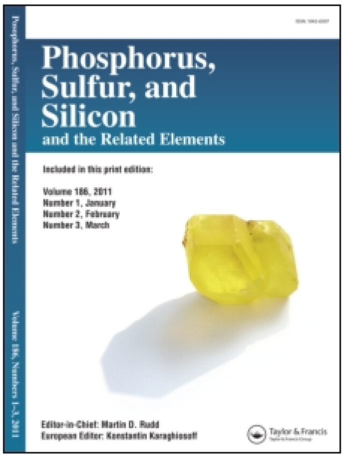

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E. Kleinpeter[a]; W. Schroth[a]
[a] Sektion Chemie, Martin-Luther-Universitat Halle-Wittenberg, Halle, Saale, GDR

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DYNAMIC NMR STUDY OF THE ELECTRONIC STATE OF HETEROAROMATICS VI.† COMPETING *C,N* AND *C,C* BARRIERS TO ROTATION OF PUSH–PULL ETHYLENES WITH AROMATIC TRANSITION STATES IN THE 1,3-THIAZINE SERIES

E. KLEINPETER‡ and W. SCHROTH
Sektion Chemie, Martin-Luther-Universität Halle-Wittenberg, Weinbergweg 16, DDR-4050 Halle (Saale), GDR

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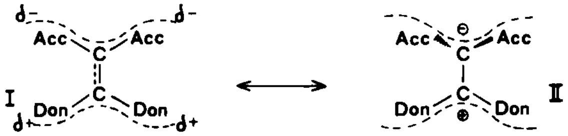
The barriers to rotation about the exocyclic partial C,N and C,C double bonds of a series of substituted 4-phenyl-2-NR_2-6-methylen-6H-1,3-thiazines were studied and found to be strongly dependent on structural influences. The C,N barrier is determined by the degree of mesomerism in the ground state of the restricted rotation, the C,C barrier, however, is dependent on the capacity of the system to stabilize the negative charge of the dipolar transition state exocyclically and the positive charge endocyclically via the aromatic thiazinium 6π electron system. Hereby the mesomeric effect of the NR_2 group is of special influence. ^1H as well as ^{13}C chemical shifts parallel obtained conclusions. The π-electron acceptors $>C{=}O$, $>C{=}S$, $>C{=}C(CN)_2$ and analogues of the latter are of the same influence on the C,N barrier to rotation in line with the pseudochalcogeno analogy principle.

Key words: Rotational barriers, Restricted C,N and C,C rotations, Transition and ground state stability; Pseudochalcogeno analogy principle.

INTRODUCTION

The low C,C barriers to rotation of push-pull ethylenes I, readily obtained by means of dynamic NMR spectroscopy,[1] result essentially from the capacity of both the push ($\text{Don-}\underset{\|}{\text{C}}\text{-Don}$) and the pull part ($\text{Acc-}\underset{\|}{\text{C}}\text{-Acc}$) to stabilize the


I
II

separated charges in the dipolar transition state II.[2]

If, moreover, there is the possibility of aromatic stabilization of the transition state owing to cyclic conjugated systems with $4n + 2\pi$ electrons as the donor part and/or with $4n\pi$ electrons as the acceptor part, the lowest barriers were obtained

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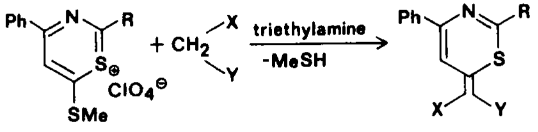
† For part V see E. Kleinpeter, R. Spitzner, W. Schroth: *Magnet. Reson. Chem.* **27**, 713 (1989).
‡ Author to whom correspondence should be addressed.

