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Malnar, Ivica; Kronja, Olga

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A Case of Concerted Formation of Five and Six Member Rings; Solvolytic Behavior of 1-Aryl-1-chloro-4,8,13,17,21-pentamethyl-4,8,12,16,20-docosapentaenes

Ivica Malnar and Olga Kronja*

Faculty of Pharmacy and Biochemistry, University of Zagreb, A. Kovačića 1,
P. O. Box 156, 10000 Zagreb, Croatia

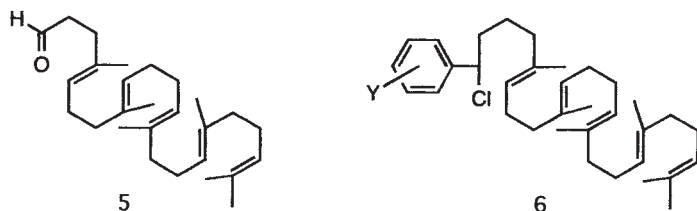
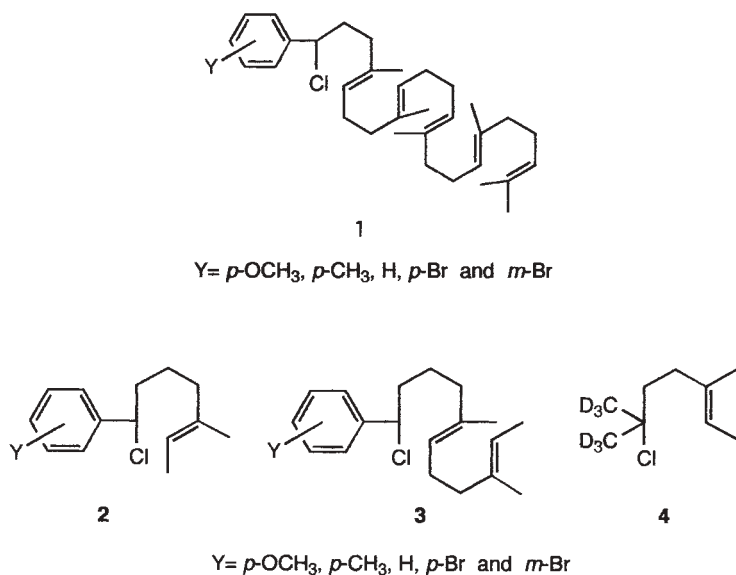
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Chlorides **1** (1-aryl-1-chloro-4,8,13,17,21-pentamethyl-4,8,12,16,20-docosapentaenes) with various phenyl substituents were prepared, and solvolysis rates were measured in 80% (*v/v*) aqueous ethanol, and in 97% (*w/w*) aqueous 2,2,2-trifluoroethanol. Hammett ρ^+ values obtained are -2.18 , -2.13 , resp., suggesting a concerted bicyclization in the rate determining step.

The solvolytic behavior of benzyl chloride **1** (1-chloro-1-phenyl-4,8,13,17,21-pentamethyl-4,8,12,16,20-docosapentaene) revealed inconsistency in some aspects, thus the reaction mechanism is ambiguous.¹ The ethanolysis rate (k_u) of **1** is practically the same as the rate of its saturated analog ($k_u / k_s = 2.5$), indicating that the reaction may proceed by way of an unassisted process. On the other hand, activation parameters obtained are consistent with the rate determining participation of at least one double bond, in which the high degree of order required in the transition state (large negative ΔS^\ddagger) is overcompensated by a rather small ΔH^\ddagger . The magnitude of $\Delta S^\ddagger = -122 \pm 13 \text{ J K}^{-1} \text{ mol}^{-1}$ obtained with **1** in aqueous ethanol ($\phi = 80\%$, 80E) is even larger than the entropy of activation obtained for the concerted monocyclization reaction with the referent benzylic chloride **2** ($\Delta S^\ddagger = -99.0 \pm 21 \text{ J K}^{-1} \text{ mol}^{-1}$),² but is lower than the one obtained with referent chloride **3** ($\Delta S^\ddagger = -194 \pm 12 \text{ J K}^{-1} \text{ mol}^{-1}$).³ It should be emphasized that, according to all methods used

* Author to whom correspondence should be addressed.

(k_H/k_S rate effects, activation parameters³ including activation volumes,⁴ β -deuterium kinetic isotope effects⁵), compounds **3** can be used as a reliable referent for concerted bicyclization. Also, chlorides **2**, except the *p*-methoxy derivative, represent confirmed referents for concerted monocyclization.



In our previous communication,⁶ we reported that tertiary chloride **4** with the double bond at C-4 from the reaction center, like chloride **1**, has a considerably reduced β -deuterium kinetic isotope effect in the solvolysis (both, in 80% vol. aqueous ethanol and 97% *w*, 2,2,2-trifluoroethanol; $k_H/k_D=1.30$) compared to its saturated analog ($k_H/k_D=1.80$). That result was attributed to the assistance of the double bond in the rate-determining formation of the five member ring. Therefore, the question arises whether the unassisted reaction takes part in solvolysis of **1**, whether the concerted formation of the

five member ring occurs, or if even a concerted bicyclization takes place, *i.e.* whether the extended π -participation mechanism is operative.

