# SYNTHESIS, KINETICS AND MECHANISM OF CYCLIZATION OF 1-(2-ARYLOXYCARBONYLPHENYL)-3-PHENYLTRIAZENES

Oldřich PYTELA and Zdeněk BAHNÍK

*Department of Organic Chemistry,*
*Institute of Chemical Technology, 532 10 Pardubice*

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Twelve substituted 1-(2-aryloxycarbonylphenyl)-3-phenyltriazenes have been synthetized and kinetics of their reactions have been measured in 52·1% (by mass) aqueous methanol at pH 3 to 11. Plots of $k_{obs}$ vs pH show three regions: noncatalyzed cyclization (pH 4 to 7), acid-catalyzed splitting of the triazene chain, and base-catalyzed cyclization. The non-catalyzed cyclization exhibits a kinetic isotope effect, the reaction constant $\varrho = 2{\cdot}69$ ($\sigma_p^-$), and $\beta_{lg} = 1{\cdot}02$, which indicates a mechanism of E1cB type with intramolecular proton transfer and a transient formation of a ketene intermediate. The base-catalyzed cyclization, on the other hand, exhibits the reaction constant $\varrho = 1{\cdot}05$ ($\sigma_p^-$), $\beta_{lg} = 0{\cdot}4$, and distinct steric effects, which indicates a cyclization by $B_{Ac}2$ mechanism with rate-limiting formation of the tetrahedral intermediate.

This present paper represents a continuation of an older one[1] dealing with synthesis and cyclization kinetics and mechanism of 1-(2-ethoxycarbonylphenyl)-3-aryltriazenes. The results given in ref.[1] showed that the cyclization mentioned was a base-catalyzed $B_{Ac}2$ process with rate-limiting splitting of tetrahedral intermediate. The alternative E1cB mechanism with a ketene intermediate and imino group in quinoid arrangement seemed less likely. Further arguments for decision about the mechanistic type of the base-catalyzed cyclization can be obtained from measurements of reactivity of the derivatives with substituents in the leaving group, i.e. 1-(2-aryloxycarbonylphenyl)-3-phenyltriazenes. These compounds and the ethyl esters mentioned have not been described yet, a survey of the literature dealing with cognate compounds was presented in ref.[1]. The title compounds can undergo, beside the base-catalyzed cyclization, a typical reaction of triazenes, viz. the acid-catalyzed splitting of the triazene chain. These reactions are summarized in refs[2,3].

The aim of this present communication is finding the cyclization mechanism of these compounds on the basis of kinetic studies of reactions of 1-(2-aryloxycarbonylphenyl)-3-phenyltriazenes at various pH values.

## EXPERIMENTAL

### Synthesis of Aryl Anthranilates

*Method A.* A solution or dispersion of 0·12 mol substituted phenol in 150 ml ice water was treated with 16 g (0·12 mol) isatoic anhydride[4], whereupon a solution of 5 g (0·12 mol) sodium hydroxide in 50 ml water was added with stirring during 30 min. The mixture was stirred for another 30 min, the separated solid was collected by suction, thoroughly washed with water, and dried in air. The raw product was purified by recrystallization.

*Method B.* A solution of 0·12 mol substituted phenol in 100 ml dioxane was treated with 16 g (0·12 mol) isatoic anhydride[4] and about 0·1 to 0·2 g solid sodium hydroxide. The mixture was refluxed for 30 min and poured into 300 ml ice water. The separated solid was collected by suction, thoroughly washed with water, dried in air, and purified by recrystallization. The liquid products were extracted with ether, the extract was dried, the solvent was distilled off, and the residue was purified by distillation under reduced pressure.

The methods adopted for the syntheses, the solvents used for the recrystallizations, the yields and melting points are presented in Table I. The identity of the compounds not yet described was verified by IR spectroscopy.