so far.[2] Several such systems with heterocyclic rings have been studied.[2] If the donor part is the heterocyclic ring component, the transition state stabilizing effect of pyridinium,[3,4,6] pyrylium[4,5,6] and thiopyrylium ions[4,5,6,7] was estimated; in the case of the acceptor part as a heterocyclic ring component, the adequately stabilizing capacity of pyrazolones,[2,8] isoxazolones[2] and related 5- and 6-membered ring systems[2,8] was determined. If there are additionally C(O)R groups in the acceptor part or NMe_2 groups in the donor part,[7,8] further restricted rotations about C_{sp^2},N or C_{sp^2},C_{sp^2} partial double bonds have been found. The separate discussion of electronic influences on the different barriers to rotation, however, was hardly possible[8] owing to steric hindrance. With this fact in mind, we became interested in heterocyclic systems of still push-pull character but the $C\overset{\cdots}{-}C$ and $C\overset{\cdots}{-}N$ bonds sufficiently separated to study structural influences on both barriers to rotation independent of steric distortions. Useful examples for this were found in the 1,3-thiazine series.[9]

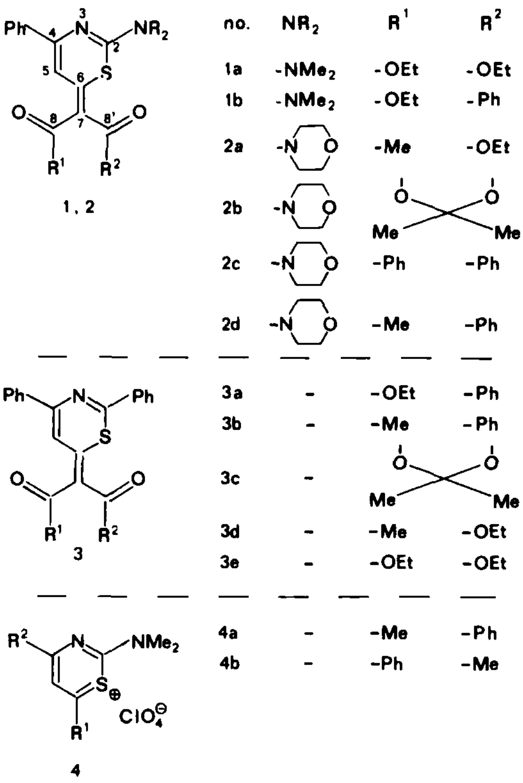
RESULTS

The 2,4-disubstituted 6-methylen-6H-1,3-thiazines **1–3** were prepared by condensation of adequately 2,4-disubstituted 6-alkylthio-1,3-thiazinium perchlorates[9a] with CH-acidic compounds (malonic acid diethylester for **1a**, **3e**; β-ketoesters for **1b**, **2a**, **3a**, **3d**; Meldrum's acid for **2b**, **3c**; and 1,3-diketones for **2c**, **2d**, **3b**).[9b,c] The 4,6-disubstituted 2-NMe_2-thiazinium perchlorates **4a,b** have been included for the purpose of comparison.[9c]



All compounds studied are shown in Scheme 1. The NMR spectra were recorded at 200.13 MHz for ^1H and 50.327 MHz for ^{13}C. The NMR parameters at ambient temperature are given in Tables I (^1H NMR) and II (^{13}C NMR). The assignments of the signals were according to usual tools as are chemical shift charts, scalar coupling behaviour, attached-proton-test and intensities subject to symmetry. In the case of **1a**, **2b** and **2c**, exemplary, also the quaternary carbon atoms C–2, C–4 and C–6 have been assigned by means of the C,H coupled ^{13}C NMR spectra (C–2: quintet or septet due to $^2J_{C\text{-}2,N(CH_n)_2}$; C-4: triplet due to $^3J_{C\text{-}4,arom.H_{ortho}}$; C-6: doublet due to $^2J_{C\text{-}6,H\text{-}5}$).

The rotational barriers for the restricted rotations about the exocyclic C^2,N and C^6,C^7 partial double bonds were determined as free energies of activation, $\Delta G_c^{\neq}$, at the coalescence temperature T_c, by the Gutowsky-Holm and Eyring equations[1] from the line shape variations of the N–C_α, O–C_α or carbonyl carbon atoms. The chemical shift differences in the slow exchange region, $\Delta\nu$, were extrapolated to the coalescence temperature and were sufficiently large to give free energies of activation, which are readily comparable to CLSA values.[10]



SCHEME 1 Compounds studied.

