urethane-NH group. In addition, the differences in chemical shift of the $COOCH_3$ and Boc signals of species *I* and *II* (Table II) may reflect the different geometries of the helix-A- and helix-B-type structures, but they may also be a consequence of the different (bonded vs. free) states of the relevant carbonyl groups in the helical structures of opposite handedness (Table I).

As for the monomeric species *III*, it is probably a mixture of various interconverting conformers. This is suggested by the position of the NH resonances, most of which fall (Table II) in a range (between 7.16 and 7.8 ppm) close to that observed[46] for such alternating oligopeptides as Boc-D-Val-(L-Val-D-Val)$_2$-OMe and Boc-(L-Val-D-Val)$_3$-OMe that are presumably not long enough to form stable regular structures in solution. IR spectra measured[38] on chloroform solutions of different concentrations indicate for species *III* an amide I band centered at 1665 cm^{-1}.

Concluding Remarks

The results presented in this paper convincingly demonstrate that the species of Boc-(L-Val-D-Val)$_4$-OMe that predominates in the apolar cyclohexane has a left-handed $\uparrow\downarrow$ $\beta^{5.6}$ structure with 14 interstrand hydrogen bonds similar, if not identical, to the structure formed by the octapeptide in the crystalline state. These results correct a preliminary report[35] that attributed a β-helical structure with a left-handed sense of twist to this species, but considered the structure to be monomeric and not dimeric, as has now been established. The results obtained indicate that this structure occurs also in chloroform; however, in this solvent it is markedly less stable. The difference in stability may derive, in part at least, from the fact that contacts between the polar peptide backbone and chloroform are less unfavorable, permitting monomeric structures with less shielded backbones to occur in this solvent.

There are a number of aspects in this helical structure that need further investigation. One concerns the hydrogen bonding pattern and the choice between the alternative helix-A- and helix-B-type structures. Another aspect is the interaction with water. Traces of water present in the deuterated solvents used—especially chloroform—seem to be responsible for some differences in the NMR parameters of the β-helical structure in solutions of different concentrations (Table II). We plan to comment further on these aspects.

Acknowledgment. Partial financial support for this investigation by the Swiss National Science Foundation (Projects Nos. 2.884-0.77 and 2.414-0.79) is gratefully acknowledged. The editing of the manuscript by B. Straub is deeply appreciated.

Registry No. Boc-(L-Val-D-Val)$_4$-OMe, 65519-02-0.

Communications to the Editor

Correlation of the Rate of Thermal Cis–Trans Isomerization of *p*-Nitro-*p'*-dialkylaminoazobenzenes with Solvent *Z* Value Applied To Study Polarity in Aqueous Surfactant Solutions

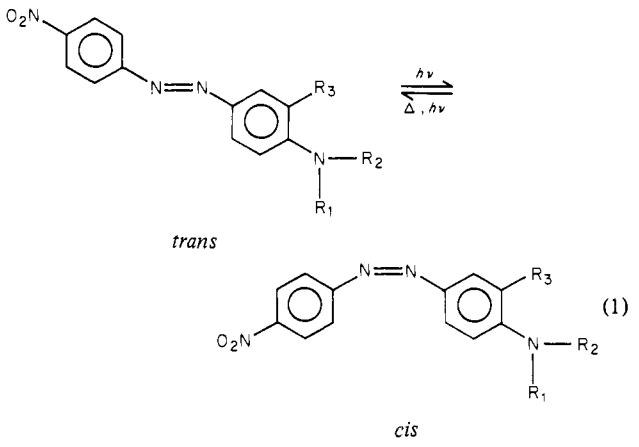
Kirk S. Schanze, T. Fleming Mattox, and David G. Whitten*

Department of Chemistry, University of North Carolina Chapel Hill, North Carolina 27514

Received November 23, 1981

The site of probe solubilization and microenvironmental effects in aqueous micellar and vesicle solutions is a topic of considerable interest.[1-3] It is frequently observed that changes in chemical and physical characteristics of probe molecules accompanies their incorporation into organized media. Numerous studies have utilized chemical and spectroscopic probes to determine the micropolarity and the degree of water penetration into aqueous surfactant assemblies.[1-6]