### Synthesis of 1-(2-Aryloxycarbonylphenyl)-3-phenyltriazenes

A mixture of 0·022 mol aryl anthranilate, 7·7 ml conc. hydrochloric acid and 5·5 ml water was cooled to 5°C and a solution of 1·55 g (0·0225 mol) sodium nitrite in 7 ml water was added dropwise with stirring at the temperature not exceeding 5°C. The diazonium salt solution prepared was added portionwise to a mixture of 2·1 g (0·0226 mol) aniline and 15 g ammonium acetate in 30 ml water with intensive stirring. The product was collected by suction as quickly as possible, carefully washed with a solution of sodium hydrogen citrate, and dried in air. The crystallization purification could be applied only to the derivatives with electron-donor substituents, whereas the other compounds on crystallization distinctly changed in their appearance, melting point, and in that the characteristic triazene band in electronic spectra (360–365 nm) disappeared. The products thus obtained were not identified, but it can be presumed that they are cyclization products. The same reaction is observed also during TLC on alumina (see also ref.[10]) and on the reversed phase in the system methanol–water during high-pressure liquid chromatography. The substances prepared underwent decomposition also in solid phase within several days after the syntheses, and therefore they were prepared always immediately before the kinetic measurements. Table II gives the yields of syntheses, solvents used for recrystallizations, and melting points.

*Kinetic measurements.* The measurements were carried out in buffers of the McIlvaine type[11] in 52·1% (by mass) aqueous methanol in the pH range from 3·00 to 11·34. The pH values were measured with a glass electrode and a PHM apparatus (Radiometer, Copenhagen). A cell placed in the thermostated cell compartment of a VSU 2P spectrophotometer (Zeiss, Jena) was charged with 2 ml buffer at 25·0 ± 0·1°C, whereupon 1 to 10 μl freshly prepared solution of the compound in dioxane was injected thereto by means of an Hamilton 701 N syringe (the concentration of this solution was adjusted so that the initial absorbance value at the wavelength $\lambda$ = 364 nm (the triazene band) might roughly be equal to one). The decrease of the compound was recorded by means of an external TZ 4100 recorder (Laboratorní přístroje, Prague) for a period of at least four halflives. The rate constant was evaluated in usual way[12] for a pseudo-first-order reaction.

*Calculation of catalytic constants.* The catalytic constants were obtained by optimizing[13] the parameters in the model derived on the basis of the reaction mechanism for description of experimental pH profiles.

TABLE I

The synthetic methods, solvents used for recrystallizations, yields, and melting points of the aryl-anthranilates 2-$NH_2$-$C_6H_4$-$COOC_6H_4X$

| X | Method | Solvent | Yield % | Melting point °C |
|---|---|---|---|---|
| 4-$N(CH_3)_2$ | *B* | ethanol–acetone 1 : 1 | 6 | 159—163 |
| 4-$OCH_3$ | *B* | heptane | 90 | 100—102 |
| 4-$C(CH_3)_3$ | *B* | hexane | 84 | 139—140 |
| 4-$CH_3$ | *A* | hexane | 83 | 74—75 |
| 3-$CH_3$ | *B* | hexane | 68 | 69—71[a] |
| H | *A* | cyclohexane | 73 | 70·5—71[b] |
| 3-$OC(CH_3)_3$ | *B* | ethanol | 77 | 137—140 |
| 3-$OCH_3$ | *B* | — | 69 | oil |
| 3-$NHCOCH_3$ | *B* | ethanol | 64 | 184—185 |
| 4-Cl | *B* | hexane | 93 | 80—80·5[c] |
| 4-Br | *B* | hexane | 91 | 79·5—80·5[d] |
| 3-Cl | *A* | hexane | 75 | 68—69[e] |

[a] Ref.[5] m.p. 71—72°C; [b] ref.[6] m.p. 70°C, ref.[7] m.p. 71°C; [c] ref.[5] m.p. 80·5—81·5°C, ref.[8] m.p. 79—80°C; [d] ref.[5] m.p. 80—81·5°C; [e] ref.[9] m.p. 63—65°C.

