Transannular Interactions in Difunctional Medium Rings, 9[+]

Spectroscopic and Theoretical Investigations of Bicyclic Dioximes and Dimethoximes with Eight-Membered Rings

Andrea Strenge[a] and Paul Rademacher*[a]

Dedicated to Professor Reiner Sustmann on the occasion of his 60th birthday

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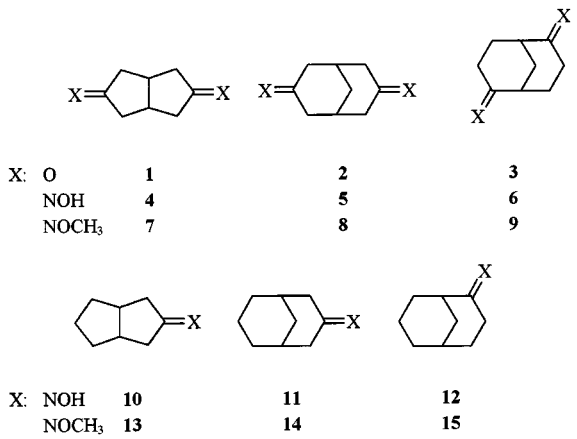
The bicyclic dioximes **4–6** and dimethoximes **7–9**, which contain the functional groups in opposite positions of bridged eight-membered rings, were synthesized. Their conformational properties and transannular interactions were investigated by spectroscopic (PE, ^{13}C NMR) and theoretical (MMX, AM1, ab initio HF, and B3LYP) methods. While in the 3,7-disubstituted bicyclo[3.3.1]nonane derivatives **5** and **8** the eight-membered ring has a CC conformation favourable for through-space interactions of the π(C=N) orbitals, in the bicyclo[3.3.0]octane derivatives **4** and **7** as well as the 2,6-disubstituted bicyclo[3.3.1]nonanes **6** and **9** the functional groups are in geometric orientations that are unfavourable for such interactions. Through-space orbital interactions in the molecules with favourable conformations lead to a splitting of the π(C=N) MOs of 0.4–0.6 eV.

1. Introduction

In the preceding paper of this series,[1] we have shown that transannular interactions occur in dioximes and dimethoximes provided the functional groups are in favourable geometrical orientations. For monocyclic compounds, this was only found in 1,5-disubstituted eight-membered rings. In this paper, we report on our investigations by the same techniques on bicyclic compounds containing an eight-membered ring with the functional groups in different, but always in opposite positions. We have studied the bicyclo[3.3.0]octane derivatives **4**, **7** and the bicyclo[3.3.1]-nonane derivatives **5**, **6**, **8**, **9**.

2. Syntheses

Starting materials for the synthesis of the dioximes **4−6** and the dimethoximes **7−9** were the diketones **1−3**. *cis*-Bicyclo[3.3.0]octane-3,7-dione (**1**) is obtained in good yield as described by Bertz et al.[2] The synthesis of bicyclo[3.3.1]-nonane-3,7-dione (**2**) was achieved according to the method of Bertz.[3] In the synthesis of bicyclo[3.3.1]nonane-2,6-dione (**3**) the improved method of Quast et al.[4] was used. The diketones were treated with hydroxylamine hydrochloride or with *O*-methylhydroxylamine hydrochloride to generate the dioximes **4−6** or the dimethoximes **7−9**, respectively. The solid dioximes were recrystallized from ethanol, and it was possible to isolate pure configurational isomers that were identified by their ^{13}C-NMR spectra because the isomers are expected to have different numbers of signals: **4*E***, **5*Z***, **6*E***. Compounds **7−9** were purified by distillation in vacuo and in all cases mixtures of (*E*) and (*Z*) isomers were obtained. While the geometrical isomers of compound **8** could be separated by column chromatography on silica gel using dichloromethane/ethyl acetate (1:1) as eluent, this technique failed for the other compounds. The dimethoximes have not been previously described in the literature.



Scheme 1. Formulas of compounds **1−15**

The monoximes **10−12** and the monomethoximes **13−15** were synthesized in an analogous manner from the corresponding ketones. The synthesis of bicyclo[3.3.1]nonane-2-one oxime (**12**) was described in the literature.[5]

[+] Part 8: Ref.[1]

[a] Institut für Organische Chemie, Universität GH Essen, D-45117 Essen, Germany
Fax: (internat.) + 49(0)201/183-4252,
E-mail: radem@oc1.orgchem.uni-essen.de

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3. Results

3.1 Structures

The conformational properties of medium rings have been investigated by experimental and theoretical methods.[6−10] For all molecules studied here, several conformations have to be considered. As a first orientation, the corresponding diketones were used.

The common structure element of the bicyclic compounds **4**−**6** and **7**−**9** is the 1,5-disubstituted cyclooctane ring. *cis*-Bicyclo[3.3.0]octane has two conformers, the chair-boat (CB) and the chair-chair (CC) form, that differ in energy by only about 1.0 kJ mol^{-1}.[9,11,12] The 3,7-dione **1** can adopt similar conformations as the monocyclic diketone except for the twist-boat-chair (TBC) form that is replaced by the twist-twist (TT) form. This is the most stable conformer of **1** with a rather long transannular distance between the atoms C-3 and C-7, and accordingly no through-space orbital interaction (OITS) has been observed by PE spectroscopy.[13] In the bicyclic diketones bicyclo[3.3.1]nonane-3,7-dione[14][15] (**2**) and bicyclo[3.3.1]nonane-2,6-dione[16] (**3**), the eight-membered rings adopt a flattened CC conformation.

