, aiming at the establishment of structure-activity relationships based on cyanopropenamides. The C=C bond of these compounds has two electron-withdrawing groups (CN, CONHR) on one sp^2-C-atom, the other carrying two electron-donating groups (O, alkyl). This push-pull substitution pattern is expected to strongly polarize the C=C bond and to reduce its double-bond character. As a consequence, a dramatic decrease of the activation barrier of (*Z*)/(*E*)-isomerization can be envisaged, allowing it to occur even at room temperature[2]) [4]. This report describes the synthesis and the conformational preferences of such compounds. It establishes that, at room temperature, the 2-cyano-3-hydroxy-alk-2-enamides **1**–**3** adopt a single, stable conformation, while the 2-cyano-2-

[1]) Compound **1** is the bioactive metabolite of the clinically tested drug leflunomide. In *in vivo* systems leflunomide is converted to **1** (> 90%) within 10 min after oral administration.

[2]) This feature has been extensively studied with compounds containing an enamine moiety. For *N*,*N*-disubstituted acrylate derivatives, see [3a]; for aromatic ketene aminals, see [3b].

(tetrahydrofuran-2-ylidene) and 2-cyano-2-(tetrahydropyran-2-ylidene)acetamides undergo (*Z*)/(*E*)-isomerization which is dependent on the solvent as well as on the *N*-substituent.



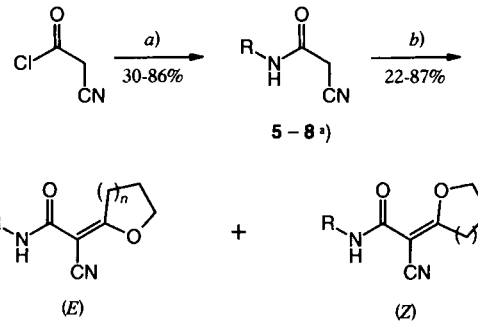
1 R^1 = H, R^2 = CF_3, R^3 = Me

2 R^1 = Me, R^2 = CN, R^3 = H_2C=CH—CH_2

3 R^1 = H, R^2 = H, R^3 = Br—$(CH_2)_3$—CH_2

Results. – *Synthesis.* Compounds **1** and **2** were prepared according to the procedure described in [2]. The target compounds were obtained in two steps starting from cyanoacetic acid. The latter was transformed to the corresponding cyanoacetamides **5**–**7** *via* cyanoacetyl chloride [5] and subsequent reaction with the corresponding amines. This method failed for the synthesis of the *N*-methyl-acetamide **8** which was obtained by reaction of methyl cyanoacetate with an excess of $MeNH_2$. Treatment of **5**–**8** with 2.2 equiv. of BuLi at −78° and acylation of the resulting dianion with 3 equiv. of either 4-bromobutanoyl chloride or 4-bromopentanoyl chloride (−78° to r.t.) led, in moderate yields, to the tetrahydrofuran-2-ylidene and tetrahydropyran-2-ylidene derivatives, respectively (*Scheme 1*)[3][4]). No ring formation occurred at low temperature as shown by the isolation of intermediate **3** upon quenching of the reaction, leading to **6b** at −78°.

Scheme 1



5a R = 4-CF_3–C_6H_4, *n* = 1 **5b** R = 4-CF_3–C_6H_4, *n* = 2
6a R = Ph, *n* = 1 **6b** R = Ph, *n* = 2
7a R = *t*-Bu, *n* = 1 **7b** R = *t*-Bu, *n* = 2
8a R = Me, *n* = 1 **8b** R = Me, *n* = 2

a) RNH_2 (1.1 equiv.), pyridine (1.5 equiv.), CH_2Cl_2, 0° → r.t. b) BuLi (2.2 equiv.), THF, −78°, 30 min, then $BrCH_2(CH_2)_nCH_2COCl$, *n* = 1, 2 (1.1 equiv.), −78° → r.t.

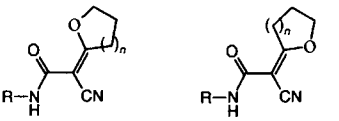
[a]) Compound **8** was obtained from the reaction of methyl cyanoacetate with $MeNH_2$.