TABLE II

The solvents used for recrystallization, yields, and melting points of the 1-(2-aryloxycarbonyl-phenyl)-3-phenyltriazenes, 2-(X-$C_6H_4OCO$)$C_6H_4$—N=N—NH—$C_6H_5$

| Compound | X | Yield % | M.p. °C | Compound | X | Yield % | M.p. °C |
|---|---|---|---|---|---|---|---|
| *Ia* | 4-$N(CH_3)_2$ | 24 | 130—134[a] | *Ig* | 3-$OC(CH_3)_3$ | 86 | 120—128 |
| *Ib* | 4-$OCH_3$ | 87 | 134—136[a] | *Ih* | 3-$OCH_3$ | 92 | 105—108 |
| *Ic* | 4-$C(CH_3)_3$ | 81 | 154—157[a] | *Ii* | 3-$NHCOCH_3$ | 81 | 115—123 |
| *Id* | 4-$CH_3$ | 79 | 104—110[a] | *Ij* | 4-Cl | 73 | 118—120 |
| *Ie* | 3-$CH_3$ | 62 | 148—151[b] | *Ik* | 4-Br | 68 | 128—132 |
| *If* | H | 83 | 113—114[a] | *Il* | 3-Cl | 71 | 78—86 |

[a] Hexane; [b] heptane.

## RESULTS AND DISCUSSION

The dependence of the observed rate constant $k_{obs}$ on pH has – for the individual derivatives – a characteristic shape with a plateau roughly in the pH region from 4 to 7 and with two branches (one in more acidic and the other in more basic region) indicating the respective catalyses. The derivative *Ia* (X = 4-$N(CH_3)_2$) represents an exception: its pH profile shows no plateau and the acidic branch is shifted by about 3 units to higher pH values. With respect to the structure of the molecule the acid-induced decomposition cannot be affected by substituents in the leaving phenol moiety. The reason must be looked for in the basicity of dimethylamino group ($pK_a$ of N,N-dimethylaniline is 4·16 in 50% ethanol[14]) which is protonated just in the experimental region. The increase in the observed rate constant $k_{obs}$ with increasing acidity of medium is due to the change in character of the substituent (the electron-donor group $N(CH_3)_2$ is converted into the electron-acceptor group $(NH(CH_3)_2)^{(+)}$) in a reaction going by the same mechanism as that of the other substituents in the region of the plateau.

On the basis of the earlier studies of triazene derivatives (see Introduction) the pH profiles found (except that of *Ia*) can be described by the equation

$$k_{obs} = k_H[H^+] + k_0 + k_{OH}K_T/(K_T + [H^+]), \qquad (1)$$

where $k_H$ stands for the catalytic rate constant of the acid-catalyzed decomposition, $k_0$ stands for the rate constant of spontaneous cyclization, $k_{OH}$ means the catalytic rate constant of the base-catalyzed cyclization, and $K_T$ is the dissociation constant of the proton in the triazene. As the processes taking place in the triazene chain will not be affected by the substituents in the leaving phenol moiety, the parameters in Eq. (*1*) can be optimized simultaneously for all the substituted derivatives except *Ia*, the $k_H$ and $K_T$ values being common to all of them. Table III presents the rate constants obtained in this way. The optimized $k_H$ constant has the value $k_H = (9{\cdot}22 \pm 0{\cdot}68)\ l\ mol^{-1}\ s^{-1}$. This result agrees well with the values found for other triazene derivatives ($k_H$, $l\ mol^{-1}\ s^{-1}$: 1,3-diphenyltriazene[15] in 20% ethanol 4·55, 3-methyl-1,3-diphenyltriazene[16] in 40% ethanol 2·44, 1,3-bis(4-methylphenyl)-triazene[2] in ethanol 47·3). The $K_T$ value obtained by the optimization is equal to $(4{\cdot}02 \pm 0{\cdot}20) \cdot 10^{-10}$, hence $pK_T = 9{\cdot}40$. Also this value agrees reasonably with the literature data for dissociation of 1,3-diphenyltriazene[15] ($pK_T = 13{\cdot}26$ in 20% ethanol, $\varrho = 1{\cdot}52$ with application of the $\sigma_p^-$ substituent constants).