The stereochemical problem of the dioximes **4**−**6** and the dimethoximes **7**−**9** becomes even more complicated since these compounds can adopt (*E*) and (*Z*) configurations.[17][18] For each compound, there are three configurational isomers, one (*Z*) and two (*E*) forms. Except for compounds **6** and **9**, the latter two isomers are enantiomers and as such will not differ in their transannular interactions and their electronic structures. The (*Z*) and (*E*) isomers are stable and can − at least in principle − be separated. We have investigated the structures of these compounds by various theoretical methods: The molecular mechanics method MMX[19] was used to study all relevant conformational and configurational variations. For the more stable conformers, AM1[20] calculations were performed, and selected conformers were also investigated by ab initio calculations with different basis sets and levels of theory. The results[21] are far too manifold in order to give a complete account in this paper where only those that seem to be most important are presented.

As representative examples, the conformers of the dimethoximes **7**, **8**, and **9** and their strain energies as calculated by the MMX method are displayed in Figures 1−3. In Table 1, the results of different methods for the two most important conformers of the dioximes **4**−**6** and the dimethoximes **7**−**9** are summarized. In each case, the enthalpies of formation or the total energies of the conformers are given together with the transannular N=C···C=N distance that is the most relevant parameter with respect to transannular interaction.

With regard to the relative stabilities of the conformers, the data indicate that for all compounds there is a single prevailing conformer, usually the CC form, only for the bicyclo[3.3.0]octane derivatives **4** and **7** it is the TT form. For the latter compounds, the structures of the TT and the BC

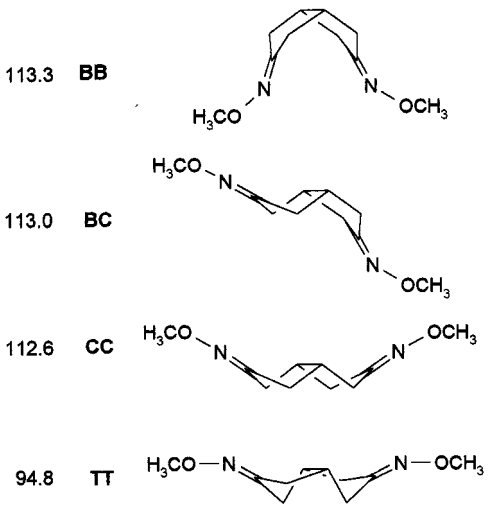

Figure 1. Conformers of bicyclic dimethoxime **7** with MMX strain energies [kJ mol^{-1}]

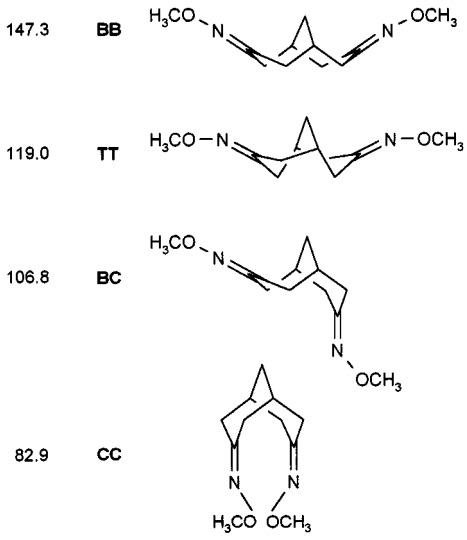

Figure 2. Conformers of bicyclic dimethoxime **8** with MMX strain energies [kJ mol^{-1}]

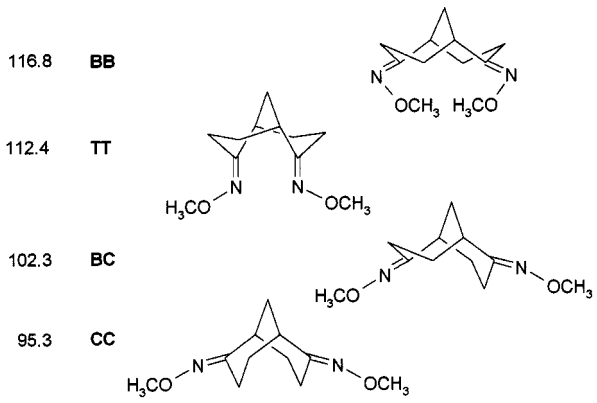

Figure 3. Conformers of bicyclic dimethoxime **9** with MMX strain energies [kJ mol^{-1}]

form could be optimized separately with the ab initio HF and the B3LYP methods only when a smaller basis set (3-

Table 1. Enthalpies of formation ΔH_f [k]mol^{-1}], total energies E [au] and transannular N=C···C=N distances d [pm] of bicyclo[3.3.0]octane-3,7-dione dioxime (**4**), bicyclo[3.3.0]octane-3,7-dione bis[*O*-methyloxime) (**7**), bicyclo[3.3.1]nonane-3,7-dione dioxime (**5**), bicyclo[3.3.1]nonane-3,7-dione bis(*O*-methyloxime) (**8**), bicyclo[3.3.1]nonane-2,6-dione dioxime (**6**), and bicyclo[3.3.1]nonane-2,6-dione bis(*O*-methyloxime) (**9**)