In 1972 it was reported that the rate of cis–trans thermal isomerization (k_{ct}, eq 1) of **1** is extremely solvent sensitive; rate enhancement of 10^4 occurs on changing solvent from hexane to DMF.[7] Similar effects were also reported for **4** and **5**.[8] Dyes **1–3** also exhibit solvochromism accompanying changes in solvent polarity. In the present paper we report results of a study of k_{ct} and the absorption maxima of **1–3** in a number of organic solvents



1, $R_1 = R_2 = CH_2CH_3$; $R_3 = H$
2, $R_1 = CH_2CH_3$; $R_2 = C_6H_5$; $R_3 = H$
3, $R_1 = CH_3$; $R_2 = n\text{-}C_{12}H_{25}$; $R_3 = H$
4, $R_1 = R_2 = CH_3$; $R_3 = H$
5, $R_1 = R_2 = CH_2CH_3$; $R_3 = CH_3$

and in aqueous micellar and vesicle solutions. These results indicate that these neutral azobenzene dyes are solubilized in relatively polar sites; however, a most interesting aspect of this study is an extrapolation that suggests that water is expelled concurrent with the solubilization process.

Dyes **1** and **2** were provided by G. Irick and their purity was checked by TLC and melting point analysis. Dye **3** was prepared by alkylation of *N*-methylaniline followed by coupling of the alkylated aniline with *p*-nitrobenzenediazonium chloride. Purification of **3** was carried out by HPLC; its purity was checked by HPLC and FT NMR. Most isomerization rates were measured by the flash photolysis technique[7] in a 2.5-cm cell thermostatted at 25 °C. Rates in benzene and heptane were measured with a Perkin-Elmer 576 spectrometer at 25 °C as previously described. Dye concentrations were 5×10^{-6} to 1×10^{-5} M. SDS was electrophoresis grade, recrystallized once from ethanol; CTAB

(1) Mukerjee, P.; Cardinal, J. R.; Desai, N. R. "Micellization, Solubilization and Microemulsions"; Mittal, K. L., Ed.; Plenum: New York, 1977; pp 241–261.
(2) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111–117.
(3) Fendler, J. H. *Acc. Chem. Res.* **1980**, *13*, 7–13.
(4) Ray, A.; Mukerjee, P. *J. Phys. Chem.* **1966**, *70*, 2138–2143.
(5) Mukerjee, P.; Ray, A. *J. Phys. Chem.* **1966**, *70*, 2144–2149.
(6) Südholter, E.; Engberts, J.; Hoekstra, D. *J. Am. Chem. Soc.* **1980**, *102*, 2467–2509.
(7) Wildes, P.; Pacifici, J. G.; Irick, G.; Whitten, D. *J. Am. Chem. Soc.* **1971**, *93*, 2004–2008.
(8) Nishimura, N.; Sueyoshi, T.; Yamanaka, H.; Imai, E.; Yamamoto, S.; Husegawa, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1381–1387.

0002-7863/82/1504-1733$01.25/0

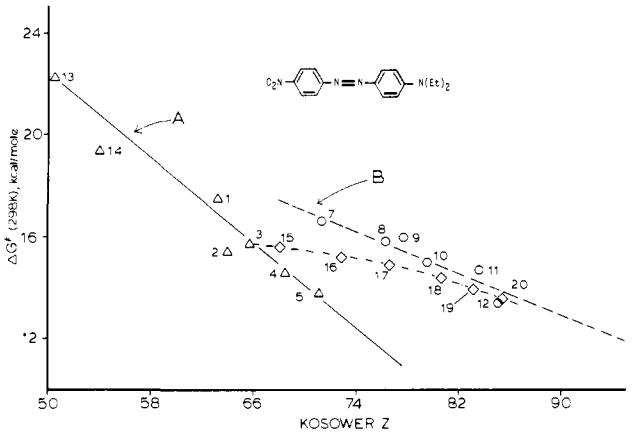


Figure 1. $\Delta G_{ct}^{\ddagger}$ (298 K) vs. Z values for **1**: line A (—), aprotic solvents; line B (---), protic solvents for **1**. Solvents: (1) $CHCl_3$, (2) pyridine, (3) acetone, (4) DMF, (5) CH_3CN, (7) *t*-BuOH, (8) 1-butanol, (9) 2-propanol, (10) ethanol, (11) methanol, (12) ethylene glycol, (13) *n*-heptane, (14) benzene. Acetone:H_2O mixtures (v/v): (15) 99:1, (16) 95:5, (17) 9:1, (18) 8:1, (19) 7:1, (20) 6:1.

