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INTERCONVERSION AND PREPARATIVE SEPARATION OF ENANTIOMERIC ENAMIDES

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Barriers to rotation about the =C-N single bond of enamides (Table 1) are rationalised. The barriers of 7 and 8 allow separations of the enantiomers.

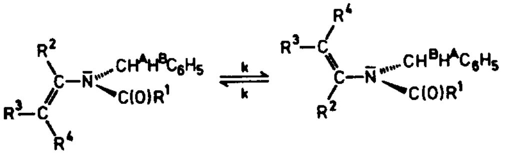
N-Alkylidenecarbamoyl chlorides, e.g. 1 (Table 1), exhibit anisochronous methylene protons H^A and H^B and are therefore non-planar, i.e. chiral[4]. Further investigations showed this property to be a general one for enamides $R^3R^4C{=}CR^2{-}\overline{N}R{-}CR^1{=}O$ (Table 1). Since the $-\overline{N}R{-}CR^1{=}O$ part of these molecules can be considered to be planar, the overall nonplanarity must be the consequence of a twist between the amide and the alkene π-planes. Consequently, the ground-state steric structures of highly substituted 1,3-butadienes[3] and enamides are analogous.

With increasing temperature, the H^A and H^B signals broaden and coalesce reversibly; in most cases of Table 1, the sharpening at still higher temperatures could be observed. $\Delta\nu$, the shift difference of H^A and H^B, depends upon temperature. Therefore, $\Delta\nu$ was extrapolated to the coalescence temperature. The topomerization investigated is due to partial rotation about the C-N single bond, the barrier depending strongly upon the substituents. Apparently, the influence of R^1 is mostly *electronic* in origin, i.e. it is qualitatively similar to the influence of R^1 upon the barrier[5] in $Me_2\overline{N}{-}CR^1{=}O$:
1 (R^1 = Cl) > 2 (R^1 = OCH_3) > 3 (R^1 = $NHCH_2C_6H_5$);
4 (R^1 = $C_6H_4NO_2[4]$) > 6 (R^1 = $C_6H_4OMe[4]$).
On the other hand, the effects of R^2, R^3 and R^4 are roughly rationalised by *non-bonding* interactions between substituents, the effects being similar to the ones encountered for rotation about the central single bond in 1,3-butadienes[3,6]:
7 (R^2 = $CHMe_2$) > 5 (R^2 = C_6H_5);
8 (R^2 = $CHMe_2$) > 9 (R^2 = C_6H_5) ≫ 10 (R^2 = H);
9 (R^4 = Me) ≫ 11 (R^4 = H);
9 (R^3 = Me) > 12 (R^3 = H).

The latter comparison reveals an *indirect* variation of the barrier by the buttressing effect[6] of R^3. The former comparisons show changes of barriers by the substituents R^2 and R^4 *directly* hindering rotation about the C-N single bond.

Besides this motion, half rotation about the N-CO partial double bond may also give rise to stereoisomers. However, two diastereomers (Scheme 1), i.e. two corresponding sets of ^1H nmr signals, were definitely detected at room temperature for enamide 7 only (Table 1). The (*E*/*Z*)assignment[7] is based, among other experiments, upon lanthanide induced shift experiments. Two similar sets of signals were also seen in the ^{13}C spectrum ($CDCl_3$, +36°C) of 7, but not of 8. We assign[7] the (*E*) configuration to enamide 8.

Table 1. $\delta(^1H)$-values (+30°C) and barriers to partial rotation about the C-N single bond of enamides 1 - 12 in d_5-nitrobenzene