		MMX ΔH_f	d	AM1 ΔH_f	d	HF/6−31+G* E	d	B3LYP/6−31+G* E	d
4*E*	TT	44.8	399.6	−93.3	416.3	−568.4455218	407.1	−571.9373227	409.8
	BC	61.8	387.7	−91.6	400.0	[b]		[b]	
	Δ[a]	17.0		1.7					
7*E*	TT	46.1	400.3	−21.4	416.4	−646.5023859	407.4	−650.5533365	410.3
	BC	64.2	382.4	−17.7	402.8	[b]		[b]	
	Δ[a]	17.9		3.7					
5*Z*	CC-3,7	11.2	291.0	−110.6	298.3	−607.4851238	306.6	−611.2576051	307.5
	BC-3,7	32.6	351.9	−104.7	355.7	−607.4785801	356.6	−611.2516608	360.6
	Δ[a]	21.4		5.9		17.16		15.59	
8*E*	CC-3,7	10.0	287.2	−38.7	292.1	−685.5419430	305.6	−689.8734383	306.6
	BC-3,7	33.9	352.9	−33.7	356.1	−685.5352327	350.9	−689.8674455	356.9
	Δ[a]	23.9	65.7	5.0		17.60		15.72	
6*E*	CC	21.0	345.5	−103.9	352.6	−607.4822520	353.4	−611.2552266	352.1
	BC	28.2	346.4	−104.6	351.3	−607.4777214	352.8	−611.2506675	353.2
	Δ[a]	7.2		−0.7		11.88		11.96	
9*E*	CC	22.4	346.7	−32.7	354.5	−685.5389283	352.1	−689.8710633	351.8
	BC	29.4	347.0	−33.5	353.5	−685.5351045	352.6	−689.8670553	353.4
	Δ[a]	7.0		−0.8		10.03		10.51	

[a] kJ mol^{-1}. − [b]No energy minimum for this conformer is found.

21G) than that given in Table 1 was used. Otherwise, only the TT form was obtained as a conformer. The data for compounds **6** and **9** obtained by AM1 deviate obviously from the results of the other methods and have to be considered as unreliable. For the bicyclo[3.3.1]nonane derivatives **5** and **8** transannular distances d of about 300 pm were computed for the CC-3,7 conformer indicating that sizeable OITS is possible. On the other hand, rather large d values (ca. 400 pm) were found for the most stable conformer of the bicyclo[3.3.0]octane 3,7-derivatives **4** and **7** that can be expected to be too large for detectable transannular interactions of the functional groups. Finally, d values of about 350 pm are calculated for the bicyclo[3.3.1]nonane 2,6-derivatives **6** and **9** that can be classified as borderline for OITS.[22]

3.2 Electronic Structures

The electronic structures of dioximes **4**−**6** and dimethoximes **7**−**9** as well as that of the corresponding monoximes **10**−**12** and monomethoximes **13**−**15** have been investigated by quantum chemical methods. The results for the most stable conformer of the molecules are summarized in Table 2. For the difunctional compounds only one (*E*)/(*Z*) isomer is considered. We will restrict the data to the two highest

Table 2. Negative orbital energies [eV] of the most stable conformers of dioximes **4**−**6**, dimethoximes **7**−**9**, monoximes **10**−**12**, and monomethoximes **13**−**15** (AM1, HF/6-31+G* and B3LYP/6-31+G* results)

	π^+(C=N)			π^-(C=N)			n^+(N)			n^-(N)		
	AM1	HF	B3LYP	AM1	HF	B3LYP	AM1	HF	B3LYP	AM1	HF	B3LYP
4*E* TT	9.96			10.00			10.92			10.97		
7*E* TT	9.72			9.75			10.73			10.83		
10 TT	9.90[a]						10.78[b]					
13 TT	9.69[a]						10.65[b]					
5*Z* CC	10.08	10.57	7.09	9.60	9.79	6.58	10.47	11.47	7.51	10.86	11.06	7.36
8*E* CC	9.81	10.20	6.70	9.37	9.55	6.29	10.58	11.29	7.37	10.36	10.89	7.18
11 CC	9.73[a]						10.51[b]					
14 CC	9.55[a]						10.42[b]					
6*E* CC	9.96	10.26	6.95	9.90	10.24	6.93	10.85	11.44	7.61	10.70	11.29	7.51
9*E* CC	9.73	9.97	6.62	9.68	9.93	6.59	10.67	11.26	7.43	10.56	11.11	7.34
12 CC		9.79[a]						10.54[b]				
15 CC		9.61[a]						10.43[b]				

[a] π(C=N). − [b] n(N).

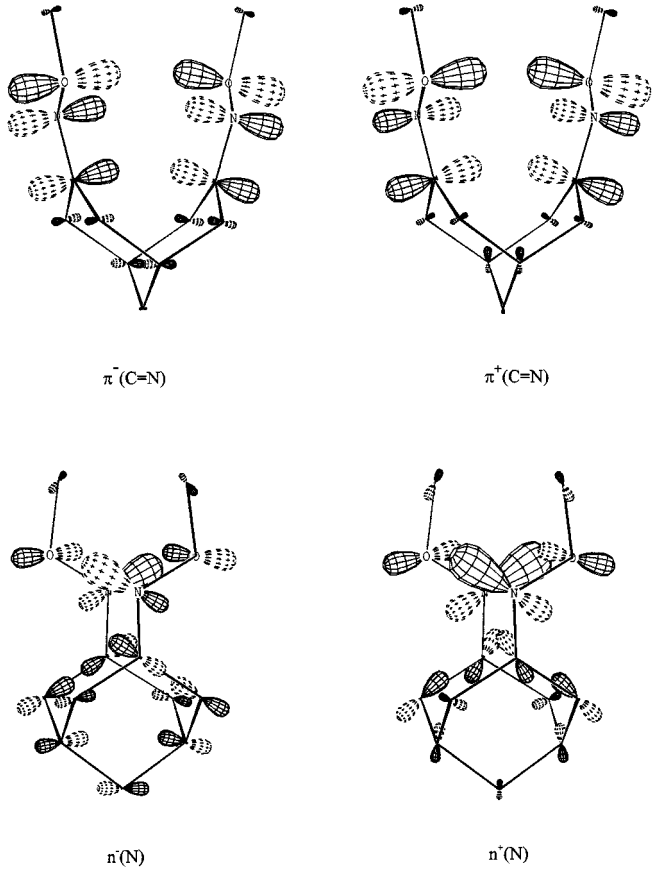

Figure 4. π(C=N) and n(N) MOs of dimethoxime **8*E*** (AM1 results); hydrogen atoms are omitted for clarity reasons