Table I. $\Delta G_{ct}^{\ddagger}$ (298 K, kcal/mol) and [λ_{max} (nm)] in Surfactant Solutions

	micellar solutions[c]			vesicles,[d]
dye	SDS[a]	CTAB[a]	Brig-35[a]	DODAB[b]
1	12.2 [515]	12.4 [515]	14.3 [509]	13.0 [515]
2	12.7 [517]		13.1 [511]	
3	13.4 [499]			14.5 [503]

[a] Surfactants at concentrations CMC + 0.02 M. [b] [DODAB] = 10^{-3} M. [c] Micelle solutions sonicated in bath sonicator for $^1/_2$ h. [d] Vesicle solutions sonicated with probe sonicator and centrifuged.

was reagent grade, recrystallized once from acetone; Brij-35 was reagent grade and was dissolved in ether, filtered, and recrystallized once. First-order plots of the change in absorbance monitored at λ_{max} for the trans isomer were linear for at least 3 lifetimes. Absorption maxima were measured at ambient temperatures in the Perkin-Elmer spectrometer.

The rate constant was measured for **1** and **2** in 13 solvents and for **1** in several acetone/water mixtures at 25 °C. Plots of $\Delta G_{ct}^{\ddagger}$ vs. Kosower Z values[9] show two linear dependences: line A for aprotic solvents and line B for protic solvents (Figure 1). The plot of $\Delta G_{ct}^{\ddagger}$ for **1** in acetone:water mixtures is curved, beginning on line A and coming to merge with line B as the acetone:water ratio decreases (Figure 1). The π,π^* absorption band for **1–3** occurs in the 450–520-nm region.[10] We have measured λ_{max} for **1** and **2** in a number of solvents. A red shift accompanies an increase in solvent polarity (e.g., for **1**, λ_{max} in hexane = 453 nm, λ_{max} in ethylene glycol = 511 nm); however, if $E_T(\pi,\pi^*)$ is plotted vs. Z the points are scattered and a good correlation (i.e., a linear fit) does not emerge.

$\Delta G_{ct}^{\ddagger}$ and λ_{max} were measured for **1–3** in aqueous surfactant solutions at 25 °C (Table I). From the $\Delta G_{ct}^{\ddagger}$ vs. Z points along with the data in Table I, values for the effective micropolarity at the site of dye solubilization can be extrapolated. Two values were obtained, each corresponding to the intersection of $\Delta G_{ct}^{\ddagger}$ (surfactant) with line A or line B. The effective Z values so obtained are presented in Table II.

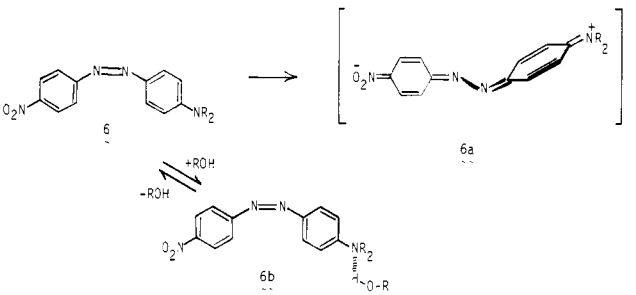
A remarkable feature that emerges from the solvent study is k_{ct}(protic solvent) < k_{ct}(aprotic solvent) for **1** and **2** for a particular Z value. The transition state in the cis–trans isomerization of **1–3** is highly polar (**6a**, Scheme I).[7,11] Stabilization of the cis isomer in protic solvents relative to aprotic solvents could be attributed to hydrogen bonding to the amino nitrogen of **6b**, which would effectively increase the N=N bond order. The dependence

Table II. Effective Z Values at Site of Dye Solubilization

	dye					
	1		2		3	
surfactant	a[a]	b[b]	a[c]	b[c]	a[a]	b[b]
SDS	75	94	74	95	72	88
CTAB	74	92				
Brij-35	70	83	72.5	92		
DODAB	72	90			69	82

[a] Line A, Figure 1 extrapolated. [b] Line B, Figure 1 extrapolated. [c] Similar extrapolations from plot for 2.

