Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

New Substituted Alkenyl-Furfuryl-Aryl Amines: Synthesis and Their Characterization

Ana Dunja Mance [a], Kresimir Jakopcić [a] & Marija Šindler-Kulyk [a]
[a] Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulićev, trg 20, HR-10000 Zagreb, Croatia
Published online: 21 Aug 2006.

To cite this article: Ana Dunja Mance, Kresimir Jakopcić & Marija Šindler-Kulyk (1996) New Substituted Alkenyl-Furfuryl-Aryl Amines: Synthesis and Their Characterization, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:5, 923-933, DOI: 10.1080/00397919608003697

To link to this article: http://dx.doi.org/10.1080/00397919608003697

SYNTHETIC COMMUNICATIONS, 26(5), 923-933 (1996)

NEW SUBSTITUTED ALKENYL-FURFURYL-ARYL AMINES: SYNTHESIS AND THEIR CHARACTERIZATION

Ana Dunja Mance, Krešimir Jakopčić and Marija Šindler-Kulyk*

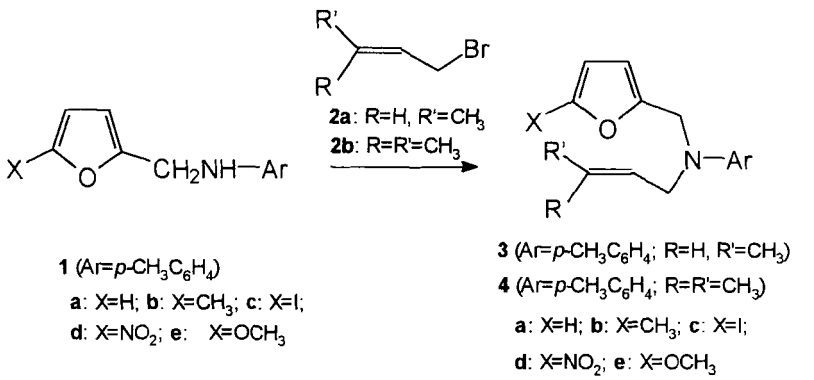
Department of Organic Chemistry,
Faculty of Chemical Engineering and Technology, University of Zagreb,
Marulićev trg 20, HR-10000 Zagreb, Croatia

Abstract: Reaction of several *N*-(5-substituted-2-furfuryl)-*p*-toluidines with the appropriate substituted allyl bromide gave new examples of tertiary amines (**3a-e**, **4a-e**) with unique capability to react spontaneously in a sense of intramolecular [4+2]cycloaddition (**IMDA**) reaction.

The paper presents the synthesis and identification of several *N*-2-butenyl and *N*-2-isopentenyl derivatives of *N*-(5-substituted-2-furfuryl)-p-toluidine. The successful preparations were important to enable the continuation of our studies on the influence of substituents in the intramolecular Diels-Alder (IMDA) reaction of tertiary allyl furfurylamines.[1] The method employed for the synthesis of tertiary amines **3** involves alkylation of readily available secondary amines **1**[8] with substituted allyl halides **2** (Scheme 1). Although the alkylation step seems to be straightforward, standard procedure[6, 8] was in the present examples strained by

*To whom correspondence should be addressed.

Scheme 1.



1 (Ar=*p*-$CH_3C_6H_4$)
a: X=H; **b**: X=CH_3; **c**: X=I;
d: X=NO_2; **e**: X=OCH_3

3 (Ar=*p*-$CH_3C_6H_4$; R=H, R'=CH_3)
4 (Ar=*p*-$CH_3C_6H_4$; R=R'=CH_3)
a: X=H; **b**: X=CH_3; **c**: X=I;
d: X=NO_2; **e**: X=OCH_3

Table 1.