occupied oxime MOs, π(C=N) and n(N), that are of the greatest relevance for the interpretation of the PE spectra (see below). In the difunctional compounds, the MOs are named π^-(C=N), π^+(C=N), n^-(N), and n^+(N). These MOs are plotted in Figure 4 for compound **8*E***.

The data in Table 2 indicate that only the π(C=N) orbital energies of the difunctional compounds **5*Z*** and **8*E*** are split nearly symmetrically from the values found for the corresponding monofunctional compounds **11** and **14** that is consistent with transannular through-space interactions. The splitting of the two π(C=N) MOs has approximately the same size as that of the n(N) MOs. However, for **5*Z*** n^-(N) is found *below* n^+(N) indicating through-bond interaction while **8*E*** shows the natural sequence with n^-(N) > n^+(N). For the other pairs of compounds, the MOs of the difunctional are stabilized relative to those of the monofunctional by less than 0.1 eV [π(C=N)] or 0.2−0.3 eV [n(N)] that can be explained by inductive effects and excludes OITS. The natural sequence of the characteristic oxime orbitals, π^-(C=N) > π^+(C=N) > n^-(N) > n^+(N), is found only in compounds **6*E***, **9*E***, and **8*E***.

3.3 Photoelectron Spectra

We have measured the PE spectra of the dioximes **4**−**6**, the dimethoximes **7**−**9**, the monoximes **11**, **12**, and the monomethoximes **14**, **15**. For the configurational isomers of compound **8**, **8*E*** and **8*Z***, which could be isolated separately, no significant differences in the spectra were observed. It is suspected that this applies also to compounds **7** and **9** which were measured as (*E*/*Z*) mixtures. Some spectra are depicted in Figures 5−7. The observed ionization potentials are listed in Table 3. The spectra of the monofunctional bicyclo[3.3.0]octane derivatives **10** and **13** could not be investigated because the compounds were not available. The spectra of the dioximes and dimethoximes were inspected for splittings of the characteristic ionization bands, and for this purpose the spectra of the monoximes were used for comparison. The ionization potentials were assigned to MOs making use of the Koopmans theorem,[23] $IP_i = -\varepsilon_i^{SCF}$, that relates vertical ionization potentials IP_i with orbital energies ε_i^{SCF} obtained by SCF MO calculations. As in the case of monocyclic dioximes and dimethoximes,[1] we will restrict the analysis on the ionizations from the two highest occupied oxime MOs, π(C=N) and n(N).

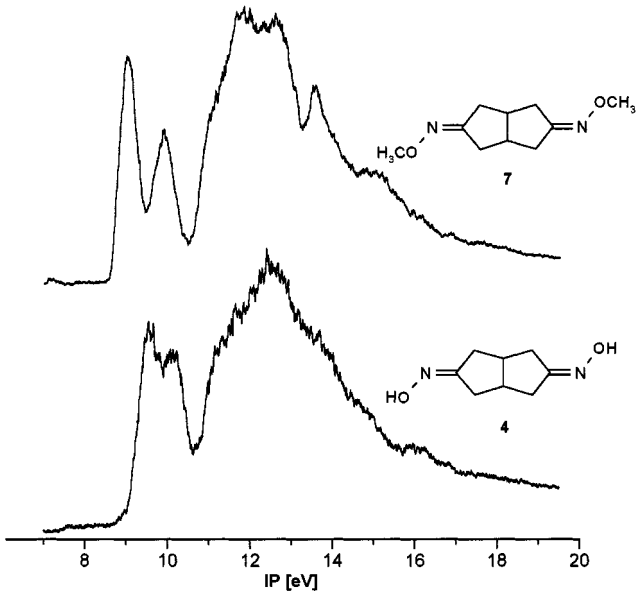

Figure 5. PE spectra of bicyclo[3.3.0]octane-3,7-dione dioxime (**4**) and bicyclo[3.3.0]octane-3,7-dione bis(*O*-methyloxime) (**7**)

In acetone oxime and acetone *O*-methyloxime, the ionization energies corresponding to π(C=N) and n(N) are 9.67 and 10.46 eV,[24] and 9.16 and 9.95 eV,[25] respectively. The IP values of the monoximes **11**, **12** and the monomethoximes **14**, **15** (Table 3) are 0.3−0.6 eV smaller than those of the two acetone derivatives owing to their larger skeletons. The spectra of the dioxime **5** and the dimethoxime **8** display three ionization bands in the lower energy section (< 11 eV) instead of two bands of the corresponding monofunctional compounds. In these difunctional compounds, the first two IPs are assigned to π^-(C=N) and π^+(C=N) that are split by 0.4−0.6 eV. The splitting of these two IPs is symmetric to the corresponding value of IP[π(C=N)] in the monoximes indicating prevailing through-space interaction of the orbitals. A split of the MOs n^-(N) and n^+(N) by about