[3]) 2-[(Carbamoyl)(cyano)methylidene]tetrahydropyran has been obtained from condensation of valerolactone diethyl acetal with cyanoacetamide at 130° [6].

[4]) 2-Methylidenetetrahydropyran derivatives have been obtained upon refluxing of butyrolactone diethyl acetal with highly acidic methylene compounds [7].

After chromatographic separation from polymeric material, compounds **5a**, **5b**, **6b**, **8a**, and **8b** were isolated as single isomers, while compounds **6a**, **7a**, and **7b** were obtained as two, easily separable isomers in the ratio 49:51, 48:52, and 23:77, respectively (*Table 1*), indicating that there is no influence of the R moiety on the product distribution within the tetrahydrofuran-2-ylidene and tetrahydropyran-2-ylidene series for R = alkyl and R = 4-CF_3–C_6H_4. However, for R = Ph two tetrahydrofuran-2-ylidene isomers (*Z*)-**6a** and (*E*)-**6a** and only one tetrahydropyran-2-ylidene isomer (*E*)-**6b** were obtained. The reason for the different product distribution of the *N*-phenyl amides as compared to that of the other derivatives is unclear.

Table 1. *Physicochemical Data of Compounds* **5a,b–8a,b**[a])



Compound	R	*n*	M.p. [°]	$\delta(CH_2O)$[b]) [ppm]	$\delta(C{=}C(O){-}CH_2)$[b]) [ppm]	*J* [Hz]	Yield [%]
(*Z*)-**5a**	4-CF_3–C_6H_4	1	190–192	4.71	3.11	6.60	22.0
(*Z*)-**6a**	Ph	1	161–162	4.68	3.10	6.60	16.0
(*E*)-**6a**	Ph	1	113–114	4.51	3.21	6.60	16.7
(*Z*)-**7a**	*t*-Bu	1	157–158	4.62	3.04	6.60	13.3
(*E*)-**7a**	*t*-Bu	1	120–121	4.45	3.14	6.60	12.1
(*Z*)-**8a**	Me	1	163–166	4.62	3.07	6.60	35.1
(*Z*)-**5b**	4-CF_3–C_6H_4	2	243–245	4.43	2.82	6.60	86.7
(*E*)-**6b**	Ph	2	109–110	3.57	2.64	6.00	53.2
(*Z*)-**7b**	*t*-Bu	2	150–152	4.39	2.75	6.00	42.7
(*E*)-**7b**	*t*-Bu	2	87–89	4.28	2.84	6.00	12.8
(*E*)-**8b**	Me	2	98–101	3.53	2.56	6.00	34.8

[a]) Satisfactory analytical data (± 0.4% for C, H, N) have been obtained for all compounds listed. [b]) ^{1}H-NMR Spectra were recorded immediately after dissolution of the compounds in (D_6)DMSO. The signals of the CH_2O and $C{=}C(O){-}CH_2$ protons appear as clearly resolved *triplets*.

Structural Studies with Conjugated Enols. A key parameter for the interpretation of the results obtained during structure-activity studies is the structural similarity of the compounds under investigation [8]. Consequently, the three-dimensional structures of the biologically active 3-hydroxy-2-cyanoalk-2-enamides **1**, **2**, and of the intermediate **3** were determined as representative acyclic compounds of this substance class. In (D_6)DMSO solution, only one of the two possible geometric isomers around the C=C bond was detected (400-MHz ^{1}H-NMR). Its conformation could not be assessed on the basis of NOE experiments, indicating that the amide NH is probably not in the vicinity of the alkyl moiety R^3. No rotamers were observed, the s-*trans* amide bond being largely favored for steric reasons as already established by spectroscopic methods both in solution and in the gas phase for acetanilide [9][10]. However, the shift of the enolic proton signal provides evidence that the conformation of **1**–**3** in solution is

governed by a strong H-bond formation in which the enol OH group is the donor. Indeed, the δ(OH) of a series of H-bonded (O–H ··· O=C), geometrically constrained cycloalkyl hydroxy-oxo-cycloalkanecarboxamides and *N*-aryl-2-hydroxybenzamides lies between 10.23 and 10.67 ppm [11]. The δ(OH) value for **1**–**3** is also in the same range (10.01, 10.10, and 9.95 ppm, resp.). Consequently, in DMSO, the 3-hydroxy-2-cyanoalk-2-enamide derivatives are locked in a planar, extended conformation stabilized by the strong O–H ··· O=C H-bonding ((*Z*)-enol).