N-trans-2-butenyl-*N*-2-furfuryl-p-toluidines (**3a-e**) and *N*-2-furfuryl-*N*-2-isopentenyl-p-toluidines (**4a-e**)

Compd.	TLC (R_f)[a]	Yield (%)[b]	m/z M^+ (%)[c]	Compd.	TLC (R_f)[a]	Yield (%)[b]	m/z M^+ (%)[c]
3 a	0.65	95	241 (84)	**4 a**	0.69	75	255 (65)
3 b	0.66	90	255 (33)	**4 b**	0.70	70	269 (71)
3 c	0.64	85	367 (86)	**4 c**	0.69	80	381 (88)
3 d	0.30	78	286 (100)	**4 d**	0.35	77	300 (43)
3 e	0.50	85	271 (12)	**4 e**	0.43	85	285 (10)

[a]Eluent: petroleum ether/ether (10:1). [b]All yields refer to isolated pure compounds. [c]In HRMS the calculated and found values for M^+ were within 0.013.

side-reactions like spontaneous rearrangement and alkyl exchange, especially when a less reactive secondary amine or a surplus of the unsaturated alkyl halide is required.

Treating the secondary amines with a slight excess of alkenyl halide gives the tertiary amines in good yields (Table 1), but the results greatly depend on the nucleophilicity of the amines. The substituents in the furan ring influence the

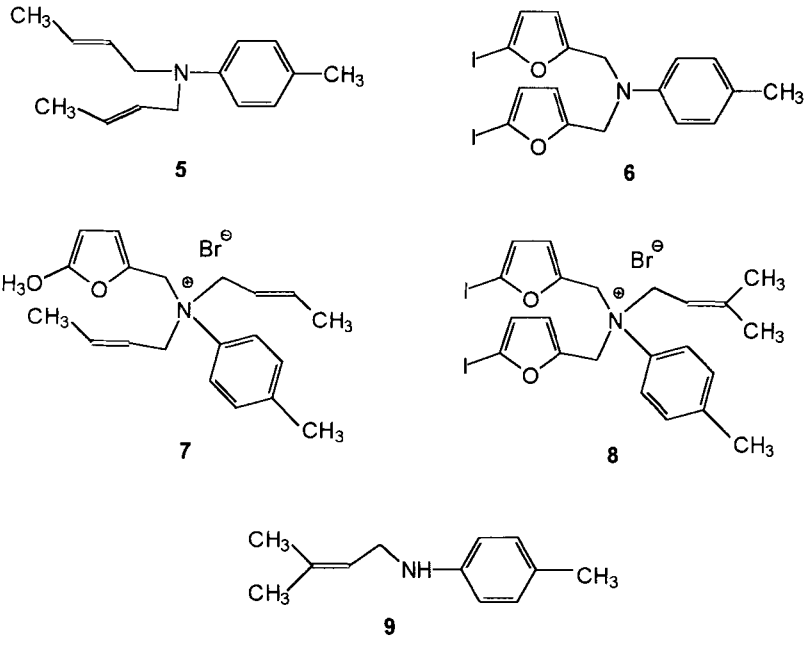
reactivity of the secondary amines. The alkylation is accelerated with electron releasing substituents in the secondary amine, and retarded with the bulky substituents in the alkyl halide. It should be noted that the separation procedures deserve great attention due to the very small differences in R_f values. Some of the substituents enhanced spontaneous IMDA reaction of the tertiary amines **3c-e**, **4c-e** at reaction conditions and/or purification, decreasing the yield.

We also observed the tendency of the prepared tertiary amines to undergo the alkyl exchange reaction depending on the polar effects of the substituents. For the illustration, in the preparation of the iodo (**3c, 4c**) and methoxy (**3e, 4e**) derivatives the amines **5** and **6** (FIG. 1.) were isolated as by-products in 5% and 10% yield respectively, if the equimolar quantity of reactants were used.[9]

The formation of *N,N*-di-*trans*-2-butenyl-*p*-toluidine (**5**) was explained by the reaction of the amine **3e** with *trans*-2-butenyl bromide in excess to give quaternary salt **7** followed by the cleavage of 5-methoxy-2-furfuryl bromide *via* the resonance stabilised 5-methoxy-2-furfuryl cation. On the other hand, *N,N*-di-(5-iodo-2-furfuryl)-*p*-toluidine (**6**), rather unexpected amine, could be formed in the reaction of **4c** with the hydrobromide salt of the unreacted secondary amine *via* quaternary salt **8**. This pathway was supported by the presence of *N*-2-isopentenyl-*p*-toluidine (**9**).

