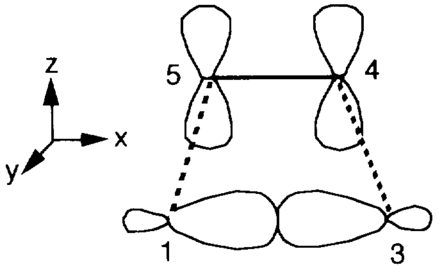
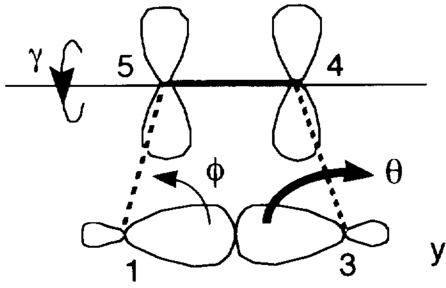


$$\Gamma(S_0) = A'$$
$$\Gamma(T_1^y) = A'$$
$$\Gamma(R_x) = A''$$
$$\Gamma(R_y) = A''$$
$$\Gamma(R_z) = A'$$

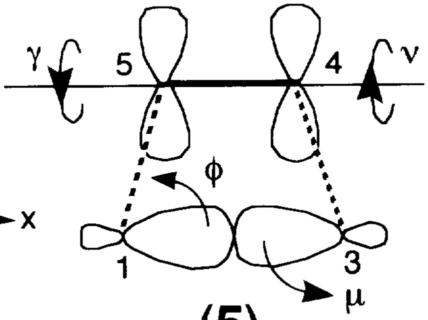
(3)

case-(A) :



(4)

case-(B) :



(5)

Also, we examine the case-(B), which can lead to the cyclopentadiene as in (**1**-(**B**)). Since the MO model of case-(B) is the same as that of case-(A), the symmetry requirements for the former is applicable to the latter (see (**5**)). Likewise, in order to obtain the nonvanishing SO coupling matrix element, a geometric distortion is needed. In contrast, however, the distortion for case-(B) may involve a disrotation of the π bond and a conrotatory cleavage of the σ bond. Further, the HOMO and the LUMO may be expressed as a function of the cleavage angle φ and μ (σ bond) and the rotation angle γ and ν (π bond) as shown in (**5**)[9(c)].

The relative SO coupling efficiency of the mechanisms can be estimated by evaluating the MO angular momentum ($\hat{l}_k$) matrix elements[10,11]:

$$\left\langle \hat{H}_{SO} \right\rangle_k = C \cdot \left\langle HOMO \left| \frac{\hat{l}_k \cdot \hat{s}_k}{r^3} \right| LUMO \right\rangle \qquad \left(C = \frac{Z_N^* e^2}{2m^2c^2}; k = x, y, z \right) \tag{2}$$

where HOMO and LUMO are the highest occupied and lowest unoccupied delocalized MOs of the molecular system, respectively[5]. Hence, the y and x components of the SO coupling matrix elements for case-(A) and case-(B), respectively, are given by

$$case-(A): \left\langle \hat{H}_{SO} \right\rangle_y = \frac{\hbar^2 C}{2\sqrt{2}} \cdot \left[\left(a^2 - b^2\right) V_{14}^{\pi} \cos\phi + \left(a^2 - b^2\right) V_{35}^{\pi} \cos\gamma \cos\theta \right.$$

$$+\left(a^2+b^2\right)V_{15}^{\pi}\cos\gamma\cos\phi+\left(a^2+b^2\right)V_{34}^{\pi}\cos\theta+ab\left(V_{13}^{\sigma}+V_{13}^{\pi}\right)\sin\theta\cos\phi\Big] \qquad (3)$$

$$case-(B):\left\langle\hat{H}_{SO}\right\rangle_x=\frac{-i\hbar^2C}{4\sqrt{2}}\cdot\Big[\left(a^2+b^2\right)\left(V_{15}^{\sigma}+V_{15}^{\pi}\right)\cos\gamma\sin\phi$$

$$+\left(a^2+b^2\right)\left(V_{34}^{\sigma}+V_{34}^{\pi}\right)\cos\nu\sin\mu+\left(a^2-b^2\right)\left(V_{14}^{\sigma}+V_{14}^{\pi}\right)\cos\nu\sin\phi$$

$$+\left(a^2-b^2\right)\left(V_{35}^{\sigma}+V_{35}^{\pi}\right)\cos\gamma\sin\mu+4abV_{45}^{\pi}\sin(\gamma+\nu)\Big] \qquad (4)$$

