

## The Influence of Substituents on The Rate of the Intramolecular Diels-Alder Reaction of Allylaryl(2-furfuryl)amines<sup>a, b</sup>

Ž. Klepo and K. Jakopčić

Laboratory of Organic Chemistry, Faculty of Technology, and Institute of Organic Chemistry and Biochemistry, University of Zagreb, 41000 Zagreb, Croatia, Yugoslavia

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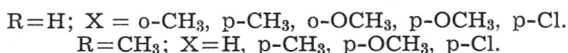
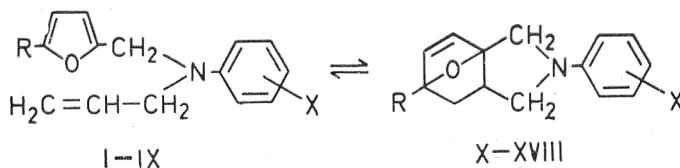
Some new examples of intramolecular Diels-Alder reaction of allylaryl(2-furfuryl)amines are given, and the influence of substituents on the rate of the reaction is studied. Unlike *para* substituents, *ortho* substitution of the *N*-aryl group or substitution in position 5 of the furan nucleus decrease the rate of the [4 + 2] cycloaddition.

Since the first example of the intramolecular Diels-Alder reaction in the furan series has been reported<sup>1</sup>, a steady interest for this [4 + 2] cycloaddition can be observed in the chemical literature. An interesting example of such a reaction was observed in the case of suitably substituted tertiary amines<sup>2,3</sup>.

The spontaneous reaction of the furan nucleus and the double bond of the allyl group playing the role of diene and dienophile respectively, started as soon as the particular allylaryl(2-furfuryl)amine was prepared. Bilović and Hahn<sup>3</sup> claimed marked difference in the rate of the reaction depending on the aryl substituent.

Having in mind that this qualitative conclusion was based on only three examples (aryl being phenyl, *p*-tolyl and *p*-methoxyphenyl) and that the solidification of oily allylaryl(2-furfuryl)amine was the sole measure of the cycloaddition rate, we reexamined this difference with more examples, monitoring the course of reaction by i. r. spectroscopic measurements.

Here we report the results of our experiments on the intramolecular [4 + 2] cycloaddition of allylaryl(2-furfuryl)amines substituted in the *ortho* or *para* position of the aryl group and/or position 5 of the furan nucleus:



<sup>a</sup> Studies in the Furan Series. XV; Part XIV: G. Karminski-Zamola and K. Jakopčić, *Croat. Chem. Acta* **46** (1974) 71.

<sup>b</sup> Taken in part from the Ph. D. Thesis of Ž. Klepo, University of Zagreb, 1972.

The characteristic i. r. spectra of the [4 + 2] cycloaddition products (Table III, X—XVIII) with a very well separated band in the 873—862  $\text{cm}^{-1}$  area, a band which is absent in the starting allylaryl(2-furfuryl)amines, made it possible to follow the course of the cycloaddition by i. r. spectroscopic measurements of the concentration of the epoxyisoindoline. The cycloadditions were carried out at 20 and 50  $^{\circ}\text{C}$  (Fig. 1 and 2). The first order rate constants are tabulated in Table I.

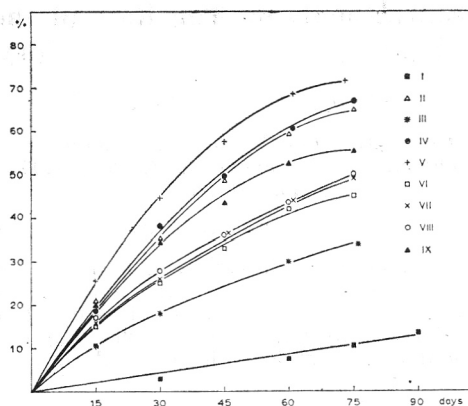


Fig. 1. Progress of cycloaddition of allylaryl(2-furfuryl)-amines (I—IX) at 20  $^{\circ}\text{C}$ .