Scheme I



of $\Delta G_{ct}^{\ddagger}$ on Z in acetone:water mixtures (Figure 1) shows that the dyes are quite sensitive to the presence of protic solvents. The point for 1% water deviates markedly from the aprotic line, and upon addition of >15% water the behavior of the solvent mixture parallels that of protic solvents.

The sensitivity of the position of the π,π^* absorption and of k_{ct} for NAAB dyes makes them attractive probes for exploring polarity and other microenvironmental effects in micelles and vesicles. Experiments with viscous solvents (ethylene glycol, cyclohexanol, mineral oil, and glycerol) show that k_{ct} is not viscosity dependent. Thus, the dyes shold be sensitive only to polarity and hydration effects in the surfactant assemblies. λ_{max} and k_{ct} for **1–3** in surfactant solutions qualitatively suggest that the dyes are solubilized in polar sites (Table I). When the results in the various surfactant assemblies (charged micelles, uncharged micelles, and vesicles) are compared, it appears that the sites of solubilization are similar in polarity. These results agree with other probe studies of polarity in micelle and vesicle solutions.[3-6]

Several different probe molecules have been utilized to examine micropolarity effects in surfactant solutions. Studies with amphiphilic alkylpyridinium iodides[4-6] in surfactant solutions indicate that the ionic headgroups of these probes experience an average micropolarity of Z = 70–80 in micelles and Z = 65–75 in doped natural phosphatidylcholine vesicles. Presumably the chromophore of these probes resides at an interfacial site; thus the Z values reflect an "interfacial Z value", not a Z value for the interior of the micelle.

The micellar $\Delta G_{ct}^{\ddagger}$ of 12.2 kcal/mol (dye **1**) corresponds to a Z value of 75 or 94 depending upon whether line A for aprotic or line B for protic solvents in Figure 1 is used for extrapolation. Based on the similarity of the "line A" Z values to micellar Z values obtained with other probes, it is tempting to conclude that the NAAB dyes reside in a site that resembles a polar aprotic solvent.[12] Since our work as well as other investigations suggest that there is extensive water penetration and/or hydrocarbon water contact in simple micelles,[2,14-17] this suggests that the dyes are

(9) Kosower, E. M. *J. Am. Chem. Soc.* **1958**, *80*, 3253–3261.
(10) Gabor, G.; Fischer, E. *J. Phys. Chem.* **1971**, *75*, 581–583.
(11) Asano, T. *J. Am. Chem. Soc.* **1980**, *102*, 1205–1206.

(12) The binding constant of **1** with SDS micelles is reported as 4×10^3 at 60 °C.[13] Dyes are insoluble in water even after prolonged sonication. These facts suggest that **1–3** are solubilized in or near the surfactant pseudophase, not in the bulk water phase.
(13) Biedermann, W.; Daytner, A. *J. Coll. Interface Sci.* **1981**, *82*, 276–285.
(14) Worsham, P. R.; Eaker, D. W.; Whitten, D. G. *J. Am. Chem. Soc.* **1978**, *100*, 7091–7093.
(15) Whitten, D. G., et al. "Biomimetic Chemistry and Transition State Analogs: Approaches to Understanding Enzyme Catalysis"; Green, B. S., Ed.; Elsevier: Amsterdam, in press.

solubilized concomitant with expulsion of water. This is in accord with other studies that show that solubilization is due to a hydrophobic effect involving elimination of hydrocarbon–water interfaces similar to the micellization process itself.[18,19]

Acknowledgment. We are grateful to the National Science Foundation (Grant No. CHE7823126) for support of this work.

Registry No. (*E*)-**1**, 80631-72-7; (*Z*)-**1**, 80631-73-8; (*E*)-**2**, 80631-74-9; (*Z*)-**2**, 80631-75-0; (*E*)-**3**, 80631-76-1; (*Z*)-**3**, 80631-77-2.

(16) Russell, J. C.; Whitten, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 3219–3220.
(17) Foreman, T. K.; Sobol, W. M.; Whitten, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 533–5336.
(18) Part 27: Bonilha, J. B. S.; Foreman, T. K.; Whitten, D. G. *J. Am. Chem. Soc.*, in press.
(19) Photochemical Reactivity in Organized Assemblies. Part 28.