We demonstrated that the value of the reaction constant (Hammett ρ^+)⁷ can be used as a powerful tool in testing the concertedness of solvolytic reactions.⁸ Roughly, as presented in the Table, the values of ρ^+ are: $\rho^+ \approx -6$ when an unassisted process occur (obtained with the saturated analog **2S** of the referent chloride **2**), $\rho^+ \approx -4$ when the concerted monocyclization takes part, as it is the case of the referent chloride **2**, and $\rho^+ \approx -2$ when the concerted bicyclization exists as with substrate **3**. It seems that each additional double bond that takes part in the rate determining step lowers the negative value of the reaction constant by approximately 2 units.

In order to obtain the ρ^+ values for the benzylic system **1**, a series of benzylic chlorides **1** were prepared ($Y = p\text{-OCH}_3, p\text{-CH}_3, \text{H}, p\text{-Br}$ and $m\text{-Br}$). The parent alcohols of **1** were obtained by addition of the corresponding bromobenzene to aldehyde **5** (prepared according to the earlier described procedures^{1,9}) in the presence of lithium. The alcohols were converted to chlorides, which were subjected to solvolysis in 80% (*v/v*) aqueous ethanol (80E) and in 97% (*w/w*) aqueous 2,2,2-trifluoroethanol (97T). Reactions were monitored by titration of the liberated acid with an automatic pH-stat at three different temperatures. All reaction rates were extrapolated to 25 °C, which values were used to calculate the Hammett ρ^+ values using the sim-

TABLE
Linear Free Energy Correlation of Some Benzylic Chlorides at 25 °C

Compound	Solvent ^a	n^b	ρ^{+c}	r^d
2S	97T	5	-6.28 ± 0.25	0.997
2	97T	4	-3.93 ± 0.10	0.998
		2	-6.21	
3	80E	5	-1.45 ± 0.03	0.999
	97T	5	-1.76 ± 0.04	0.999
4	80E	5	-1.81 ± 0.05	0.999
	97T	5	-1.56 ± 0.04	0.999
1	80E	5	-2.18 ± 0.07	0.998
	97T	5	-2.13 ± 0.07	0.998

^a80E is aqueous ethanol ($\phi = 80\%$); 97T is aqueous 2,2,2-trifluoroethanol ($w = 97\%$); ^bNumber of data points with ($n = 5$) or without ($n = 4$) the rate of the *p*-anisyl derivative. $n = 2$ ρ^+ was obtained from *p*-anisyl and *p*-toluyl derivatives; ^cUncertainties are standard errors of estimate.

^dCoefficient of correlation.

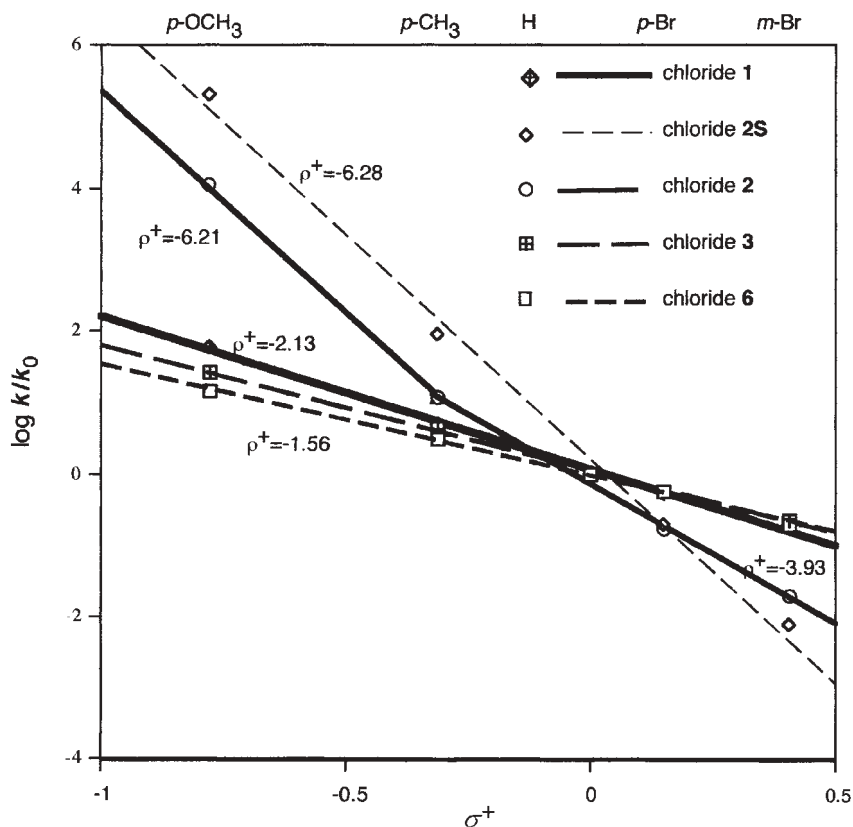


Figure. Hammett $\sigma^+\rho^+$ plots for some benzylic chlorides in 97% (*w/w*) aqueous 2,2,2-trifluoroethanol.

ple regression analysis. The results are presented in the Table and in the Figure, together with some other important referent data.