Plotting of $\log k_0$ (Table III) against the Hammett $\sigma$ constants[17] gives a linear dependence with a remote value for the derivative *Ig* (the residual standard deviation $s = 0{\cdot}207$). After excluding the deviated value we obtain the Hammett equation in the following form:

$$\log k_0 = -(1{\cdot}94 + 0{\cdot}05) + (2{\cdot}38 \pm 0{\cdot}24)\,\sigma\,, \qquad (2)$$
$$n = 10\,,\quad s = 0{\cdot}148\,,\quad r = 0{\cdot}961\,.$$

A distinctly closer correlation is obtained with the dual constants $\sigma_p^-$ (Eq. (3)):

$$\log k_0 = -(2{\cdot}01 \pm 0{\cdot}02) + (2{\cdot}69 \pm 0{\cdot}11)\,\sigma(\sigma_p^-) \qquad (3)$$
$$n = 10\,,\quad s = 0{\cdot}059\,,\quad r = 0{\cdot}993\,.$$

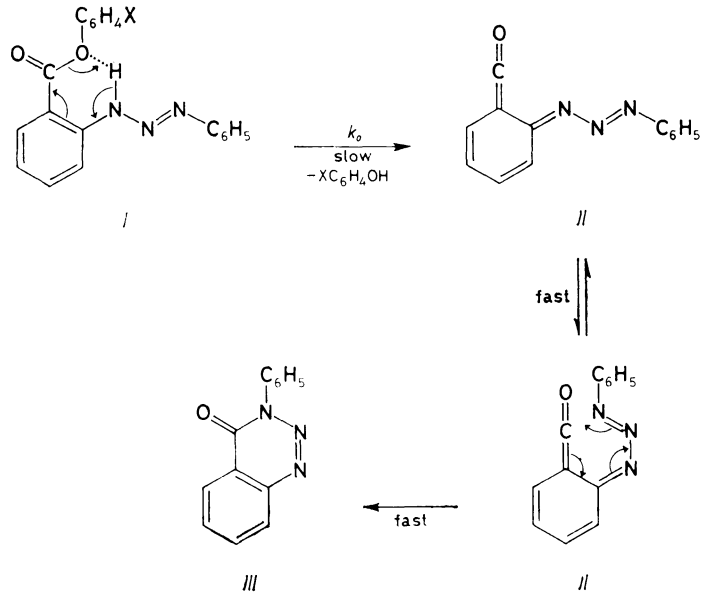
The residual standard deviation in this case is within the limits of precision of the Hammett equation (ref.[17], p. 88). The value found for the reaction constant $\varrho$ is unexpectedly high as compared with that found for the noncatalyzed solvolysis of phenyl acetates[18,19] (60% acetone, 30°C, $\varrho = 1{\cdot}15$; water, 30°C, $\varrho = 1{\cdot}16$) or for the base-catalyzed solvolysis of the same compounds[19,20] (28% ethanol, 30°C, $\varrho = 1{\cdot}0$; water, 30°C, $\varrho = 1{\cdot}1$) or for aryl benzoates[21] (water–acetonitrile 2 : 1, 25°C, $\varrho = 1{\cdot}28$). On the other hand, the reaction constant $\varrho$ from Eq. (3) is very close to those found for the base-catalyzed solvolyses going by the E1cB mechanism,e.g. with N-methylcyrbamates[22,23] (20% dioxane, 25°C, $\varrho = 3{\cdot}17$; water, 25°C, $\varrho = 2{\cdot}80$). Also the value $\beta_{lg} = 1{\cdot}02$ ($\varrho$ for dissociation of phenols in 50% methanol is equal to 2·65, ref.[24]) is high and indicates a considerable extent of splitting of the bond to the leaving group in the transition state[25,26]. The rate constants obtained by the