The strong negative $\Delta S^{\neq}$ values, which are expected for the C,C barriers and which are limiting the reliance of the $\Delta G^{\neq}$ values, had been found to increase with $\Delta H^{\neq}$ in series of related compounds;[2] thus the $\Delta G^{\neq}$ and the $\Delta H^{\neq}$ values fall in the same order and the discussion of structural influences in terms of $\Delta G^{\neq}$ will be acceptable. Acid catalysis of the C,C isomerization, sometimes mentioned, was not observed. The dynamic NMR parameters and rotational barriers are given in Table III.

DISCUSSION

Structural Influences on the Barriers to Rotation; C,N Rotational Barrier

As usual, the C,N barriers to rotation are larger when employing NMe_2 instead of morpholino as the NR_2 substituent (comp. **1** and **2**) due to the sterically and electronically destabilized ground state in the case of the latter.[10] The acceptor part of the push-pull ethylenic fragment $=C^7(X)(Y)$ is only of small influence on the C,N barrier. The highest value along the series studied, **1**–**3**, was obtained for the Meldrum's acid derivative **2b** probably due to the most stable ground state; the ring closure of the acceptor fragment in **2b** forces this part of the

TABLE I

^{1}H NMR parameters at ambient temperature of the compoun

				Chemical shifts δ/ppm/		
Comp.	Solvent	H-5	—NR$_2$	R^1		
1a	CDCl$_3$	6.81	3.21	4.15; 4.30 (q)[a]	and	1.26;
1b	CDCl$_3$	7.24	3.34	3.96 (q)[a] 0.83 (t)[a]		7.45–
2a	CDCl$_3$	7.24	3.78 (t); 3.92 (t)	2.33		4.36 (q
2b	CDCl$_3$	8.64	3.51 (t); 3.68 (t)		1.35	
2c	CDCl$_3$	7.36	3.78 (t); 3.97 (t)			7.17–
2d	CDCl$_3$	7.26	3.75 (t); 3.90 (t)	2.06		
3a	CDCl$_3$	7.24	—	4.09[b] (3.99)[c] (q)[a] 0.96[b] (0.81)[c] (t)[a]		7.37–
3b	CDCl$_3$	6.72	—	2.15		7.24–
3c	CDCl$_3$	9.51	—			1
3d	DMSO-d_6	7.39	—			2.28[d] (4.39[d] (1.34[d] (
3e	CDCl$_3$	7.24	—			1.31[a] (t 4.27 (q)
4a	CD$_3$CN	7.72	3.39; 3.55	2.14		8.34 7.63–
4b	CD$_3$CN	7.68	3.43; 3.62	7.61–7.94 (m)		2

[a] $^3J_{CH_2CH_3} = 7.2$ Hz.

[b] Major isomer (68%).

[c] Minor isomer (32%).

[d] Major isomer (86%).

[e] Minor isomer (14%).

TABLE II

^{13}C chemical shifts δ/ppm/ at ambient temperature in CDCl$_3$ of the compo

Comp.	C-2	C-4	C-5	C-6	C-7	C-8/C-8′	NR$_2$	R^1
1a	156.0	161.9	96.3	152.4	105.7	165.9; 166.9	38.5	60.2 14.3
1b	[a]	[a]	95.8 97.1	[a]	109.7 110.6	191.3; 194.5	38.1 39.2	59.8 13.0
2a[c]	158.3[b]	162.4[b]	98.3	154.4[b]	113.5	193.7; 168.5	44.7 (45.5) 66.4	14.1
2b	166.0	163.9	102.4	162.5	102.9	163.3	46.1 66.1	91.3 and
2c[d]	162.5	159.0	99.4	156.2	119.2	196.7; 192.0	45.7 66.3	140.7 140.1 138.1
2d	[a]	[a]	99.3	[a]	[a]	[a]	45.9 66.4	28.9
3a[e]	165.8[b]	152.3[b]	105.1	151.0[b]	115.9	194.1; 167.0	—	60.5 13.9
3b	167.6[b]	153.3[b]	106.2	150.3[b]	124.6	196.8; 193.1	—	29.2
3c	161.4[b]	159.2[b]	108.0	171.6[b]	103.5	163.9; 165.6	—	95.4 26.9
3d[e]	168.0[b]	154.3[b]	106.1	153.2[b]	117.9	193.9; 167.7	—	24.4
3e	166.0[b]	152.2[b]	104.8	150.7[b]	11.2	165.4; 166.7	—	60.8 61.4 14.3
4a	169.7[b]	168.5[b]	113.9	162.6[b]	—	—	40.7 40.5	23.3
4b	179.7[b]	170.1[b]	116.6	159.5[b]	—	—	41.5	134.1 (i) 128.4 131.0 134.6(

[a] Not further assigned owing to too many signals.