	R^1	R^2	R^3	R^4	δ_A	δ_B	$\Delta\nu$[a] [Hz]	T_c [°C]	$\Delta G^{\ddagger}$[b] [kJ/mol]
1[4]	Cl	Cl	Me	Me	4.37	4.92	~38	>+200	>101
2	OCH_3	Cl	Me	Me	4.34	4.92	42	+164	91
3	$NHCH_2C_6H_5$	Cl	Me	Me	4.27	5.28	72	+123	81
4	$C_6H_4NO_2$ [4]	C_6H_5	Me	Me	3.92	5.38	85	+136	83
5	C_6H_5	C_6H_5	Me	Me	3.84	5.42	101	+132	81
6	C_6H_4OMe [4]	C_6H_5	Me	Me	3.82	5.45	102	+129	81
7	C_6H_5	$CHMe_2$	Me	Me	c	c	~24	>+210	>102
8	CH_3	$CHMe_2$	Me	Me	4.07	5.20	~57	>+200	>98
9	CH_3	C_6H_5	Me	Me	3.51	5.26	103	+167	89
10[d]	CH_3	H	Me	Me	4.56		100[e]	<-110[f]	<31[f]
11[d,g]	CH_3	C_6H_5	Me	H	4.42		180[h]	- 56	42
12[g]	CH_3	C_6H_5	H	Me	3.65	5.50	139	+120	78

[a] Shift difference of H^A and H^B at 100 MHz, extrapolated to the coalescence temperature T_c by linear regression. [b] Calculated for T_c from $k = \pi(\Delta\nu^2 + 6J_{AB}^2)^{0.5}/\sqrt{2}$, whereby J_{AB} = 14 Hz. Errors of $\Delta G^{\ddagger}$ range from ±1 to ± 2 kJ/mol.

[c] In this case, the signals of (*E*)-7 (δ_A = 4.40, δ_B = 5.22, ~85 %) and (*Z*)-7 ($\delta_{A'}$ = 4.67, $\delta_{B'}$ = 4.30, ~15 %) appear at +30°C (see text and cf. Scheme 1).

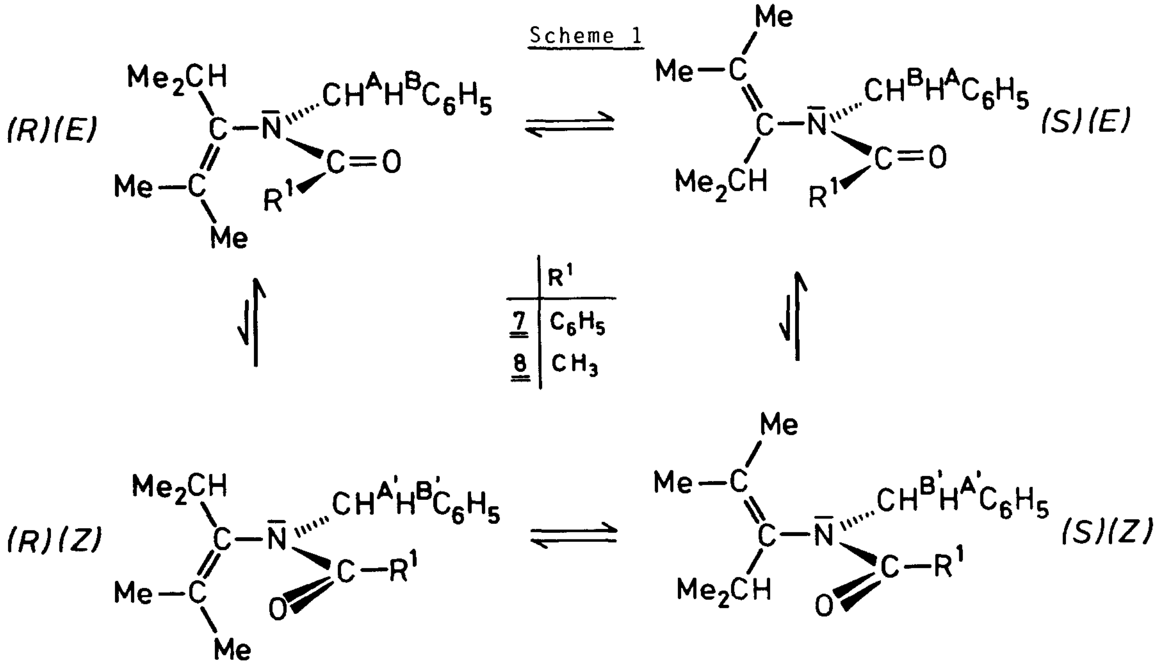
[d] Solvent CD_2Cl_2. [e] Estimated $\Delta\nu$-value. [f] Sample solidified as a glass.