TABLE III

The rate constants $k_0$ and $k_{OH}$ and their standard deviations $s_0$ and $s_{OH}$ obtained by optimization according to Eq. (*1*) (modification (*4*) was used for the derivative *Ia*), numbers (*n*) of experimental points in the pH profiles

| No. | Compound | $k_0 \cdot 10^3$ $s^{-1}$ | $s_0 \cdot 10^3$ $s^{-1}$ | $k_{OH}$ $l\,mol^{-1}\,s^{-1}$ | $s_{OH}$ $l\,mol^{-1}\,s^{-1}$ | *n* |
|---|---|---|---|---|---|---|
| 1 | *Ia* | — | — | 10·9 | 0·6 | 38 |
| 2 | *Ib* | 4·72 | 0·17 | 25·1 | 1·5 | 32 |
| 3 | *Ic* | 4·75 | 0·16 | 11·0 | 0·5 | 41 |
| 4 | *Id* | 4·26 | 0·15 | 23·2 | 1·3 | 31 |
| 5 | *Ie* | 5·26 | 0·18 | 12·4 | 0·6 | 39 |
| 6 | *If* | 8·95 | 0·31 | 31·3 | 1·9 | 31 |
| 7 | *Ig* | 6·58 | 0·22 | 13·8 | 0·7 | 38 |
| 8 | *Ih* | 19·3 | 0·6 | 31·4 | 2·0 | 33 |
| 9 | *Ii* | 20·4 | 0·6 | 21·6 | 1·1 | 40 |
| 10 | *Ij* | 48·0 | 1·5 | 67·0 | 4·2 | 34 |
| 11 | *Ik* | 52·1 | 1·5 | 54·8 | 4·7 | 34 |
| 12 | *Il* | 96·2 | 2·9 | 42·0 | 3·8 | 31 |

measurements in methanol ($6{\cdot}71 \cdot 10^{-4}\ s^{-1}$) and in O-[$^2$H]-methanol ($2{\cdot}12 \cdot 10^{-4} \cdot s^{-1}$) for the derivative *Ic* unequivocally indicate the existence of kinetic isotope effect. This effect cannot be the isotope effect of solvent (which rather would be reversed, since deuteriomethanol is a stronger acid) because the reaction proceeds at a measurable rate also in anhydrous aprotic solvents (*k*, *Ic*: dimethyl sulfoxide, $1{\cdot}08 \cdot 10^{-3}\ s^{-1}$; dioxane $8{\cdot}71 \cdot 10^{-5}\ s^{-1}$). From the results given it follows that the intermolecular cyclization takes place in a single step with simultaneous hydrogen transfer from the triazene chain to the leaving phenoxide anion. This reaction is retarded by steric effects, which can be seen from the $k_0$ value of the derivative *Ig* synthetized for this purpose. The whole mechanism of spontaneous cyclization of the compounds studied can be described by Scheme 1, the first step being rate-limiting and the splitting of bond to the leaving phenoxide moiety being distinctly




SCHEME 1

more advanced than the proton transfer. If we return back to the dimethylamino derivative *Ia*, we can make estimates from the Hammett equation (*3*) for the non-protonated substituent ($k_0^N \approx 1{\cdot}3 \cdot 10^{-3}\ s^{-1}$) and for its protonated form ($k_0^{NH} \approx$ $\approx 3{\cdot}7\ s^{-1}$). The $k_0^N$ value is ca 5× smaller than the lowest experimental value in the pH profile. Obviously the spontaneous cyclization does not make itself felt with this derivative. On the other hand, the $k_0^{NH}$ value exceeds the region of measurement accessible by usual techniques. For these reasons the optimization of the param-

eters in Eq. (*1*) with $k_0$ modified as follows:

$$k_0(4\text{-N(CH}_3)_2) = (k_0^N K_N + k_0^{NH}[H^+])/(K_N + [H^+]), \quad (4)$$

where $K_N$ means the dissociation constant of the substrate protonated at the dimethylamino group, gave no reasonable results for $k_0^N$ ($3{\cdot}5 \cdot 10^{-3}$ s$^{-1}$) and $k_0^{NH}$ ($2{\cdot}1 \cdot 10^{-1}$ s$^{-1}$). On the other hand, it was possible to find a relatively reasonable value $pK_N = 3{\cdot}97$ ($pK_a = 4{\cdot}16$ for N,N-dimethylaniline in 50% ethanol[14]).