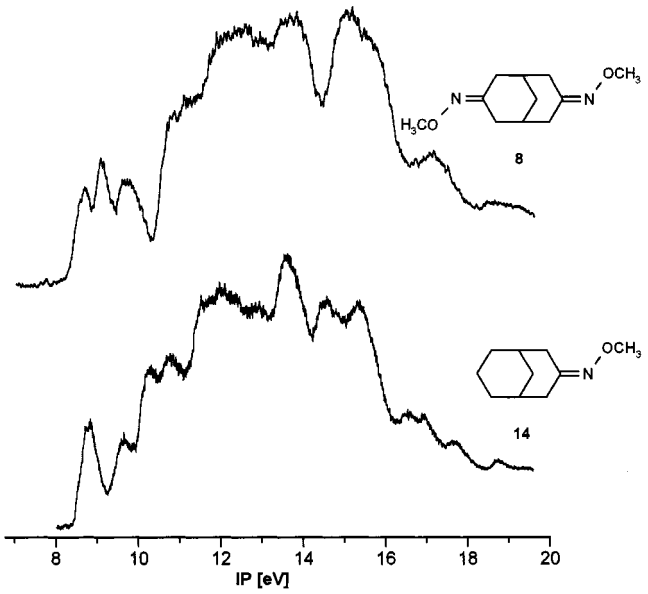

Figure 6. PE spectra of bicyclo[3.3.1]nonane-3,7-dione bis(*O*-methyloxime) (**8**) and bicyclo[3.3.1]nonane-3-one *O*-methyloxime (**14**)

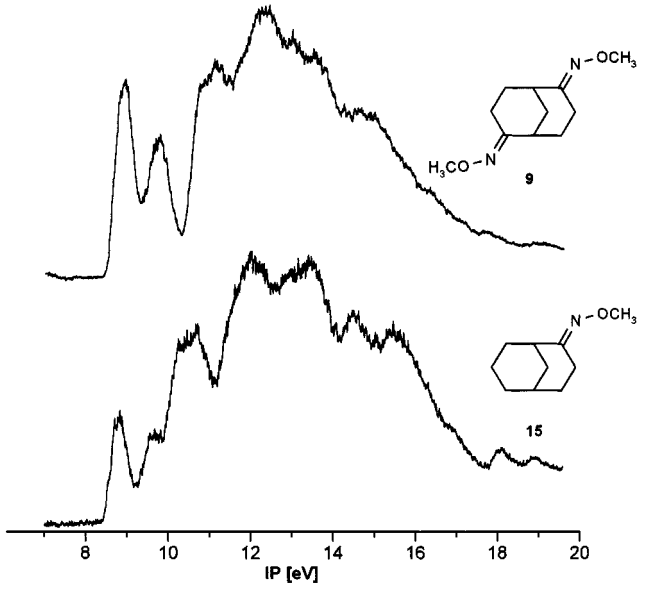

Figure 7. PE spectra of bicyclo[3.3.1]nonane-2,6-dione bis(*O*-methyloxime) (**9**) and bicyclo[3.3.1]nonane-2-one *O*-methyloxime (**15**)

0.2 eV is determined only for compound **8** that has a rather broad third ionization band. On the other hand, the spectra of compounds **4**, **7**, **6**, and **9** exhibit no indication of splitted π(C=N) and n(N) ionizations, and in the last two compounds the IPs are only 0.02−0.16 eV higher than in the monoxime **12** and the monomethoxime **15** that can be attributed to inductive stabilization of the orbitals by the second electronegative oxime group. Probably, the bicyclic skeleton connecting the functional groups is favourable for such effects.

The PE spectra of the dioximes and dimethoximes studied here, indicate sizeable OITS effects for the bicyclic compounds **5** and **8**. These compounds have an eight-membered ring in the CC conformation, favourable for through-space interaction of the functional groups. On the other hand, in the bicyclic compounds **4**, **7**, **6**, and **9** the puckering of the eight-membered ring disfavours the "contact" of the oxime groups and because of this no splitting of the orbitals occurs. The PE-spectroscopic findings confirm the results of the quantum chemical calculations outlined in the preceding section.

Table 3. Vertical ionization potentials [eV] of dioximes **4**−**6**, dimethoximes **7**−**9**, monoximes **11**, **12**, and monomethoximes **14**, **15**

	π^-(C=N)	π^+(C=N)	n^-(N)	n^+(N)
4*E*	9.53		10.12	
7[a]	8.99		9.88	
5*Z*	9.02	9.61	9.99	
8*E*	8.62	9.05	9.56	9.72
11	9.18[b]		9.88[c]	
14	8.78[b]		9.60[c]	
6*E*	9.37		9.96	
9[a]	8.88		9.73	
12	9.21[b]		9.94[c]	
15	8.75[b]		9.67[c]	

[a] Mixture of (*E*) and (*Z*) isomers. − [b] π(C=N). − [c] n(N).

3.4 ^{13}C-NMR Spectra

In Table 4, the ^{13}C-NMR δ values of the oxime carbon atoms of dimethoximes **8**, **9**, and methoximes **14**, **15** are summarized. In addition, Δδ values are given for the investigated systems that are obtained as the differences of the δ values of the mono- and the difunctional compounds, Δδ = δ(monofunctional) − δ(difunctional), and the transannular distances *d*. In both cases, there is a high-field shift in the difunctional compounds as compared to the monofunctional, and the size of Δδ is dependant on the distance *d* of the chromophores indicating strong transannular interactions in compound **8** and considerably smaller interactions in **9**. However, the result for the last compound seems to be questionable in view of the long distance *d* and the PE-spectroscopic results (see above). This is not the first time that NMR spectroscopy seems to lead to less reliable results for transannular effects,[22] and alternative interpretations of the experimental findings are likely.[26−28]

Table 4. ^{13}C-NMR δ values of the oxime carbon atoms of dimethoximes **8**, **9** and methoximes **14**, **15** (in $CDCl_3$), and transannular distances *d* [pm]

	δ(C=N)	*d*[a]		δ(C=N)	Δδ
8[b]	155.89	287.2	**14**	161.09	5.20
9[b]	160.88	346.7	**15**	163.10	2.22

[a] MMX results (from Table 1). − [b] Mixture of (*E*) and (*Z*) isomers.