[b] Or reversed.

[c] Obtained at 213 K.

[d] Obtained at 260 K.

[e] Major isomer only.

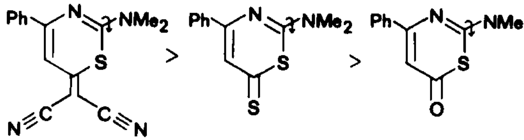
TABLE III

Dynamic NMR parameters (T_c, $\Delta\nu$) and rotational barriers ($\Delta G_c^{\neq}$) for restricted rota
C,C and C,N double bonds of compounds **1–4**

Comp.	Restricted rotation about C^2,N					Restricted r
	Solvent	T_c(K)	$\Delta\nu$ (Hz)	$\Delta G_c^{\neq}$ (kJ/mol)	Solvent	T_c (K)
1a	CD_2Cl_2	242	18.5	51.3	DMSO-d_6	335[a]
						337[b]
1b	CD_2Cl_2	257	54	52.3	CD_2Cl_2	278[a]
						278[c]
2a	$CDCl_3$	222[d]	52[d]	45.0		[e]
		213[a]	21.5[a]	44.7		
2b	$CDCl_3$	243[d]	56[d]	49.3	$CDCl_3$	273[b]
		238[a]	31.5[a]	49.4		
2c	CD_2Cl_2	226[a]	21[a]	47.6	$CDCl_3$	297[b]
		233[d]	54[d]	47.3		
2d	CD_2Cl_2	222[d]	63[d]	44.7		[e]
		212[a]	23[a]	44.4		
3a[f]	—	—	—	—	DMSO-d_6	408[c]
3e	—	—	—	—	DMSO-d_6	430[c]
4a	DMSO-d_6	>440	—	>95	—	—
4b	DMSO-d_6	435[g]	17.5[g]	94.6	—	—

[a] Obtained from OÇH_2. [b] Obtained from ÇO. [c] Obtained from ethoxy-ÇH_3. [d] NÇH
phenomena near to ambient temperature but preferred isomer (≥95%). [f] Population o
line shape studied.

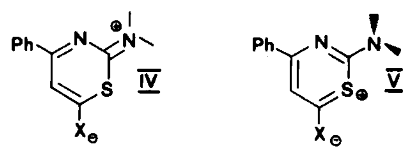
molecule into a common plane and thereupon the mesomerism is expected to get strengthened adequately. In the cases of the other C^6 substituents there is no doubt that one or two acceptor substituents are twisted out of the double bond plane[6] to reduce the mesomerism at least partly. The barrier differences between the latter compounds, however, are too small to discuss meaningfully. The highest C,N barrier to rotation were obtained for the thiazinium perchlorates **4** as the result of the strongly increasing π-electron deficiency of the aromatic ring in the case of these compounds[12] compared with **1**–**3**. The barriers to C,N rotation of the 6-methylene-6H-1,3-thiazine **1** and the values obtained for the corresponding 6-chalcogeno analogues are approximately of the same size:



62,7 kJ/mol [17] 59,1 kJ/mol [16] 57,7 kJ/mol [15]

This result suggest similar electronic influences of oxygen, sulphur and $C(CN)_2$ or the analogues of the latter on the rotational barriers studied in line with the pseudochalcogeno analogy principle[18,19] and indicate the heteroaromatic 6π electron system involved in balancing very effectively differences expected which were still substantial in analogous urea[4,13] and formic aldehyde[4,13] derivatives. Even the very characteristic C,N barrier difference between amides and thioamides (or vinylogues) of ca. 10–20 kJ/mol owing to the greater polarizibility of sulphur is no longer acceptable for the compounds present.