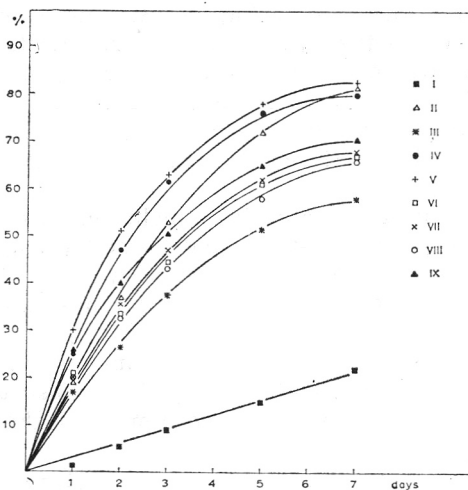


Fig. 2. Progress of cycloaddition of allylaryl(2-furfuryl)-amines (I—IX) at 50  $^{\circ}\text{C}$ .

In contrast to previous qualitative observations<sup>3</sup>, the influence of *para* substituent was not significant, and the differences in the rates of cycloaddition ( $\text{X}=\text{H}$ ,  $p\text{-CH}_3$ ,  $p\text{-OCH}_3$  and  $p\text{-Cl}$ ) were too small to support any conclusion about their electronic effects. Such results were not surprising since the  $2\pi$  system is well separated from the aryl nucleus. On the other hand, the presence of a methyl or methoxy group in the *ortho* position of the aryl group slowed markedly the reaction at 20 and at 50  $^{\circ}\text{C}$ . Similarly,

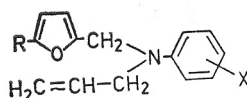
TABLE I.

Rate constants for the intramolecular [4 + 2] cycloaddition of allylaryl(2-furfuryl) amines

No.	R	X	$k/10^{-7}s^{-1}$ (20 °C)	$k/10^{-6}s^{-1}$ (50 °C)
I	H	<i>o</i> -CH <sub>3</sub>	0.17 ± 0.01	0.38 ± 0.01
II	H	<i>p</i> -CH <sub>3</sub>	1.71 ± 0.07	2.78 ± 0.11
III	H	<i>o</i> -OCH <sub>3</sub>	0.72 ± 0.08	1.73 ± 0.13
IV	H	<i>p</i> -OCH <sub>3</sub>	1.79 ± 0.06	3.34 ± 0.28
V	H	<i>p</i> -Cl	2.20 ± 0.08	3.73 ± 0.42
VI	CH <sub>3</sub>	H	1.09 ± 0.11	2.25 ± 0.18
VII	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>	1.12 ± 0.07	2.37 ± 0.22
VIII	CH <sub>3</sub>	<i>p</i> -OCH <sub>3</sub>	1.18 ± 0.10	2.09 ± 0.11
IX	CH <sub>3</sub>	<i>p</i> -Cl	1.49 ± 0.12	2.69 ± 0.35

TABLE II.

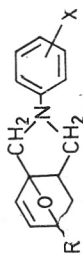
Allylaryl(2-furfuryl)amines



No.	R	X	Yield %	B. p. (°C/mmHg)	$n_D^{20}$	Formula	Mol. weight	Calc'd Found	
								%C	%H
I	H	<i>o</i> -CH <sub>3</sub>	63	132—134/4	1.5479	C <sub>15</sub> H <sub>17</sub> NO	227.3	79.25 79.28	7.54 7.58
II	H	<i>p</i> -CH <sub>3</sub>	81	151—154/4 <sup>a</sup>	—	C <sub>15</sub> H <sub>17</sub> NO	227.3		
III	H	<i>o</i> -OCH <sub>3</sub>	63	153—154/4	1.5638	C <sub>15</sub> H <sub>17</sub> NO <sub>2</sub>	243.3	74.05 73.80	7.04 7.28
IV	H	<i>p</i> -OCH <sub>3</sub>	62	181—184/5 <sup>b</sup>	—	C <sub>15</sub> H <sub>17</sub> NO <sub>2</sub>	243.3		
V	H	<i>p</i> -Cl	62	182—183/6	—	C <sub>14</sub> H <sub>14</sub> ClNO	247.7	67.88 68.14	5.69 5.72
VI	CH <sub>3</sub>	H	55	160—161/5	1.5697	C <sub>15</sub> H <sub>17</sub> NO	227.3	79.26 79.08	7.54 7.45
VII	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>	72	166—167/5	1.5621	C <sub>16</sub> H <sub>19</sub> NO	241.3	79.62 79.60	7.94 7.92
VIII	CH <sub>3</sub>	<i>p</i> -OCH <sub>3</sub>	64	187—188/6	1.5633	C <sub>16</sub> H <sub>19</sub> NO <sub>2</sub>	257.3	74.67 74.35	7.44 7.46
IX	CH <sub>3</sub>	<i>p</i> -Cl	50	187—188/7	—	C <sub>15</sub> H <sub>16</sub> ClNO	261.8	68.82 68.95	6.16 6.14

<sup>a</sup>) Lit.<sup>3</sup> b. p. 178—181 °C/14 mmHg,  $n_D^{20} = 1.5682$ ; <sup>b</sup>) Lit.<sup>3</sup> b. p. 192—194 °C/13 mmHg,  $n_D^{20} = 1.5699$ .