High Diastereoselection in the Alkylation of Siloxy-Substituted Methyl Cyclopropanecarboxylates: Consequence of a Pyramidal Ester Enolate Anion?

Hans-Ulrich Reissig*† and Ingrid Böhm

Institut für Organische Chemie der Universität Am Hubland, D-8700 Würzburg, West Germany

Received November 19, 1981

Recently we reported[1] on the reaction depicted in Scheme I, which to our best knowledge is the first example of a successful deprotonation and alkylation of an alkyl cyclopropanecarboxylate.[2] This transformation makes available a great variety of siloxy-substituted cyclopropanes of type **2**, which are useful building blocks in organic synthesis.[3] At first sight one would expect both diastereomers, (*E*)-**2** and (*Z*)-**2**, in the alkylation reaction (Scheme I). Yet we demonstrate here with suitable model compounds that (*E*)-**2** is formed in large excess or even exclusively.

A 1:1 mixture of (*E*)- and (*Z*)-methyl 2-phenyl-2-trimethylsiloxycyclopropanecarboxylate (**1a**) was deprotonated with LDA (1.5 equiv) in THF at −78 °C (2 h), and the resultant enolate was treated with iodomethane (Table I, entry 1).[4] Only (*E*)-**2a** could be detected by ^1H and ^{13}C NMR spectrometry in the reaction mixture. Similarly, addition of other electrophiles El–X, e.g., Me_2SO_4, *n*-BuI, $CH_2{=}CHCH_2Br$, and $PhCH_2Br$, to the enolate **1a** also resulted in the exclusive formation of the corresponding *E* isomers (*E*/*A* > 95:5) in excellent yields (73–89%).[5] Protonation of the enolate is less selective (NH_4Cl/H_2O: (*E*)-**1a**:(*Z*)-**1a** = 76:24).[7]

Deprotonation and methylation of the cyclopropanes **1c** and **1d** also gave only the *E* diastereomers (entries 3, 4). Since the same sequence applied to **1b**, **1e**, and **1f** led to 92:8, 90:10, and 90:10 *E*:*Z* mixtures, respectively (entries 2, 5, 7), the reaction of the enolate **1f** with other electrophiles was studied. Entries 6–13 show a large to moderate preference for (*E*)-**2f**α to (*E*)-**2f**ϵ in all cases.[8] The diastereoselectivity decreases with more reactive electrophiles (entries 7, 8, 11, 12) but also seems to be sensitive to the bulkiness of El–X (entries 7, 9, 10). As expected, the same *E*:*Z* mixture was obtained in the alkylation regardless of the diastereomeric composition of the starting material (entries 6, 7).

Table I. Diastereoselectivity in the Alkylation of 1 → 2 According to Scheme I

entry	educt	*E*:*Z*	El–X[a]	product(s)	*E*:*Z*[b]	yield,[c] %
1	1a	50:50	Me–I	2a	>97:3	84
2	1b	53:47	Me–I	2b	92:8	70
3	1c	52:48	Me–I	2c	>97:3	92
4	1d	58:42	Me–I	2d	>95:5	65
5	1e	75:25	Me–I	2e	90:10	85
6	1f	>98:2	Me–I	2fα	88:12	86
7	1f	75:25	Me–I	2fα	90:10	87
8	1f	75:25	$Me–OSO_3Me$	2fα	85:15	66
9	1f	75:25	Et–I	2fβ	88:12	90
10	1f	75:25	*n*-Bu–I	2fγ	81:19	77
11	1f	75:25	allyl–Br	2fδ	82:18	81
12	1f	75:25	allyl–I	2fδ	72:28	76
13	1f	75:25	benzyl–Br	2fϵ	65:35	81

[a] Reaction conditions: THF:hexane = 3:1; −78 °C; 6–40 h. [b] Ratio determined by ^1H and ^{13}C NMR spectrometry. Control experiments showed that the *E*:*Z* ratios are reproducible to within ±2%. [c] Isolated yield of purified product after bulb-to-bulb distillation. Satisfactory spectra and combustion analyses were obtained for all compounds.