In the solid state, X-ray crystal-structure analysis confirmed that the enols **1** and **3** adopt an extended conformation and have a (*Z*)-enol structure with a strong H-bond between the OH and the amide C=O moieties (*Fig. 1*). It is interesting to note that, although the aromatic ring of **1** is almost coplanar with the plane of the conjugated system [8] and in line with that observed in the crystal structure of acetanilide (17°) [12], the Ph ring of **3** deviates by 55° (*Fig. 1*). Not surprisingly, the electron density along the 3-hydroxy-2-cyanoalk-2-enamide moiety is delocalized as evidenced by the short bond lengths between the atoms involved. Indeed, **1** has C–CN, (CN)C–C(CO), and (OH)C–C(CN) bond lengths of 1.431, 1.458, and 1.373 Å, respectively, while the corresponding values for **3** are 1.429, 1.477, and 1.376 Å. In addition, the short intramolecular O–H ··· O bond is also indicative of an extended π delocalization of the H-bonded conjugated systems (*d*(O–O) is 2.474 and 2.491 Å for **1** and **3**, resp.). In fact, the experimental data obtained fully supports the RAHB (resonance-assisted hydrogen bonding) model which emphasizes the interplay between intramolecular H-bonding

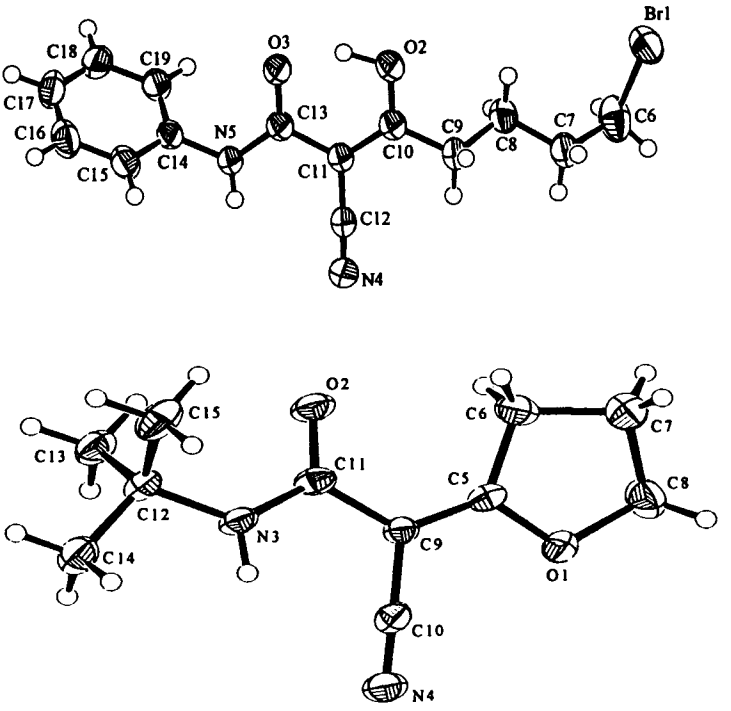
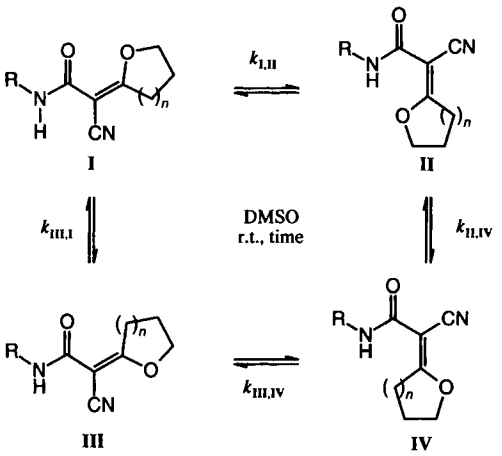


Fig. 1. *ORTEP Plots of* **3** *and* (E)-**7a**. The ORTEP plot of **1** has been described in [8].

distance, NMR spectroscopic data, and electron-density delocalization for 1,3-diketone enols and related systems irrespective of their molecular complexity and the number of additional conjugated systems [13].