4. Discussion

It was the main purpose of this investigation to study the conformational properties of bicyclic dioximes and dimethoximes in which the two functional groups are in opposite positions in an eight-membered ring. Depending on their relative geometric orientation, transannular orbital interactions between the π and the n MOs are possible. These features have been studied by quantum chemical calculations and by PE spectroscopy. In addition, ^{13}C-NMR spectroscopy was used. The conformational properties have been analysed comprehensively by molecular mechanics (MMX) and by semiempirical quantum chemical AM1 calculations. For the most important conformers also ab initio HF and B3LYP calculations were performed. The results of the latter methods were generally in better accordance with those of the MMX than those of the AM1 method. It was, however, unimportant to include electron correlation, i.e. the B3LYP results were rather the same as the HF results.

The electronic structures were analysed by the same theoretical methods as well as by PE spectroscopy. For the dioxime **5** and the dimethoxime **8**, significant transannular interactions could be established unequivocally by PE spectroscopy. The spectra of the difunctional compounds comprise an additional π(C=N) ionization band as compared to the corresponding monofunctional compounds. The observed effects are ascribed to through-space orbital interactions (OITS) caused by the favourable geometric orientations of the functional groups. On the other hand, no indications for such interactions were found in the PE spectra of compounds **4**, **6**, **7**, and **9**. All these results are in accord with the results of the quantum chemical calculations that indicate unfavourable conformations for the latter molecules to establish OITS. In this respect, it can be mentioned that for the interpretation of the PE spectra the MO energies calculated by the AM1 and the B3LYP method are superior to those of the HF method, indicating that inclusion of electron correlation is advantageous.

The results of our ^{13}C-NMR-spectroscopic analyses indicate that this technique is not the method of choice to study the conformational properties of cyclic dioximes and transannular interactions. The data give evidence for transannular effects in compounds **8**, however, it is difficult to differentiate these results from those for compound **9** where such effects are absent

Experimental Section

General: For details see ref.[1]

Bicyclo[3.3.0]octane-3,7-dione Dioxime (4): A solution of hydroxylamine hydrochloride (24.30 g, 0.35 mol) and sodium acetate (30.50 g, 0.37 mol) in water (200 mL) was added dropwise to a well-stirred solution of bicyclo[3.3.0]octane-3,7-dione (10.00 g, 72.4 mmol) in methanol (220 mL). Immediately a colourless precipitate occurred. The mixture was stirred at 25°C for 24 h and then the solid was filtered off, washed with water, and recrystallized from ethanol. Yield 10.91 g (90%), m.p. 172°C. − ^{1}H NMR ([D$_6$]DMSO): δ = 1.99−2.17 (m, 4 H, CH_2), 2.49−2.57 (m, 6 H, CH_2/CH), 10.32 (s, 2 H, =NOH). − ^{13}C NMR ([D$_6$]DMSO) (**4*E***): δ = 31.53 (CH_2), 35.33 (CH_2), 39.64 (CH), 163.20 (C=N). − IR (KBr): $\tilde{\nu}$ = 3250 (ν_{O-H}), 2959, 2914 (ν_{C-H}), 1684 ($\nu_{C=N}$), 1473, 1440, 1413 (δ_{CH2}), 1217 (δ_{O-H}), 972, 953, 908 cm^{-1}. − MS (70 eV, EI); *m*/*z* (%): 168 (26) [M$^+$], 151 (6) [M$^+$ − OH], 110 (60), 79 (100), 41 (22).

Bicyclo[3.3.1]nonane-3,7-dione Dioxime (5): A solution of bicyclo-[3.3.1]nonane-3,7-dione (2.00 g, 6.6 mmol) in ethanol (33 mL) was added dropwise to a well-stirred solution of hydroxylamine hydrochloride (3.64 g, 52.4 mmol) and sodium acetate (2.79 g, 34.0 mmol) in water (40 mL). The resulting reaction mixture was stirred at 60°C for 24 h. Ethanol was removed by evaporation and after addition of water (40 mL) the aqueous solution was extracted three times with dichloromethane. The dichloromethane extracts were combined, dried with sodium sulfate, and the solvent was evaporated. Recrystallization of the residue from ethanol afforded colourless crystals. Yield 1.08 g (89%), m.p. 241°C (ref.[29] 240−243°C). − ^{1}H NMR ([D$_6$]DMSO): δ = 1.83 (m, 4 H, CH_2), 2.25 (m, 6 H, CH_2), 3.04 (m, 2 H, CH), 10.04 (s, 2 H, =NOH). − ^{13}C NMR ([D$_6$]DMSO) (**5*Z***): δ = 27.52 (CH), 29.40 (CH), 30.03 (CH_2), 32.50 (CH_2), 36.72 (CH_2), 153.53 (C=N). − IR (KBr): $\tilde{\nu}$ = 3196 (ν_{O-H}), 2914 (ν_{C-H}), 1664 ($\nu_{C=N}$), 1485, 1456, 1430 (δ_{CH2}), 1356, 1281 (δ_{O-H}), 1066, 961 cm^{-1}. − HR-MS: $C_9H_{14}N_2O_2$, M$^+$: calcd. 182.1055; found 182.1044. − $C_9H_{14}N_2O_2$ (182.1): calcd. C 59.32, H 7.74, N 15.37; found C 59.31, H 7.90, N 15.21.