The dependence of the catalytic rate constants $k_{OH}$ on the Hammett substituent constants was not found simultaneously for all the derivatives (Fig. 1). As it can be seen from Fig. 1 the *meta*-substituted derivatives with roughly the same $\sigma$ values exhibit distinctly lower $k_{OH}$ values depending on the magnitude of substituent. This can be seen very well if one compares the derivatives 3-$OCH_3$ (point **8**), 3-$NHCOCH_3$ (**9**), and 3-$OC(CH_3)_3$ (**7**); the last derivative, which was synthesized specially for this purpose, exhibits the greatest deviation in general. Similar behaviour is observed also with the derivatives carrying 4-$N(CH_3)_2$ and 4-$C(CH_3)_3$ substituents. These results show that steric effect markedly affects the rate-limiting step. As this effect is not much significant in the non-catalyzed cyclization, the catalyzed cyclization obviously proceeds by another mechanism. If the reaction constant is estimated with application of 5 substituted derivatives with the least steric hindrance, the result is $\varrho = 1{\cdot}05$ ($s = 0{\cdot}046$, $r = 0{\cdot}981$, for $\sigma_p^-$). This value is in accordance with the above-mentioned reaction constants of solvolyses of aryl esters proceeding by the $B_{Ac}2$ mechanism. For the compounds studied this mechanism can be described by Scheme 2. With regard to the low substituent sensitivity (as far as the substituents in the leaving group are concerned; cf. the value of $\varrho$ constant and $\beta_{lg} = 0{\cdot}4$) and also with regard to the marked manifestations of steric effects it can be stated that

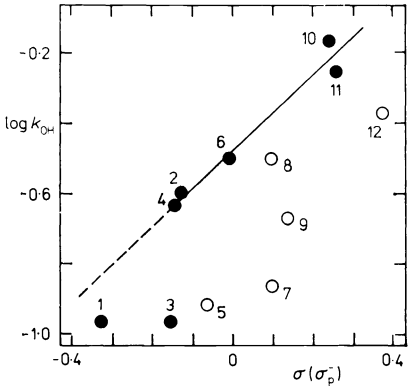
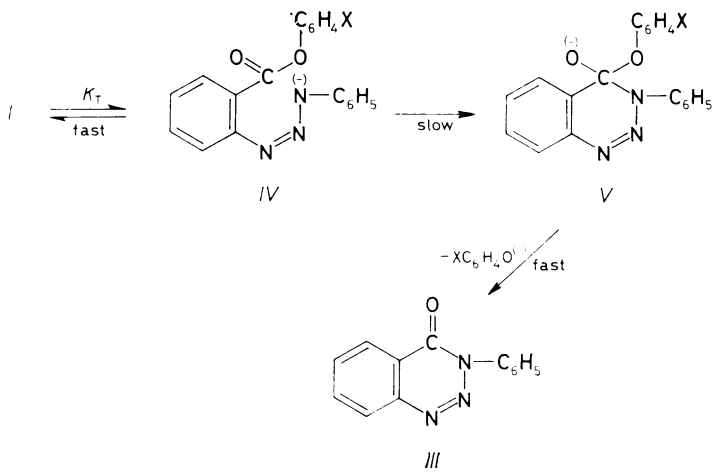



FIG. 1

The dependence of log $k_{OH}$ on the Hammett substituent constants (for numbers see Table III), ● the *para*-substituted and non-substituted derivatives, ○ the *meta*-substituted derivatives



SCHEME 2

the base-catalyzed cyclization of 1-(2-aryloxycarbonylphenyl)-3-phenyltriazenes proceeds by the mechanism of $B_{Ac}2$ type with formation of the tetrahedral intermediate *V* in the rate-limiting step. This conclusion agrees with the results obtained for the base-catalyzed cyclizations of 1-(2-ethoxycarbonylphenyl)-3-aryltriazenes[1].

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