For convenience, we use V^{σ} and V^{π} to describe σ- and π-interactions, respectively[5(d,e)]. That is,

$$V_{mn}^{\sigma}=\left\langle p_{my}\left|\frac{1}{r_m^3}+\frac{1}{r_n^3}\right|p_{ny}\right\rangle,\ V_{mn}^{\pi}=\left\langle p_{mz}\left|\frac{1}{r_m^3}+\frac{1}{r_n^3}\right|p_{nz}\right\rangle,\ldots\ldots\ldots\ldots\ldots\ldots\ldots etc.$$

where m and n are positions of the atomic centers. Additionally, V^{σ} and V^{π} behave similarly to the corresponding atomic overlap integral such that, in general, $|V^{\sigma}| > V^{\pi} > 0$ and $V^{\sigma} < 0$ [5(d)].

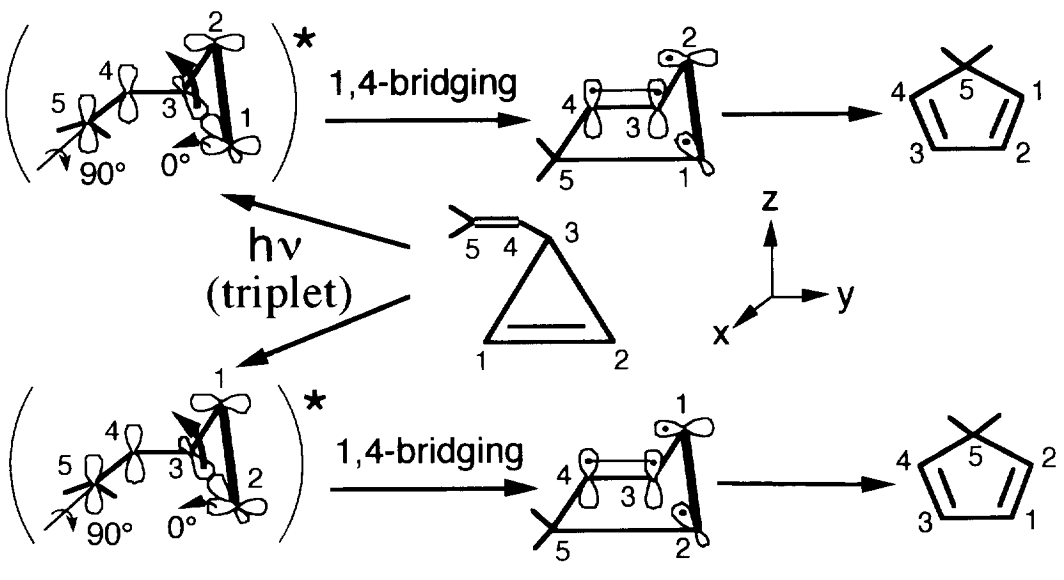
For case-(A) the last term, $(V_{13}^{\sigma}+V_{13}^{\pi})$, is negative and will not add to the other terms in eq(3). Similarly, the last term in eq(4) is not additive. Consequently, the qualitative aspects of this spin-inversion efficiency may be summarized as follows:

(i) Supposing that a ≈ b (and thus 2ab ≈ a^2+b^2), which corresponds to the interacting valence MOs being electronically similar[9(b,c)]. Then eq(3) reaches a maximum as given by

$$case-(A)(\theta=\gamma=90^\circ,\phi=0^\circ):\left\langle\hat{H}_{SO}\right\rangle_{y,\max}=\frac{\hbar^2C}{2\sqrt{2}}\cdot\left[ab\left(V_{13}^{\sigma}+V_{13}^{\pi}\right)\right] \qquad (5)$$