The oximes **6** and **11** were synthesized in an analogous manner as described for cyclohexane-1,4-dione dioxime.[1]

Bicyclo[3.3.1]nonane-2,6-dione Dioxime (6): Dione **3** (10.00 g, 65.7 mmol) and hydroxylamine hydrochloride (18.20 g, 0.26 mol) afforded 9.69 g of **6** (81%), m.p. 215°C. − ^{1}H NMR ([D$_6$]DMSO): δ = 1.70 (m, 4 H, CH_2), 1.79 (m, 2 H, CH_2), 1.92−2.06 (m, 2 H, CH_2), 2.63 (m, 2 H, CH), 3.10 (m, 2 H, CH_2), 10.32 (s, 2 H, = NOH). − ^{13}C NMR ([D$_6$]DMSO) (**6*E***): δ = 21.25 (CH_2), 29.65 (CH_2), 33.33 (CH_2), 34.77 (CH), 159.04 (C=N). − IR (KBr): $\tilde{\nu}$ = 3199 (ν_{O-H}), 2933, 2869 (ν_{C-H}), 1651 ($\nu_{C=N}$), 1458 (δ_{CH2}), 1355, 1289 (δ_{O-H}), 1055, 999, 965 cm^{-1}. − MS (70 eV, EI); *m*/*z* (%):182 (23) [M$^+$], 165 (100) [M$^+$ − OH], 148 (21) [M$^+$ − 2 OH], 106 (12) [$C_7H_8N^+$], 94 (25), 41 (18) [$C_2H_3N^+$]. − $C_9H_{14}N_2O_2$ (182.1): calcd. C 59.32, H 7.74, N 15.37; found C 59.28, H 7.78, N 14.90.

Bicyclo[3.3.1]nonane-3-one Oxime (11): Bicyclo[3.3.1]nonane-3-one (0.50 g, 3.6 mmol) and hydroxylamine hydrochloride (0.50 g, 7.2 mmol) afforded 0.43 g of **11** (78%), m.p. 107°C. − ^{1}H NMR ($CDCl_3$): δ = 1.32−1.73 (m, 8 H, CH_2), 2.01 (m, 1 H, CH_2 bridge), 2.14 (m, 2 H, CH), 2.44 (m, 2 H, CH_2), 3.17 (m, 1 H, CH_2 bridge), 8.80 (br. line, 1 H, =NOH). − ^{13}C NMR ($CDCl_3$): δ = 18.70 (CH_2), 28.19 (CH), 28.92 (CH), 29.72 (CH_2 bridge), 31.80 (CH_2), 32.77 (CH_2), 33.88 (*C*H_2C=N), 36.96 (*C*H_2C=N), 161.12 (C=N). − IR (KBr): $\tilde{\nu}$ = 3256 (ν_{O-H}), 2919, 2834 (ν_{C-H}), 1667 ($\nu_{C=N}$), 1444, 1417 (δ_{C-H}), 1350, 1289 (δ_{O-H}), 922 cm^{-1}. − HR MS: $C_9H_{15}NO$, M$^+$: calcd. 153.1154; found 153.1153.

The methoximes **7**, **8**, **9**, **14**, and **15** were synthesized by the procedure described for cyclohexane-1,4-dione bis(*O*-methyloxime).[1]

Bicyclo[3.3.0]octane-3,7-dione Bis(*O*-methyloxime) (7): Dione **1** (3.00 g, 21.7 mmol) and *O*-methylhydroxylamine hydrochloride (4.18 g, 50.0 mmol) afforded 1.86 g of **7** (44%), b.p. 92°C/0.27 hPa. − GC/MS analysis indicates a mixture of (*E*)/(*Z*) isomers, **7*E*/7*Z*** ≈ 1.2:1. − ^{1}H NMR ($CDCl_3$): δ = 2.12−2.33 (m, 4 H, CH_2), 2.60−2.73 (m, 6 H, CH_2/CH), 3.84 (s, 6 H, =$NOCH_3$). − ^{13}C NMR ($CDCl_3$) (two isomers): δ = 32.32 (CH_2), 33.20 (CH_2), 35.18 (CH_2), 35.99 (CH_2), 40.36 (CH), 40.51 (CH), 61.52 (= $NOCH_3$), 164.84 (C=N). − IR (liquid film): $\tilde{\nu}$ = 2942, 2815

(ν_{C-H}), 1651 ($\nu_{C=N}$), 1465, 1422 (δ_{CH2}), 1048 (ν_{C-O}), 886 cm^{-1}. − HR MS: $C_{10}H_{16}N_2O_2$, M^+: calcd. 196.1212; found 196.1238. − $C_{10}H_{16}N_2O_2$ (196.1): calcd. C 61.20, H 8.22, N 14.27; found C 61.23, H 8.82, N 14.24.