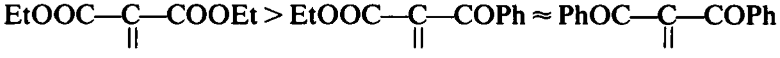
To conclude, the π-electron acceptor groups $=O$, $=S$ and $=C(X)(Y)$ are of approximately the same capacity to stabilize both the ground state (IV) and the transition state (V) of the restricted C,N rotation.



Consequently, the general validity of the pseudochalcogeno analogy principle,[18,19] which has been used very successfully for the estimation of the reactivity of compounds in a large number of anomalous reactions, is corroborated from another point of view.

C,C Rotational Barrier

In **1** and **2**, the C,C barriers to rotation and the corresponding C,N barriers are approximately of the same size. According to the capacity of the push-pull ethylenic acceptor part to stabilize the negative charge in the transition state, the following series of decreasing C,C barriers to rotation is obtained:



$$\underset{\|}{\mathrm{EtOOC{-}C{-}COOEt}} > \underset{\|}{\mathrm{EtOOC{-}C{-}COPh}} \approx \underset{\|}{\mathrm{PhOC{-}C{-}COPh}}$$

This sequence is related to the σ_R^- values of the present acceptor substituents.[6]

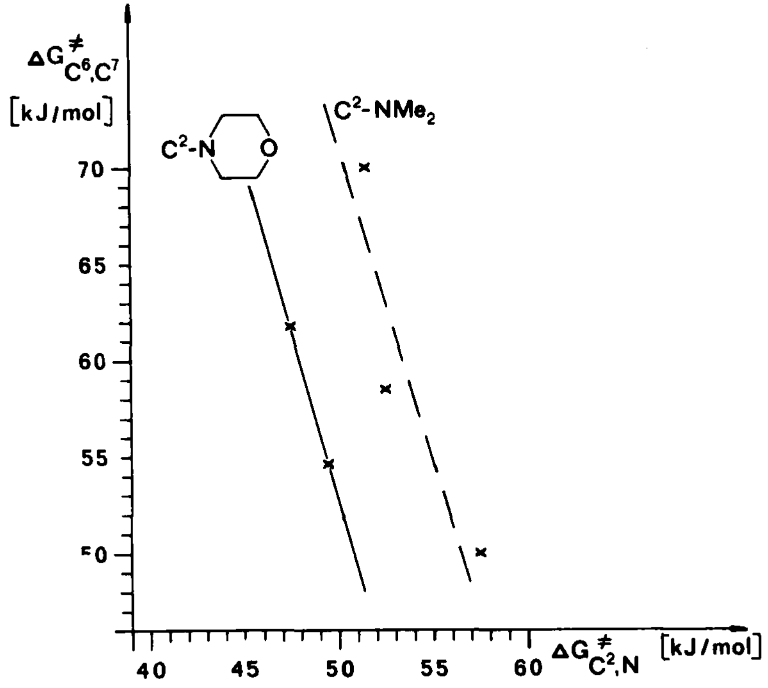
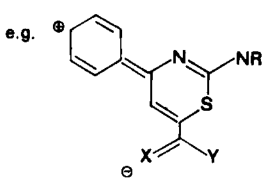


FIGURE 1 Correlation of C^6,C^7 barriers to rotation vs. the corresponding C^2,N barriers to rotation in the 2-NMe_2-4-phenyl-6-methylene-6H-1,3-thiazines **1** (full line) and 2-morpholino-4-phenyl-6-methylene-6H-1,3-thiazines **2**.