TABLE III.  
N-Aryl-4H-5,7a-epoxyisoindolines



No.	R	X	Yield (%)		M. p. (°C)	I. r. band <sup>a</sup> (cm <sup>-1</sup> )	Formula	Mol. weight	Anal. %C	Calc'd Found	
			20 °C 60 days	50 °C 3 days						%H	%N
X	H	<i>o</i> -CH <sub>3</sub>	10	8	85—86	868	C <sub>15</sub> H <sub>17</sub> NO	227.3	79.25 79.54	7.54 7.72	6.16 6.39
XI	H	<i>p</i> -CH <sub>3</sub>	75	72	104—105 <sup>b</sup>	862	C <sub>15</sub> H <sub>17</sub> NO	227.3	74.05	7.04	5.75
XII	H	<i>o</i> -OCH <sub>3</sub>	35	36	110—111	862	C <sub>15</sub> H <sub>17</sub> NO <sub>2</sub>	243.3	73.92	7.13	5.85
XIII	H	<i>p</i> -OCH <sub>3</sub>	76	66	137—138 <sup>c</sup>	862	C <sub>15</sub> H <sub>17</sub> NO <sub>2</sub>	243.3	67.88	5.69	5.65
XIV	H	<i>p</i> -Cl	90	88	127—128	864	C <sub>14</sub> H <sub>14</sub> ClNO	247.7	67.65	5.89	5.74
XV	CH <sub>3</sub>	H	47	52	96—97	873	C <sub>15</sub> H <sub>17</sub> NO	227.3	79.26 79.05	7.54 7.52	6.16 6.39
XVI	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>	57	55	107—108	873	C <sub>16</sub> H <sub>19</sub> NO	241.3	79.62 79.92	7.94 7.81	5.81 5.95
XVII	CH <sub>3</sub>	<i>p</i> -OCH <sub>3</sub>	50	49	117—118	871	C <sub>16</sub> H <sub>19</sub> NO <sub>2</sub>	257.3	74.67 74.84	7.44 7.18	5.45 5.74
XVIII	CH <sub>3</sub>	<i>p</i> -Cl	77	82	142—143	873	C <sub>15</sub> H <sub>16</sub> ClNO	261.8	68.82 68.59	6.16 6.45	5.35 5.18

<sup>a</sup> Frequency of characteristic i. r. band used for quantitative measurements.

<sup>b</sup> Lit.<sup>3</sup>, m. p. 104—105 °C, yield 100%. <sup>c</sup> Lit.<sup>3</sup> m. p. 136—138 °C, yield 100%.

methyl group in position 5 of the furan nucleus decreased the rate of the cycloaddition. These results can be rationalized in terms of unfavourable steric effects, most likely in the reaction transition state.

The preparation of mostly new tertiary amines (Table II, I—IX) was performed by known<sup>4</sup> or modified procedures, and will be reported elsewhere. Here, the details of the preparation and isomerization of *N*-allyl-*N*-(5-methyl-2-furfuryl)-4-chloroaniline (IX) will be given as an example. Other compounds listed in Tables II and III were prepared by essentially the same methods described for the preparation of IX and XVIII.

#### EXPERIMENTAL

Melting points are uncorrected. I.r. spectra were taken on a Perkin-Elmer 137 Infracord spectrophotometer using 0.2 mm NaCl-window cels. UV spectra were recorded on a Unicam SP 800 spectrophotometer. Refraction indices were measured using a Carl Zeiss — Jena refractometer.