A three-dimensional picture of this mechanism is presented in Scheme I. It begins with π–π bridging (1–4 bridging) in the excited state, with the terminal carbon of the vinyl group bonding to one end of the excited cyclopropene double bond, accompanied by fission of the σ bond (C-1–C-3 or C-2–C-3 in Scheme I). It then undergoes the formation of a π bond to give the cyclopentadiene products as shown in (**1**-(**A**)). It should be noted that the mechanistic interpretation for case-(A), which undergoes a concerted process, bears a strong similarity to the triplet "mechanism A" proposed by Zimmerman *et al.*[1,2], although they also suggested that the latter occurs in a non-concerted process involving an intermediate houseane diradical.

On the other hand, for case-(B) two extremes can be easily distinguished in eq(4). These are, γ = ν = 45°, μ = φ = 0° and γ = ν = μ = 45°, φ = 0°. The former leads only to maximization of the last term in eq(4), where the C=C bond of the vinyl group twists perpendicularly. In this geometry, however, the system inverts



Scheme I.

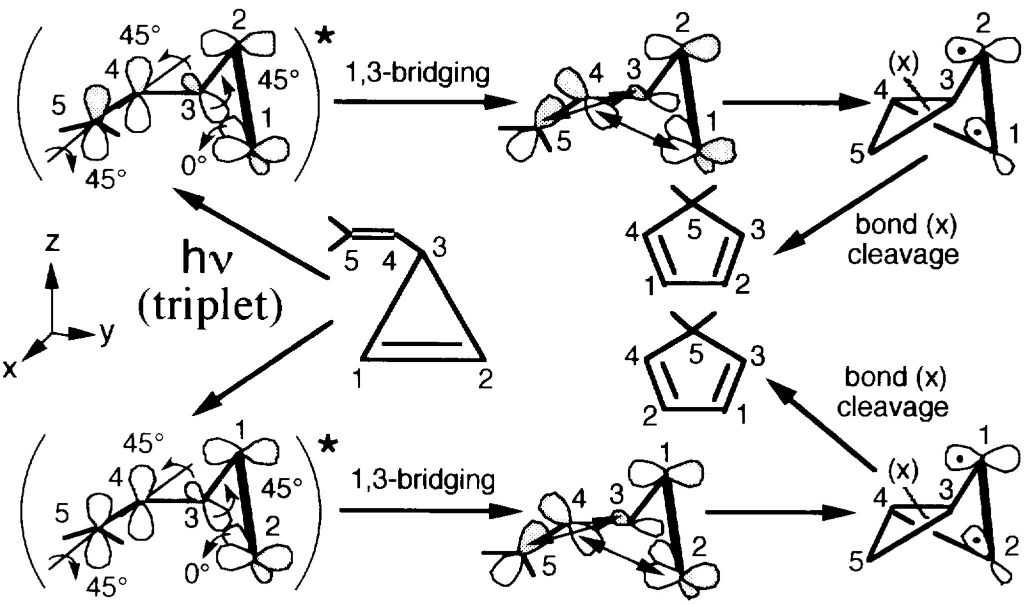
a spin and relaxes to a ground state reactant. In contrast, the latter reaches a higher value leading to the expression

$$case-(B)(\gamma = \nu = \mu = 45^\circ, \phi = 0^\circ):$$

$$\left\langle \hat{H}_{SO} \right\rangle_{x,\max} = \frac{-i\hbar^2 C}{4\sqrt{2}} \cdot \left[0.50(a^2 + b^2)(V_{34}^{\sigma} + V_{34}^{\pi}) + 4abV_{45}^{\pi} \right] \tag{6}$$

A schematic representation of a distortion complex corresponding to those angular characteristics is shown in Scheme II using the coloring convention of the *p* AOs to indicate the directional changes. The double headed arrows indicate the bonds to be formed. In such a geometry all the rotational orbitals are aligned to form the new bonds (i.e., 1,3-bridging)[12]. This then can either revert to the reactant if ring closure requires a higher barrier or proceed onward to give the cyclopentadiene product as shown in (**1**-(**B**)). It is notable that the case-(B) mechanism proposed here is analogous to the triplet "mechanism C", involving the formation of the cyclobutenyloxy diradical, as suggested by Zimmerman et al[1,2].