The values of ρ^+ for chlorides 1 obtained in both solvents, 80E and 97T (different nucleophilicity), are essentially the same, excluding the possibility that this significant result is due to the rate determining displacement by the solvent.¹⁰

The reaction constant is generally considered to be the measure of the charge »seen« by the aromatic ring at the reaction center, which is closely related to charge delocalization. If π -participation of the neighboring double bond(s) occurs, the charge is delocalized from the reaction center, and thus the lower negative ρ^+ value is obtained. The Hammett ρ^+ values obtained in both solvents ($\rho^+ = -2.18$ in 80E and $\rho^+ = -2.13$ in 97T) unambiguously demonstrate that π -participation occurs in the rate determining step with

chlorides **1**. Even though the negative values of ρ^+ obtained are slightly higher than those of referent **3**, they are drastically lower than the ρ^+ obtained for concerted monocyclization with chloride **2**, indicating that the transition state has less positive charges on the benzylic carbon than a simple benzylic carbocation. The latter conclusion demonstrates that this cannot be an unassisted solvolysis, and may suggest that the concerted bicyclization may take place with substrate **1**.

As it was shown earlier, the concerted monocyclization was proved for all derivatives of **2** but the one with the *p*-methoxy group. In the case of *p*-anisyl derivative, the participation of the neighboring double bond is eliminated by the strongly electron donating *p*-methoxy substituent. However, both, the coefficient of correlation (r) and the statistical test Ψ^{11} indicate that the *p*-methoxy variant of **1** should be included into correlation (Table). The facts that drastically different reaction constants were obtained with **1** than with the model for the concerted monocyclization **2** (-2.13 vs. -3.93 in 97T), and that the *p*-methoxy derivative solvolytic behavior is different than that of **2**, are in accord with a previously drawn conclusion about the possible concerted bicyclization.

Since the structure of chloride **1** is closely related to the squalene derivative **6** (the structures differ in one methylene group), it is advantageous to compare the ρ^+ value obtained with the corresponding reaction constant of chloride **5**. For the latter, extended π -participation mechanism was established not only on the basis of the Hammett ρ^+ value,⁹ but also on the basis of lack of the β -deuterium kinetic isotope effect obtained with the tertiary counterpart of **5**.¹² The behavior of the two species is almost the same in solvolysis and is comparable with the referent chloride **3**. Both have a similar reaction constant in magnitude, and also in both cases the electron donation of the *p*-methoxy groups does not cancel out the assistance of double bonds.

Probably the most obvious support for the possible extended participation mechanism of **1** comes from the careful study of the superimposed Hammett plots presented in the Figure. It is evident that, according to the slopes of the plots, three different mechanisms can be traced down. Breakdown of the linear relation occurs with the plot that corresponds to chlorides **2** when the mechanism is changed from concerted monocyclization to unassisted reaction with the *p*-methoxy derivative. The plot obtained after the breakdown caused by the *p*-methoxy variant is almost parallel with the plot obtained with **2S**, which also reacts with the lack of the neighboring olefinic bond participation. It can be seen that the slope of the Hammett plot with all derivatives of **2** ($Y=CH_3$, H, *m*-Br, and *p*-Br, resp.) but the methoxy variant is drastically less steep, indicating the concerted monocyclization mechanism. Further profound decrease of the slope occurs for all

three other compounds: the investigated chlorides **1**, the referent chlorides **3**, and the squalene derivatives **6**, respectively, suggesting that they all proceed by way of the extended π -participation mechanism.

Slightly larger $-\rho^+$ of chlorides **1** than of the referent chlorides **3** can be rationalized in terms of the distribution of the charge if the »earlier« transition state of **1** is considered. In that case, the concentration of the positive charge on the reaction center is somewhat larger than in the case of **3**, in which the transition state is more akin to tertiary cyclohexyl cation. Once again it has been proven that only a large rate effect can be taken as a proof of the neighboring group participation¹³ Moderate, as obtained with **1** ($k_u/k_s=2.5$), or even inverse rate effect can conceal some considerable participation that can be proven by other methods.

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SAŽETAK

Primjer usklađenog zatvaranja petero- i šesteročlanog prstena; solvolitsko ponašanje 1-aril-1-klor-4,8,13,17,21-pentametil-4,8,12,16,20-dokosapentaena*Ivica Malnar i Olga Kronja*

Pripravljene su kloridi **1** (1-aril-1-klor-4,8,13,17,21-pentametil-4,8,12,16,20-dokosapentaeni) s različitim supstituentima na fenilnom prstenu. Izmjerene su konstante brzine solvolize u 80% (vol./vol.) vodenom etanolu te u 97% (w) vodenom 2,2,2-trifluoretanolu. Dobivene Hammettove vrijednosti ρ^+ od $-2,18$, odnosno $-2,13$ upućuju na usklađeni proces ciklizacije dviju dvostrukih veza u stupnju koji određuje brzinu reakcije.