The C,C barrier to rotation of the Meldrum's acid derivative **2b** is the lowest along the series studied as opposed to the C,N barrier of this compound. This inverse behaviour of the two barriers is obtained generally—see Fig. 1. Two straight lines are visible (owing to two different NR_2 substituents) to conclude therefrom on large C,C barrier variations accompanied by small and inverse ones of the corresponding C,N barriers. This result is in line with the general figure of the two dynamic processes: the variable acceptor part of the push-pull ethylenes in these widely delocalized systems changes the ground state of the two barriers only moderately (due to mesomerism along the whole system) but the transition state of the C,C barrier dramatically (because of being now limited to stabilize the negative charge only along the acceptor part of the push-pull ethylenic moiety). Thereupon the C,N barrier changes only slightly (due to ground state control), the C,C barrier, however, changes dramatically (due to transition state control). This is properly supported by the compounds **3**. The C,C barrier difference between **3a** and **3e** is approximately the same as between **1b** and **1a** owing to the respectively identical acceptor parts of the push-pull ethylenic fragments. The C,C barrier difference between comparable compounds **1** and **3** however, is dramatical ($\Delta G^{\neq}$ (**3a**) ca. 30 kJ/mol larger than $\Delta G^{\neq}$ (**1b**)). There is no doubt that both the ground and the transition state of the restricted C,C rotation are destabilized if NMe_2 (in **1**) is structurally replaced by phenyl (in **3**). However, the transition state is destabilized to a much larger amount, because the positive charge is delocalized in **3** along the thiazinium moiety only and the lost donor capacity of NMe_2 is missed strongly. The ground state balances the latter activity of the NMe_2 group via mesomerism along the whole conjugated system much more easier; the difference between the two states, the C,C barrier to rotation, increases adequately.

Steric Influences on the Barriers to Rotation

The transition states of the two restricted rotations should be strainfree due to twist angles of 90°. The same seems to be true for the C,N rotational barrier ground state (twist angle of 0°) due to absent ortho substituents and protons as well.[12] In the case of the ground state of the C,C rotation, however, any steric twist from the optimal plane of mesomerism cannot be excluded (vide supra). The ^1H chemical shifts of the protons H-5 are rather informative for this purpose. In spite of the being $\delta = 7.20–7.30$ ppm usually (see Tab. I), H-5 is low field shifted to $\delta = 8.64$ ppm in the Meldrum's acid derivative **2b** as a consequence of forcing the carbonyl groups of the acceptor part into a common plane (H-5 low field shifted under influence of the carbonyl anisotropy effect). The usual high field position of H-5 in **2a,c,d** with respect to **2b** can be explained by steric twist or by different conformations of the substituents in the acceptor part, which are obligatory Z,Z in **2b**. The E,Z conformation seems to be acceptable[13] due to attractive interactions of one partially negative carbonyl oxygen and the partially positive ring sulphur atom, as stated previously[7]; the E,E conformation seems less probable because of destabilizing dipole, dipole repulsion.[14] The low field position of H-5 in the Meldrum's acid derivatives as the consequence of the location within the deshielding part of the carbonyl anisotropy cone is confirmed by the normal position of the C-5 carbon atom in the ^{13}C NMR spectra.



III

The ^{13}C chemical shift of the para phenyl carbon atom is a very sensitive probe of the degree of mesomerism heterocyclic system/2-phenyl—see III. Approximately the same C_{para} chemical shifts have been obtained along the studied **1–3**; increased mesomerism in the case of **4**, however, causes C_{para} to shift to low field by an amount expected. With regard to these data, a common plane heterocyclic system/2-phenyl and the absence of remarkable steric twist should be concluded even if H-5 and the ortho hydrogen atoms of the 2-phenyl substituent are spatially very close as proved to be true by NOE experiments.[15]

EXPERIMENTAL

2,4-disubstituted 6-methylene-6H-1,3-thiazines **1–3**. A mixture of 0.001 mol of the 2,4-disubstituted 6-methylthio-1,3-thiazinium perchlorate[9a] and 0.0025 mol of the CH-acidic compound in 50 ml dry acetonitril is stirred at ambient temperature for 30 minutes while 0.25 g (0.0025 mol) of dry triethylamine dissolved in ca. 10 ml of the same solvent is introduced dropwise. The mixture is heated at a rate at which moderate refluxing takes place. After cooling to room temperature, the acetonitril is distilled off under reduced pressure and the residue extracted with 5 drops of dry ethanol, methanol or n-hexane. The precipitated thiazines **1–3** have been recrystallized from solvents, useful therefore, and identified via IR, UV, NMR and mass spectrometry.

NMR: The ^1H NMR (at 200.13 MHz) and ^{13}C NMR spectra (at 50.253 MHz) were recorded on a Bruker WP-200 NMR spectrometer at various temperatures in the solvents mentioned in the relevant Tables. The temperature was kept constant (±2 K) by the variable temperature unit of the Bruker equipment and checked carefully by reference samples (ethylene glycol, high temperatures; methanol, low temperatures.)

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