Since the case-(A) mechanism competes with the case-(B) mechanism, it would be instructive to compare their SO coupling expressions. One may easily obtain $|(\text{eq}(10))^2| \geq |(\text{eq}(9))^2|$ owing to $|2V_{45}^{\pi}| > |V_{13}^{\sigma} + V_{13}^{\pi}| > (|V_{34}^{\sigma} + V_{34}^{\pi}|)/2$ [5(b)]. Namely, the SO coupling expressions for the case-(A) and the case-(B) mechanisms in a nonpolar event are comparable. Nevertheless, case-(A) is expected to be kinetically favorable as a result of its better initial orbital overlaps as well as the less geometric motions (see Scheme I and



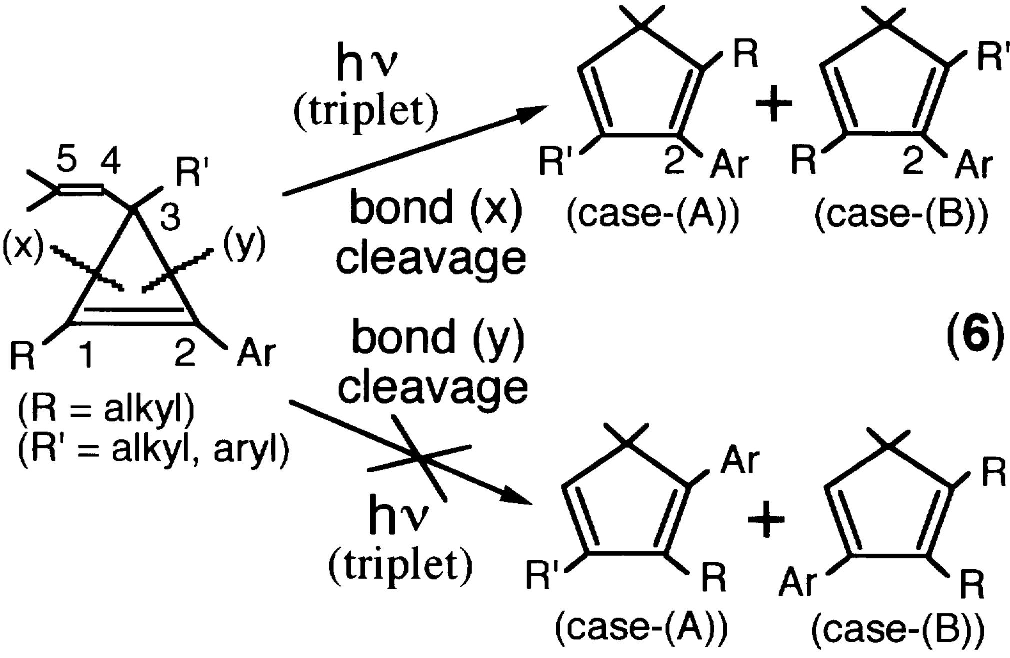
Scheme II.

II). It is therefore concluded that *the case-(A) pathway will in general be more efficient than the case-(B) route in nonpolar environments and may dominate where both are a priori possibilities.* This predictions has been verified in the 3-vinylcyclopropene system as shown in (**1**)[1]. Furthermore, one striking result of these rearrangements is that regioselectivity was encountered when the cyclopropene π bond was unsymmetrically substituted[1(a-c)]. Here the preference is for new carbon to carbon bond formation at the three-membered-ring π-bond position bearing the alkyl rather than the aryl group as illustrated in (**6**). This result can be understood in terms of the case-(A) and case-(B) mechanisms outlined in Scheme I and II respectively, where there is a preference for the C-1 or C-2 position to be aryl rather than alkyl as a consequence of the demand for odd-electron delocalization by the aryl substituent.