No definitive explanation of the high *E* diastereoselectivity can be given; however, a number of interesting conclusions concerning the structure of the methyl cyclopropanecarboxylate anion may be drawn. Three limiting principal structures of the anion[9] are shown in Scheme II: (1) the "normal" planar ester enolate anion[10] **3**; (2) the pyramidal ester enolate anions[10] (*E*)-**4** and (*Z*)-**4**; (3) the pyramidal cyclopropyl anions (*E*)-**5** and (*Z*)-**5** with the carbomethoxy group in a bisected conformation.

If it is assumed that the reaction is governed only by steric effects,[11] entries 1–5 ($OSiMe_3 < R^1$) are in accordance with the type-**3** planar anions. However, the results of entries 6–13 ($OSiMe_3 > R^1 = H$), which show a marked preference for the electrophile to be introduced cis to the sterically more demanding group, imply that pyramidal species such as **4** and **5** are involved. On the other hand, the configurational instability of the anions concluded from all entries makes a cyclopropyl anion of type **5** unlikely. Furthermore, the changing product *E*/*Z* ratios arising from different electrophiles (entries 6–13) suggest a mobile equilibrium of the intervening anionic species. Probably (*E*)-**4** is the most reactive[12] among the postulated enolates affording (*E*)-**2** as main product.[13] In summary our present experimental data are best rationalized in terms of a configurationally labile pyramidal ester enolate **4** as intermediate.

† Liebig Fellow, 1979–1982.
(1) Böhm, I.; Hirsch, E.; Reissig, H.-U. *Angew. Chem.* **1981**, *93*, 593. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 574.
(2) For the deprotonation of cyclopropanecarboxylates and alkylation attempts see: Pinnick, H. W.; Chang, Y. H.; Foster, S. C.; Govindan, M. *J. Org. Chem.* **1980**, *45*, 4505 and literature cited therein.
(3) For a review see: Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27. See also ref 1 and Reissig, H.-U. *Tetrahedron Lett.* **1981**, *22*, 2981 and literature cited therein.
(4) For description of a typical experiment see ref 1.
(5) The cis relationship of the carbomethoxy function and the phenyl group in (*E*)-**2a** derivatives is clearly demonstrated by the high-field methoxy singlet ($CDCl_3$, δ 3.18–3.40); see ref 6.
(6) Booth, H. "Progress in Nuclear Magnetic Resonance Spectroscopy"; Pergamon Press: Oxford, England, 1969; Vol. **5**, p 149.
(7) This result and a comparable product ratio in the protonation of the **1f** enolate (*E*/*Z* = 71/29) suggest at least partial *O*-protonation followed by nonstereoselective H shift to carbon.
(8) In isomers (*E*)-**2f**α to (*E*)-**2f**ϵ R^1 = H is shifted to lower field ($CDCl_3$, δ 3.57–3.85) due to the cis-located carbomethoxy group, whereas the respective protons in the *Z* isomers appear at higher field ($CDCl_3$, δ 2.87–3.23); see ref 6.
(9) As in most work dealing with carbanionic species one can only speculate about the role of the cation. Li^+ might be coordinated to oxygen in **3** and **4** and to carbon in **5**. Also the kind of ion pair involved and the degree of aggregation are not certain. These unknown factors, however, should not distract from our argumentation regarding the geometry of the reacting anion.
(10) Only one of the two possible isomers concerning the enolate C–C bond is shown. We see no obvious mechanism showing how this factor could control the diastereoselectivity.
(11) The E_s value for $OSiMe_3$ should be in the order of that of *O*-alkyl ≈ 0.55; for E_s values see: Fujita, T.; Nishioka, T. *Progr. Phys. Org. Chem.* **1976**, *12*, 49. For empirical substitutent parameters see: Knorr, R. *Chem. Ber.* **1980**, *113*, 2441.
(12) If the cation is coordinated to the carbonyl oxygen of the enolate, favorable complexation to the siloxy group seems possible in (*Z*)-**4** but not in (*E*)-**4**, which might be the reason for its higher reactivity; however, see footnote 9.
(13) Retention of configuration with respect to the nucleophilic carbon, as mostly observed in electrophilic substitution, is assumed. Also, (*E*)-**4** can be regarded as a system with a nonplanar C–C double bond interacting with El–X via its larger orbital lobe and finally giving (*E*)-**2**.

0002-7863/82/1504-1735$01.25/0