[g] From a mixture [11] : [12] = 3 : 2. [h] Measured at -80°C.

The barriers of 1, 7 and 8 are high enough to allow the separation of enantiomers (Table 1) at room temperature. Subsequent thermal racemization of these enantiomers should yield more precise values for the barriers to rotation about the C-N single bond than the ones given in Table 1.

A separation of the enantiomers via diastereomeric salts did not show much prospect of success because of the low basicity of enamides. Therefore we applied low-pressure liquid chromatography on microcrystalline, swollen triacetylcellulose[8,9] with ethanol/H_2O (96:4) as an eluent. Separations of 200 and 500 mg quantities of (±) - 7 and (±) - 8, respectively, were performed by the recycling technique[9] using two equal columns (30 cm length, 2.5 cm i.d.) and yielded 50 to 100 mg of both enriched enantiomers (Table 2). The enantiomeric purities P of the samples of 8 could be measured by means of the $C\underline{H}_3CO$ nmr signals in the presence of an auxiliary compound (Table 2). No suitable signal was found for 7; however, the comparision of chromatograms[8,9] and specific rotations of the 7 and 8 samples gives a rough estimate of 10% and 30% for the P-values of (+)- and (-)-7, respectively.

Scheme 1



	R^1
7	C_6H_5
8	CH_3

$\rightleftharpoons$ represents partial rotation about the C-N single bond.

$\downarrow\uparrow$ represents half rotation about the N-CO partial double bond.

Thermal racemizations of the above samples were monitored during 2 half-lifes by polarimetry. They turned out to be of the first order and resulted in

Table 2: Partially separated enantiomers of enamides **7** and **8**; barriers to partial rotation about their C-N single bond, obtained by thermal racemizations in benzene solutions, monitored by polarimetry at 365 nm

Predominant enantiomer	R^1	$[\alpha]^{22}$ (λ)[nm][a]	P [%]	10^4k $[s^{-1}]$	T [°C]	$\Delta G^{\ddagger}$ [kJ/mol]
(+)-**7**	C_6H_5	$+2.7^\circ \pm 0.8^\circ$ (365)	∼10[b]	1.09	+25.0	95.5 ± 0.2
(-)-**7**	C_6H_5	$-6.2^\circ \pm 1.8^\circ$ (365)	∼30[b]	1.16		
(+)-**8**	CH_3	$+88^\circ \pm 4^\circ$ (589)	40 ± 2[c]	1.00	+59.6	107.1 ± 0.1
(-)-**8**	CH_3	$-111^\circ \pm 5^\circ$ (589)	47 ± 2[c,d]	1.04		

[a] 0.4 g/100 ml of CCl_4. [b] Estimated enantiomeric purity (see text). [c] Enantiomeric purity, measured by means of the $C\underline{H}_3CO$ signals ($\delta_{(+)} = 6.03$, $\delta_{(-)} = 5.60$) of **8** in CCl_4 with 0.4 equivalents of (+)-tris(3-heptafluorobutyryl-*D*-camphorato)europium(III). [d] CD (*n*-hexane, 25°C, calc. for P = 100%): $\lambda_{max} = 214$ nm ($\Delta\varepsilon = -15.0$ l cm^{-1} mol^{-1}).

the barriers to partial rotation about the C-N single bond given in Table 2. The agreement with the nmr results (Table 1) is satisfactory if the different conditions are taken into account. In accordance with the above mentioned electronic influence of R^1, the order of barriers is **8** ($R^1 = CH_3$) > **7** ($R^1 = C_6H_5$).

Further investigations are in progress in order to find out, *which* elementary step or steps (cf. Scheme 1) determine the rate of the overall enantiomerization $(R) \rightleftharpoons (S)$ described in Tables 1 and 2.

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