Structural Studies with Conjugated Cyclic Ethers. In contrast to the enols, the tetrahydrofuran-2-ylidene and tetrahydropyran-2-ylidene derivatives, **5a–8a** and **5b–8b**, respectively, are expected to be more flexible, since they have no possibility of H-bond formation *via* participation of the amide C=O group. Thus, each of the compounds can adopt four diastereoisomeric structures **I–IV** (*Scheme 2*) which correspond to two pairs of conformers (**I**/**II** and **III**/**IV**) and two pairs of geometric isomers (**I**/**III** and **II**/**IV**). The extended (*Z*)- and (*E*)-isomers **I** and **III** are expected to be energetically favored. In spite of the potential NH ··· O H-bond in **II**, this structure is not expected to be favored, since the acceptor is a vinylogous carbamidyl moiety. Nevertheless, molecular-mechanics calculations [5]) performed on the structures depicted in *Scheme 2* using **6a** and **6b** as model compounds indicate that the energy differences between **I–IV** do not exceed 3 kcal/mol, and, thus no quantitative predictions concerning the corresponding conformation populations can be made.

Scheme 2



As with the enolic compounds, **5a,b–8a,b** possess an essentially planar geometry in the ground state in order to maximize electron delocalization along the conjugated π system. Indeed, all compounds exhibit intense UV absorption bands in the region of 248–279 nm which can be assigned to the $\pi \rightarrow \pi^*$ transition. The potential for internal rotation of these olefins as well as their solution structures were investigated by ^{1}H-NMR (400 MHz) both in $CDCl_3$ and (D_6)DMSO at room temperature. The spectra of the compounds in $CDCl_3$ showed only one set of clearly resolved signals indicating the presence of a single geometric isomer and the lack of amide-bond rotamers. No time-dependent changes were observed in the spectra up to 72 h. For establishing the structures of **5a,b–8a,b**, ROESY experiments [14] were performed which should allow the identifi-

[5]) The molecular modeling program packet SYBYL 6.22 from *Evans & Sutherland, Tripos Assoc. Inc.*, St. Louis, MO, was used. The geometry optimization was performed with the force-field MAXIMIN 2.

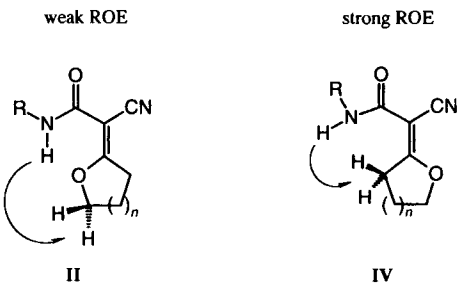


Fig. 2. *ROEs Intensities for (E)- and (Z)-isomers,* **II** *and* **IV**, *respectively*

cation of **II**- and **IV**-like geometric isomers (*Fig. 2*), the corresponding extended conformers **I** and **III** having no potential for ROE effects due to the distance constraints (distance of NH to closest $CH_2 \geq 4.7$ Å).

In all eight compounds investigated, there were no ROEs detected. Although this result did not reveal anything about the conformation of **5a,b**–**8a,b**, it suggested that the compounds might adopt one of the extended structures **I** or **III**. Experimental support for such a conformation was obtained by X-ray crystallographic studies with **7a**, the only compound of the series suitable for single-crystal analysis. Indeed, as shown in *Fig. 1*, this compound adopted a **III**-type structure with physicochemical properties similar to those of **1** and **3**. The ensemble of the experimental data is compatible with an extended conformation for **5a,b**–**8a,b** in $CDCl_3$. However, no predictions about the type of the isomerism (**I** *vs.* **III**) can be made concerning the single isomers **5a**, **5b**, **6b**, **8a**, and **8b**, while **6a**, **7a**, and **7b** have been isolated in both isomeric forms.