#### *N*-Allyl-*N*-(5-methyl-2-furfuryl)-*p*-chloroaniline (IX)

To 11.1 g (0.05 mol) of freshly distilled *N*-(5-methyl-2-furfuryl)-*p*-chloroaniline\* 6.65 g (0.055 mol) allylbromide was added during 30 min. dropwise with stirring and efficient cooling. After standing overnight at room temperature the reaction mixture was dissolved in 600 ml water and an excess of saturated aqueous sodium hydroxyde was added. Crude amine was obtained by extraction with ether and evaporation of dried ethereal solution. The residual oil was distilled at reduced pressure yielding 6.6 g (50%) of IX, b.p. 185—193 °C/7 mm Hg. After repeated fractionation, analytically pure sample b.p. 187—188 °C/7 mm Hg was obtained; u. v. spectrum:  $\lambda_{\max}$  210, 261, and 311 nm; log  $\epsilon$  4.05, 4.30, and 3.26.

*Picrate*: From 0.52 g (0.002 mol) IX and 0.46 g (0.002 mol) picric acid in 3 ml of ethanol. The product was recrystallized from ethanol. M. p. 77—78 °C.

*Anal.* C<sub>12</sub>H<sub>9</sub>ClN<sub>4</sub>O<sub>8</sub> (490.9) calc'd: C 51.38; H 3.91; N 11.41%  
found: C 51.27; H 3.82; N 11.50%

#### *N*-(*p*-Chlorophenyl)-5-methyl-4H-5,7a-epoxyisoindoline (XVIII)

2.1 g of the amine IX was allowed to stand at room temperature for 60 days or at 50 °C for 3 days. After addition of 1 ml ethanol, crystalline XVIII was separated. Yield 77% and 82%, respectively. The analytically pure sample was obtained by repeated recrystallization from ethanol; u. v. spectrum:  $\lambda_{\max}$  208, 262, and 316 nm; log  $\epsilon$  4.07, 4.41 and 3.39.

#### *I. r. measurement of N-aryl-4H-5,7a-epoxyisoindoline concentration during cycloaddition*

The intensity-concentration calibration curve was constructed from peak-heights of the characteristic i. r. band (873—862 cm<sup>-1</sup>) for each *N*-aryl-4H-5,7a-epoxyisoindoline (Table III) at various concentrations (5—80 mg/ml CCl<sub>4</sub>) against pure carbontetrachloride as reference. The accuracy of the i. r. measurements was better than 1%.

\* Prepared by reduction of 48.4 g (0.22 mol) 5-methylfurfurylidene-*p*-chloroaniline<sup>5</sup> with 26.8 g (1.1 mol) magnesium in methanol, according to the reported method<sup>4</sup>. Yield 37.5 g, b. p. 166—167 °C/6 mm Hg, m. p. 48—49 °C.

*Anal.* C<sub>12</sub>H<sub>12</sub>ClNO (221.7) calc'd: C 65.01; H 5.45%  
found: C 64.46; H 5.40%

An 80 mg sample of each freshly redistilled tertiary amine (I—IX)\*\* was dissolved in 1 ml of analytical grade carbontetrachloride and i.r. spectra were recorded. From the peak-heights of characteristic bands, using the previously constructed calibration curve, a starting concentration of the corresponding epoxy-isopindoline was established.

A number of 80 mg samples\* of each tertiary amine (I—IX) were thermostatted at 20 or 50 °C. The samples were taken out at given periods, dissolved in 1 ml of carbontetrachloride and i.r. spectra were recorded. From the peak heights of the band at 873—862  $\text{cm}^{-1}$  (Table III) taking in account a calibration curve and the starting concentration, the change in concentration was calculated and the results represented graphically (Figs. 1 and 2).

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## SAŽETAK

**Utjecaj supstituenata na brzinu intramolekularne Diels-Alderove reakcije alilaril(2-furfuril)amina**

Ž. Klepo i K. Jakopčić

Brzina intramolekularne [4 + 2]-cikloadicije supstituiranih alilaril(2-furfuril)amina praćena je pomoću i.r.-spetrometrije. Suprotno ranijim kvalitativnim opažanjima, pokazalo se da supstituenti u *para*-položaju aromatskog ostatka ne utječu bitno na brzinu reakcije. S druge strane, prisutnost metilne ili metoksi-skupine u *orto*-položaju aromatskog ostatka, odnosno metilne skupine u položaju 5 furanske jezgre smanjuju brzinu cikloadicije. Uzrok smanjenju brzine reakcije pripisan je steričkim utjecajima u prijelaznom stanju.

ZAVOD ZA ORGANSKU KEMIJU, TEHNOLOŠKI FAKULTET

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Prispjelo 23. listopada 1974.

\* With the exception of IV in which case sample of 40 mg were used, due to insufficient solubility.