Bicyclo[3.3.1]nonane-3,7-dione Bis(*O*-methyloxime) (8): Dione **2** (2.00 g, 13.1 mmol) and *O*-methylhydroxylamine hydrochloride (2.67 g, 32.0 mmol) afforded 1.58 g of **8** [mixture of (*E*) and (*Z*) isomer] (57%), m.p. 67°C, b.p. 92°C/0.20 hPa. **8*E*** and **8*Z*** were separated by column chromatography on silica gel using dichloromethane/ethyl acetate (1:1) as eluent. − ^{1}H NMR ($CDCl_3$) (**8*E***): δ = 1.88−199 (m, 4 H, CH_2), 2.34 (m, 6 H, CH_2), 3.18 (m, 2 H, CH), 3.83 (s, 6 H, $=NOCH_3$). − ^{13}C NMR ($CDCl_3$) (**8*E***): δ = 30.21 (CH_2), 30.32 (CH), 33.56 (CH_2), 38.22 (CH_2), 61.14 (=$NOCH_3$), 155.89 (C=N); (**8*Z***): δ = 28.35 (CH), 30.53 (CH), 30.92 (CH_2), 33.43 (CH_2), 37.42 (CH_2), 61.04 (=$NOCH_3$), 156.03 (C=N). − IR (KBr) (**8*E***): $\tilde{\nu}$ = 2937, 2849 (ν_{C-H}), 1636 ($\nu_{C=N}$), 1465, 1433 (δ_{CH2}), 1053 (ν_{C-O}), 883 cm^{-1}. − HR MS: $C_{11}H_{18}N_2O_2$, M^+: calcd. 210.1368; found 210.1379. − $C_{11}H_{18}N_2O_2$ (210.1): calcd. C 62.83, H 8.63, N 13.32; found C 62.05, H 8.72, N 12.71.

Bicyclo[3.3.1]nonane-2,6-dione Bis(*O*-methyloxime) (9): Dione **3** (3.00 g, 19.7 mmol) and *O*-methylhydroxylamine hydrochloride (3.76 g, 45.0 mmol) afforded 1.72 g of **9** (42%), b.p. 88°C/0.29 hPa. − GC/MS analysis indicates a mixture of three (*E*)/(*Z*) isomers (6:5:1). − ^{1}H NMR ($CDCl_3$): δ = 1.75−2.21 (m, 8 H, CH_2), 2.74 (m, 2 H, CH), 3.22 (m, 2 H, CH_2), 3.84 (s, 6 H, $=NOCH_3$). − ^{13}C NMR ($CDCl_3$) (**9*E*** prevailing isomer): δ = 21.98 (CH_2), 29.76 (CH_2), 33.27 (CH_2), 34.83 (CH), 61.19 (=$NOCH_3$), 160.88 (C=N). − IR (KBr): $\tilde{\nu}$ = 2936, 2813 (ν_{C-H}), 1628 ($\nu_{C=N}$), 1451 (δ_{CH2}), 1048 (ν_{C-O}), 900, 863 cm^{-1}. − HR MS: $C_{11}H_{18}N_2O_2$, M^+: calcd. 210.1368; found 210.1367. − $C_{11}H_{18}N_2O_2$ (210.1): calcd. C 62.83, H 8.63, N 13.32; found C 63.47, H 9.20, N 13.22.

Bicyclo[3.3.1]nonane-3-one *O*-Methyloxime (14): Bicyclo[3.3.1]nonane-3-one (1.00 g, 7.2 mmol) and *O*-methylhydroxylamine hydrochloride (0.69 g, 8.3 mmol) afforded 0.80 g of **14** (67%). − ^{1}H NMR ($CDCl_3$): δ = 1.31−1.80 (m, 8 H, CH_2), 1.99 (m, 1 H, CH_2 bridge), 2.08 (m, 2 H, CH), 2.41 (m, 2 H, CH_2), 3.01 (m, 1 H, CH_2 bridge), 3.82 (s, 3 H, OCH_3). − ^{13}C NMR ($CDCl_3$): δ = 18.81 (CH_2), 28.24 (CH), 28.96 (CH), 30.39 (CH_2 bridge), 31.83 (CH_2), 32.79 (CH_2), 33.90 (CH_2C=N), 36.98 (CH_2C=N), 61.04 (=$NOCH_3$), 161.09 (C=N). − IR (liquid film): $\tilde{\nu}$ = 2956, 2803 (ν_{C-H}), 1629 ($\nu_{C=N}$), 1465, 1412 (δ_{C-H}), 1046 (ν_{C-O}), 964, 874 cm^{-1}. − HR MS: $C_{10}H_{17}NO$, M^+: calcd. 167.1310: found 167.1306.

Bicyclo[3.3.1]nonane-2-one *O*-Methyloxime (15): Bicyclo[3.3.1]nonane-2-one (1.00 g, 7.2 mmol) and *O*-methylhydroxylamine hydrochloride (0.69 g, 8.3 mmol) afforded 0.60 g of **15** (50%), b.p. 125°C/40 hPa. − ^{1}H NMR ($CDCl_3$) (major isomer): δ = 1.47−1.89 (m, 10 H, CH_2), 1.98 (m, 1 H, CH), 2.18−2.43 (m, 1 H, CH_2 bridge), 2.62 (m, 1 H, CH), 2.97−3.12 (m, 1 H, CH_2 bridge), 3.80 (s, 3 H, OCH_3). − ^{13}C NMR ($CDCl_3$) (major isomer): δ = 21.29 (CH_2), 23.26 (CH_2 bridge), 27.55 (CH), 28.06 (CH_2), 32.28 (CH_2), 32.41 (CH_2), 33.42 (CH_2C=N), 35.16 (CH), 61.07 (=$NOCH_3$), 163.10 (C=N). − IR (liquid film): $\tilde{\nu}$ = 2913, 2803 (ν_{C-H}), 1614 ($\nu_{C=N}$), 1450 (δ_{C-H}), 1044 (ν_{C-O}), 896, 859 cm^{-1}. − HR MS: $C_{10}H_{17}NO$, M^+: calcd. 167.1310; found 167.1326.

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