(ii) Supposing that a > b, which corresponds to the interacting MOs being electronically dissimilar and polarized. In the extreme case, polarization makes 2ab zero while ($a^2 + b^2$) approaches unity. Therefore, as polarity increases, ($a^2 + b^2$) becomes larger than 2ab, which, in turn, leads to a new SO coupling expression for the case-(A) mechanism (eq(3)) as follows,

$$case-(A)(\theta = 45^\circ, \gamma = 90^\circ, \phi = 0^\circ):$$

$$\left\langle \hat{H}_{SO} \right\rangle_{y,\max} = \frac{\hbar^2 C}{2\sqrt{2}} \cdot \left[0.71(a^2 + b^2) V_{34}^{\pi} + (a^2 - b^2) V_{14}^{\pi} + 0.71ab(V_{13}^{\sigma} + V_{13}^{\pi}) \right] \qquad (7)$$



(6)

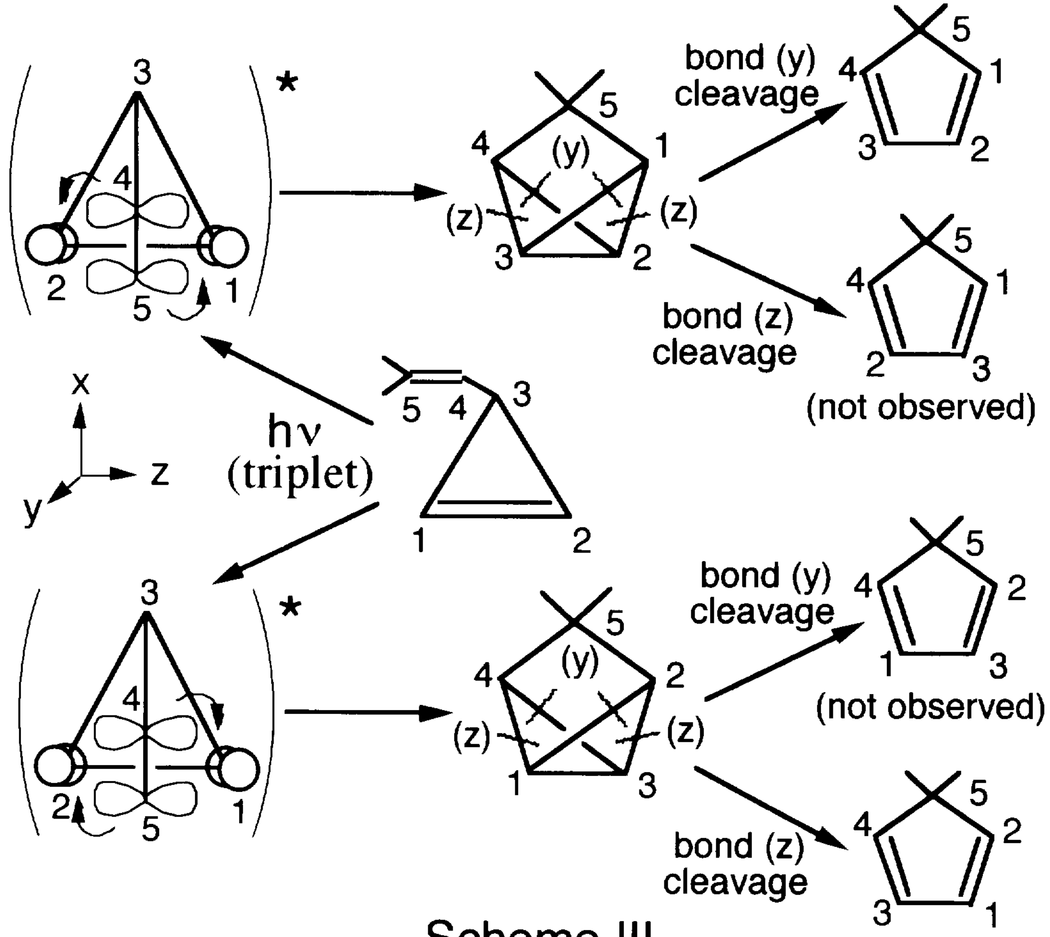
Again, in this geometry the system either returns to its ground state reactant after a spin-inversion or to a cyclopentadiene, analogous to Scheme I.