In contrast to the results obtained in $CDCl_3$, a time-dependent evolution of the resonances was observed in the (D_6)DMSO spectrum of all compounds with the exception of the *t*-Bu-substituted derivatives **7a** and **7b** (*Tables 1* and *2*). In this case, ROESY spectroscopy turned out to be a valuable tool for the determination of the structure of the diastereoisomers present. As already mentioned, compounds of type **II** or **IV** had ROEs of different intensities (*Fig. 2*). In the case of the isomers of **7a**, where no equilibration occurs, irradiation of the NH (δ 6.85, *s*) gave a strong ROE with the allylic CH_2 (δ 3.13, *t*, $J = 6.6$) demonstrating that this isomer was **7a(IV)**. Irradiation of the NH signal (δ 6.92, *s*) of the second isolated isomer of **7a** lead to a weak ROE with the CH_2O resonance (δ 4.65, *t*, $J = 6.6$) thus indicating that this compound was **7a(II)**. The structures of the two isomers of **7b** were determined in a similar manner. For rapidly equilibrating derivatives such as **5a** and **5b**, the ROE experiments were conducted after 48 h *via* irradiation of the major NH signal present.

Discussion. – The common feature of 2-cyano-3-hydroxyalk-2-enamides is their planar structure which allows them to maximize electron delocalization along the conjugated π system. Both solid-state and solution (DMSO) data obtained with the enolic compounds **1** and **3** demonstrate that they adopt similar conformations stabilized by the strong intramolecular H-bond between the OH and the amide carbonyl O-atom.

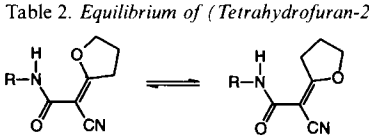
The situation is different for the 2-cyano-2-(tetrahydrofuran-2-ylidene)- and -2-(tetrahydropyran-2-ylidene)alk-2-enamides **5a**, **5b**, **6a**, **6b**, **8a**, and **8b**. These compounds

undergo (*Z*)/(*E*)-equilibration at room temperature when dissolved in (D_6)DMSO but not when dissolved in $CDCl_3$. This observation is compatible with a dipolar transition state of rotation. Indeed, the mechanism of the rotation around such olefinic systems may conceivably involve a biradical or a dipolar transition state. In contrast to the apolar $CDCl_3$, the polar (D_6)DMSO is capable of stabilizing a dipolar transition state and, consequently, increases the rate of isomerization.

The key parameter employed for the investigation of the kinetics of the **II**/**IV** equilibration and for the unambiguous assignment of the conformer structures present was the NH signal. Although only configurational isomers of type **II** and **IV** were identified by NMR, molecular-mechanics calculations performed on the structures **I**–**IV** using **6a** and **6b** as model compounds indicate that the energy differences between the four conformers do not exceed 3 kcal/mol. This low value, which does not take into account the influence of solvent effects, together with the set of experimental data obtained by X-ray crystallographic analysis of **7a** and NMR experiments in $CDCl_3$ with **5a**,**b**–**8a**,**b** indicate the existence of the extended isomers **I** and **III**. It could, therefore, be that, in (D_6)DMSO, all four structures **I**–**IV** are present and equilibrate with four different equilibrium constants. The lack of observation of **I** and **III** might be due to the very fast exchange rates $k_{I,II}$ and $k_{III,IV}$ at room temperature and/or to the low populations of these isomers. An analogous four-species equilibrium has already been observed for methyl 2-cyano-3-(*N*-methylanilino)acrylate [15].

Tables 2 and *3* summarize the equilibration behavior of the push-pull tetrahydrofuran-2-ylidene and tetrahydropyran-2-ylidene derivatives as a function of time. Interestingly, the *N*-(*t*-Bu)-substituted amides are very resistant to isomerization, emphasizing the key contribution of the substituent R (*cf. Scheme 1*) in the activation barrier of the rotation around the C=C bond. However, the factors governing the activation energy for rotation about bonds are manifold. As shown above, steric interactions are important, but electronic effects are by no means to be neglected [4].