Also, for the case-(B) mechanism (eq(4))) one may readily obtain

$$case-(B)(\gamma = \mu = \nu = 45^\circ, \phi = 0^\circ):$$

$$\left\langle \hat{H}_{SO} \right\rangle_{x,\max} = \frac{-i\hbar^2 C}{4\sqrt{2}} \cdot \left[0.50(a^2+b^2)(V_{34}^{\sigma}+V_{34}^{\pi}) + 0.50(a^2-b^2)(V_{35}^{\sigma}+V_{35}^{\pi}) + 4abV_{45}^{\pi} \right] \quad (8)$$

Similarly, this distortion complex will behave as depicted in Scheme II. Moreover, the main terms for eq(3) and eq(4) are $0.71\left(a^2+b^2\right)V_{34}^{\pi}$ and $0.50\left(a^2+b^2\right)\left(V_{34}^{\sigma}+V_{34}^{\pi}\right)$, respectively, as $\left(a^2+b^2\right)$ is the biggest coefficient and V_{34} is the largest value. Taking into account $\left(a^2+b^2\right) >> 2ab$, one may then readily prove that $|(eq(11))^2| \geq |(eq(12))^2|$. As a result, we come to the conclusion that *the case- (A) mechanism should be more efficient than the case-(B) mechanism in the photocycle reaction of 3-substituted cyclopropene in polar situations, because of its larger SO coupling expression as well as better initial orbital overlap (and the less geometric motion).* This conclusion is based on the model we used here as well as on the assumption that other controlling factors are constant. Our model prediction is in good agreement with available experimental results[2]. For instance, it was verified that placing electron-withdrawing groups at the 3-olefiniccyclopropenes



Scheme III.

(i.e., acyl, imino, etc.) yield furan and pyrrole, respectively, all deriving exclusively from the case-(A) pathway as shown in (**2**).

Further, repeating the procedure for $\langle \hat{H}_{SO} \rangle_x$ and $\langle \hat{H}_{SO} \rangle_z$ in case-(A) as well as for $\langle \hat{H}_{SO} \rangle_y$ and $\langle \hat{H}_{SO} \rangle_z$ in case-(B) lads to much smaller SO coupling expressions. Accordingly, spin inversion will occur faster only in the y sublevel for case-(A) and the x sublevel for case-(B).

We also note that there could be a third reaction mechanism involving a $2\pi + 2\pi$ cycloaddition of the vinyl group to the cyclopropene double bond as shown in Scheme III, analogous to the triplet "mechanism D" suggested by Zimmerman *et al*[1,2]. Nevertheless, this spin-inversion mechanism (Scheme III) was found to be identical to the orbital-symmetry-forbidden pathway $[{}_{\pi}2_s + {}_{\pi}2_a]$[12(b)]. Moreover, such a mechanism results in zero SO coupling expressions and may lead to the cyclopentadiene products, which were not experimentally observed as given in (**1**) and (**2**). We therefore exclude this $2\pi + 2\pi$ mechanism in the photorearrangements of 3-substituted cyclopropenes.

In summary, this work represents an attempt to apply group theory to search for the motions which lead to spin inversion, and then evaluate their relative efficiency using delocalized MOs as a semiquantitative tool. A mechanistic interpretation for such photorearrangements in terms of a concerted process via a diradical is satisfactorily reconciled with the observed stereochemical results[1,2]. It is hoped that our study will provide stimulation for further research into the subject.