Table 2. *Equilibrium of (Tetrahydrofuran-2-ylidene)acetamides in DMSO*[a])



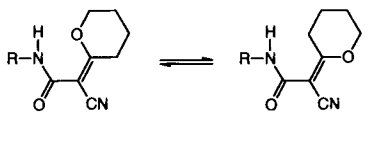
(*Z*) (*E*)

5 R = 4-CF_3–C_6H_4
6 R = Ph
7 R = *t*-Bu
8 R = Me

Compound[b])	(*Z*)/(*E*) Ratio					
	5 min	0.5 h	1.0 h	7.0 h	24 h	48 h
(*Z*)-**5**	78:22	42:58	36:64	32:68	20:80	16:84
(*Z*)-**6**[c])	100:0	81:19	75:25	51:49	41:59	39:61
(*E*)-**6**	0:100	0:100	0:100	4:96	6:94	7:93
(*Z*)-**7**	100:0	100:0	100:0	100:0	100:0	100:0
(*E*)-**7**	0:100	0:100	0:100	0:100	0:100	0:100
(*Z*)-**8**	100:0	100:0	90:10	52:48	35:65	33:67

[a]) The ratios represent the mean of two sets of integrals and were determined by ^{1}H-NMR (400 MHz). [b]) Initial major conformation of isolated compound. [c]) After six days: (*Z*)/(*E*) ratio 13:87.

Table 3. *Equilibrium of (Tetrahydropyran-2-ylidene)acetamides in DMSO*[a])



(*Z*) (*E*)

5 R = 4-CF_3–C_6H_4
6 R = Ph
7 R = *t*-Bu
8 R = Me

Compound[b])	(*Z*)/(*E*) Ratio					
	5 min	0.5 h	1.0 h	7.0 h	24 h	48 h
(*Z*)-**5b**	90:10	81:19	70:30	19:81	0:100	0:100
(*E*)-**6b**[c])	100:0	4:96	8:92	31:69	56:44	78:22
(*Z*)-**7b**[d])	100:0	100:0	100:0	96:4	94:6	93:7
(*E*)-**7b**	0:100	0:100	0:100	0:100	0:100	0:100
(*E*)-**8b**	0:100	1:99	3:97	8:92	14:86	17:83

[a]) The ratios represent the mean of two sets of intergrals and were determined by ^{1}H-NMR (400 MHz). [b]) Initial major conformation of isolated compound. [c]) The (*Z*)-isomer was exclusively present after 127 h. [d]) After 72 h and 312 h the (*Z*)/(*E*) ratio was 88:12 and 82:18, respectively.

In conclusion, this study demonstrates that, in contrast to the conformationally locked 3-hydroxy-2-cyanoalk-2-enamides, *N*-substituted tetrahydrofuran-2-ylidene and tetrahydropyran-2-ylidene derivatives can exist as two (*E*)/(*Z*)-isomers each of which has the possibility to adopt two, solvent-dependent conformations at room temperature. An analogous phenomenon has been observed with the naturally ocurring immunosuppressants cyclosporin A [16] and FK-506 [17]. Moreover, both the product distribution of the reaction leading to **5a,b**–**8a,b** as well as the rate of isomerization of the compounds in DMSO are heavily dependent on the *N*-substituent on the amide function. To gain insight into these processes, variable-temperature NMR investigations are required to obtain thermodynamic information about the energy barriers coming into play during the isomerization of these compounds. The ensemble of the data could allow establishing a relationship between structure, kinetic and thermodynamic properties of cyclic compounds structurally related to propenamides. This will be of value in understanding the mechanism of the rotational process(es) as well as the physicochemical properties of other conjugated systems.

We thank Prof. *D. Seebach* (ETH-Zürich) for his suggestions and critical reading of the manuscript, and *J. France* for initial NMR experiments.

Experimental Part

Spectroscopic Studies. ^{1}H-NMR Spectra were recorded at r.t. on a *Bruker AMX-400* or *-DPX-400* spectrometer. For the equilibration experiments, 1 mM solns. of **5a,b**–**8a,b** in (D_6)DMSO were used, and the structures of the isomers were determined by ROE [14].

*Synthesis. 2-Cyano-*N*-methylacetamide* (**8**). Methyl cyanoacetate (50.0 g, 505 mmol) and a large excess of $MeNH_2$ were placed in an autoclave and heated to 140°. After 1 h, the pressure dropped from 10 to 1 atm. The cylinder was then cooled and the crystalline mass removed. Two successive recrystallizations from MeOH yielded pure **8** [21] (23.6g, 47%). M.p. 96–98°. ^{1}H-NMR ((D_6)DMSO): 2.60 (*d*, *J* = 5.1, 3 H); 3.57 (*s*, 2 H); 8.15 (br. *s*, 1 H).

General Procedure for the Synthesis of 2-Cyano-2-(2,3,4,5-tetrahydrofuran-2-ylidene)acetamides **5a–8a** *and 2-Cyano-2-(3,4,5,6-tetrahydro-2H-pyran-2-ylidene)acetamides* **5b–8b** (see *Table 1*). To a precooled soln. (–78°) of **5–8** (10 mmol, 1 equiv.) in dry THF, a soln. of BuLi (22 mmol, 2.2 equiv.) in hexane was added. The resulting yellow soln. was stirred for 30 min. Then, 4-bromobutanoyl chloride or 4-bromopentanoyl chloride (11 mmol, 1.1 equiv.) was added dropwise. The reaction was then allowed to slowly warm to r.t. and quenched with sat. aq. NH_4Cl soln. The mixture was then extracted with 3 portions of AcOEt and concentrated *in vacuo*. The crude products were purified by flash chromatography (silica gel, hexane/AcOEt) to give **5a,b–8a,b**.

Table 4. *Data Collection and Refinement for Compounds* **3** *and* (E)-**7a**[a])

Compound	**3**	(*E*)-**7a**
Crystallized from	AcOEt/Et_2O	Et_2O/hexane
Formula	$C_{14}H_{15}BrN_2O_2$	$C_{11}H_{16}N_2O_2$
Mol. wt.	323.19	208.26
Crystal system	triclinic	monoclinic
Space group	*P*1	$P2_1/c$
a [Å]	5.963(1)	16.988(2)
b [Å]	8.107(1)	7.288(1)
c [Å]	15.004(2)	9.521(1)
α [°]	98.62(1)	
β [°]	98.61(1)	91.58(1)
γ [°]	98.16(1)	
V (Å^3)	699.0(2)	1178.3(2)
Z	2	4
F(000)	328	448
$D_{calc.}$ [g · cm^{-3}]	1.536	1.174
No. of reflections for cell parameters	25	25
Θ range for cell parameters [°]	26–32	15–20
μ [mm^{-1}]	4.012	0.663
Crystal form	platelet	needle
Crystal size (mm)	0.58 × 0.27 × 0.08	0.54 × 0.06 × 0.02
Crystal color	colorless	colorless
Diffractometer	*Enraf-Nonius CAD4*	*Philips PW1100*
Radiation (graphite monochromated)	CuK_α	MoK_α
Wavelength [Å]	1.5418	0.70926
Scan mode	$\omega/2\Theta$	$\omega/2\Theta$
Scan range (2Θ)	6–148	6–87
Absorption correction	none	none
No. of measured reflections	3134	1013
No. of independent reflections	2853	928
No. of observed reflections ($I > 2\sigma(I)$)	2597	767
R_{int}	0.067	0.021
Intensity variation	± 2%	± 1%
Refinement method	refinement on F^2	refinement on F^2
No. of parameters	172	136
R	0.077	0.046
R_w	0.174	0.118
S	1.89	0.949
Treatment of H-atoms	riding	riding
Max/min $\Delta\rho$ [eÅ^{-3}]	1.612/ –0.956	0.213/ – 0.155

[a]) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-101138. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: + 44(1223) 336 033; e-mail: deposit@ccdc.cam.ac.uk).

Crystal-Structure Determination of **3** *and* (E)-**7a** (see *Table 4* and *Fig. 2*). A *Nonius CAD4* automatic diffractometer was used for data collection with CuK_α radiation, and a graphite monochromator was used for the measurement of **3**. For the determination of the structure of (*E*)-**7a**, a *Philips PW1100* automatic diffractometer using graphite monochromated MoK_α radiation was employed. The structures were solved by direct methods [18], and the parameters were refined by full-matrix least-squares calculations [19] with anisotropic displacement parameters for all non-H-atoms. A subsequent difference *Fourier* map showed all H-atoms. For the visualization of the results, the molecular graphics software ORTEP was used [20].

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