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3. Furthermore, Zimmerman also suggested that the close relationship between the three mechanisms A, B, and C has been noted (see ref.(1(d))). This leads to the possibility of a composite mechanism embodying the features of all three extremes with timing depending upon structure and multiplicity. Such a mechanism may be seen in the present study; see case-(A) and (B) mechanisms proposed here.
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6. It must be emphasized that our focus on the stereochemical results of the spin inversion mechanisms does not imply that other factors (e.g., energy barriers, reaction intermediates, etc.) are not important. However,

treating these effects along with spin-inversion would complicate the problem enormously. Hence, in order to reduce the complexity of the problem we have chosen an idealized system in which the determining variable is the efficiency of spin inversion. Other factors, such as barriers to reorganization, can be considered later as effects which may, or may not, modify the trend.

7. Presumably, the reason for the cleavage of the σ bond is because the cyclopropene molecule is notoriously in a state of "strain" due to the "bent" bond; see Finar, I. L., "Organic Chemistry", Longman House, Essex, 1973, pp539.
8. This view is also applicable to the x component situation, but we will not consider it further since the x component path is unable to lead to the experimentally-existing molecular conformations. The same situation also applies to case-(B).
9. (a) Both HOMO and LUMO can be expressed as a function of the rotation and bending angles, see ref.(4).

   (b) For case-(A), the valence MOs are given as follows:

$$HOMO = a(p_{1x}\cos\phi - p_{1y}\sin\phi - p_{3x}\cos\theta + p_{3z}\sin\theta) + b(p_{4z} + p_{5z}\cos\gamma + p_{5y}\sin\gamma)$$

$$LUMO = b(p_{1x}\cos\phi - p_{1y}\sin\phi + p_{3x}\cos\theta - p_{3z}\sin\theta) + a(p_{4z} - p_{5z}\cos\gamma - p_{5y}\sin\gamma)$$

   (c) For case-(B), the valence MOs are given as follows:

$$\begin{aligned} HOMO = {} & a(p_{1x}\cos\phi - p_{1y}\sin\phi - p_{3x}\cos\mu + p_{3y}\sin\mu) \\ & + b(p_{4z}\cos v - p_{4y}\sin v + p_{5z}\cos\gamma + p_{5y}\sin\gamma) \end{aligned}$$

$$\begin{aligned} LUMO = {} & b(p_{1x}\cos\phi - p_{1y}\sin\phi + p_{3x}\cos\mu - p_{3y}\sin\mu) \\ & + a(p_{4z}\cos v - p_{4y}\sin v - p_{5z}\cos\gamma - p_{5y}\sin\gamma) \end{aligned}$$

10. It has to be noted that inclusion of more configurations will certainly modify features but will not alter the key conclusions. For more details, see: ref.(4).
11. Z_N^* stands for the effective nuclear charge of nucleus N. The r_{iN} stands for the distance between electron i and nucleus N. The $\hat{l}(i)$ and $\hat{s}(i)$ are the orbital and spin angular momentum operators for electron i, respectively.
12. (a) This, in principle, is similar to a formal $[{}_{\sigma}2_{a} + {}_{\pi}2_{a}]$ symmetry-allowed cycloaddition. (b) See: Woodward, R. B. and Hoffmann, R., "The Conservation of Orbital Symmetry", Verlag Chemie, Weinheim, 1970, pp65.

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A New Family of Phytoecdysteroids Isolated from Aerial Part of *Ajuga reptans* var. *atropurpurea*.[†]

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Abstract: A new family of four phytoecdysteroids have been isolated from aerial part of *Ajuga reptans* var. *atropurpurea* harvested at the beginning of autumn. These compounds show a novel 22-oxo-12β-hydroxy functionalization of the C-28 and C-29 γ-lactonic ecdysteroids. The structure of those compounds was inferred from the corresponding IR, ^{1}H and ^{13}C-NMR and HPLC-MS(TSP) spectral data.

Many plants contain phytoecdysteroids, polyhydroxysteroids with a 5β-H-7-ene-6-one system and structurally related with the ecdysone, the biosynthetic precursor of the insect moulting hormone. These compounds exhibit physiological activities in insects and also in mammals. Regulation of moulting is the best established function of ecdysteroids in insects, but other hormonal functions involve regeneration, metamorphosis, reproduction and differentiation in all arthropod taxa[1]. Furthermore, these compounds also exhibit interesting activities in mammals, such as antiulcer and antirheumatic, insulin regulation and diuretic or tonic effects[2-4].

Over 100 different related structures have so far been isolated from plants[5]. Nevertheless, the role of these compounds in plants is still an open question, a defensive activity against insect or nematode attack has been suggested, but other functions can not be ruled out.

In plants of *Ajuga* genus a variety of such compounds have been isolated[6]. Among them, cyasterone (**4**) or 20-hydroxyecdysone (**2**) are usually the most abundant, but ajugalactone (**1**) is the most characteristic one. In previous work[7-10], we have isolated, from wild specimens of *Ajuga reptans* and its *in vivo* and *in vitro* cultures, the C-27, C-28 and C-29 phytoecdysteroids summarized in Figure 1. A great variation of contents and ratios among these compounds was observed depending from the different sources used. Recently, we have extended these studies to different varieties of *Ajuga reptans*. In the present communication we report on the results obtained in the study of the *Ajuga reptans* var. *atropurpurea*.

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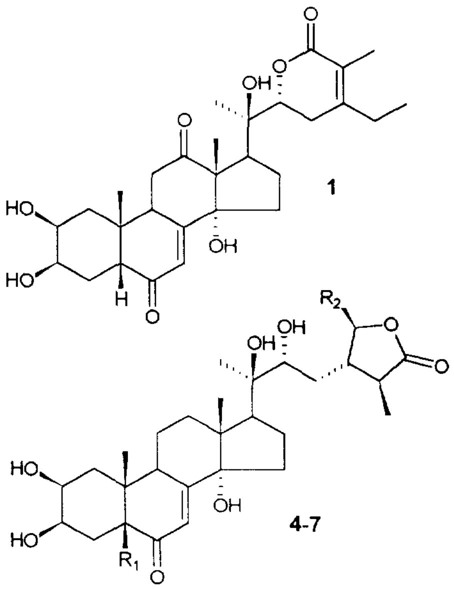

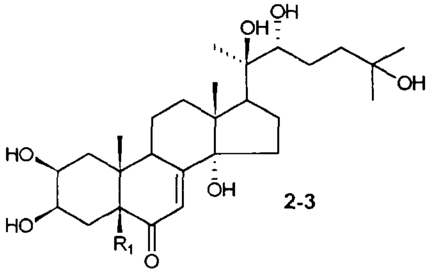

Compound	R1	R2
1: Ajugalactone	-	-
2: 20-Hydroxyecdysone	H	-
3: Polypodine B	OH	-
4: Cyasterone	H	CH3
5: Sengosterone	OH	CH3
6: 29-Norcyasterone	H	H
7: 29-Norsengosterone	OH	H

Figure 1.- Structure of previously isolated ecdysteroids from *Ajuga reptans* plants.

RESULTS AND DISCUSSION

Ajuga reptans var. *atropurpurea* is easily recognized by the red color of its leaves. Recently, the production of phytoecdysteroids by hairy roots cultures, obtained by transformation of roots with *Agrobacterium rhyzogenes*, of this variety has been studied[11]. The main ecdysteroids found in these transformed tissues were 20-hydroxyecdysone (**2**), 29-norcyasterone (**6**), cyasterone (**4**) and isocyasterone similar to those described in other *Ajuga* plants. In our study we have compared the effect of the harvesting time on the phytoecdysteroid contents of the aerial parts of the wild green variety of *Ajuga reptans*, so far used in our previous studies, with those of the *atropurpurea* variety, cultured under the same greenhouse fast growing conditions or collected in the field at the beginning of autumn when growth of aerial parts is very sparse.

A reversed phase HPLC analysis of the phytoecdysteroid contents, as described in the experimental part, is summarized in Table I. The different compounds were identified by comparison of retention times with those of authentic samples. As shown, the *A. reptans* var. *atropurpurea* exhibits a major content of 20-hydroxyecdysone and minor amounts of norsengosterone and norcyasterone the major components of the green variety. Another important feature was the occurrence in the *atropurpurea* variety, collected in autumn, of four components undetected in the other plant materials, with UV absorption compatible with an ecdysteroid