The structure of the obtained tertiary amines was determined by their ^1H and ^{13}C NMR spectra (Table 2-5). The assignments were made using the data obtained by off-resonance technique and substituent-induced shift increments[10-12] combined with the literature data for similar compounds.[13,14]

FIG. 1.

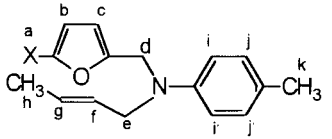


All examined amines (Table 1, M^+ given) show (except **3d** and **4d**) in the mass spectra typical fragmentation at furfuryl moiety and nitrogen[5] leading to the most resonance stabilized 5-substituted 2-furfuryl cation as the base peak.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a JEOL FX-90 Q instrument using $SiMe_4$ as internal standard in $CDCl_3$ solution. The mass spectral data were obtained on a Varian MAT CH-7 (70 eV) instrument. Silica gel (Merck 0.05-0.2 mm) and Alumina (neutral, Grade I) was used for chromatographic

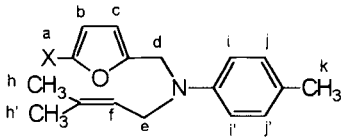
Table 2. ^{1}H NMR spectra[a)] of *N-trans*-2-butenyl- *N*-2-furfuryl- *p*-toluidine and 5-substituted 2-furfuryl derivatives



Compd.	a	b	c	d	e	f + g	h	i, i'	j, j'	k
3a X=H	7.30 dd, 1H *J'*=1.8 *J''*=0.9	6.25 dd, 1H *J*=3.2 *J'*=1.8	6.10 dd, 1H *J*=3.2 *J''*=0.9	4.37 s, 2H	3.96-3.87 m[b], 2H	5.74-5.42 m[c], 2H	1.66 d[d], 3H *J*=4.7	6.71 d, 2H *J*=8.5	6.99 d, 2H *J*=8.5	2.22 s, 3H
3b X=CH_3	2.18 s, 3H[f]	5.79 d[e], 1H *J*=2.6	5.94 d, 1H *J*=2.6	4.27 s, 2H	3.95-3.72 m[b], 2H	5.53-5.43 m[c], 2H	1.68 d, 3H *J*=4.7	6.68 d, 2H *J*=8.5	6.95 d, 2H *J*=8.5	2.18 s, 3H[f]
3c X=I		6.41 d, 1H *J*=3.2	6.02 d, 1H *J*=3.2	4.40 s, 2H	3.87-3.83 m[b], 2H	5.58-5.47 m[c], 2H	1.68 d[d], 3H *J*=4.7	6.67 d, 2H *J*=8.5	7.00 d, 2H *J*=8.5	2.29 s, 3H
3d X=NO_2		7.21 d, 1H *J*=3.8	6.32 d, 1H *J*=3.8	4.48 s, 2H	3.93-3.87 m[b], 2H	5.80-5.32 m[c], 2H	1.70 d, 3H *J*=4.7	6.66 d, 2H *J*=8.5	7.02 d, 2H *J*=8.5	2.24 s, 3H
3e X=OCH_3	3.78 s, 3H	5.01 d, 1H *J*=3.2	5.98 d, 1H *J*=3.2	4.26 s, 2H	3.96-3.82 m[b], 2H	5.58-5.47 m[c], 2H	1.68 d[d], 3H *J*=4.7	6.71 d, 2H *J*=8.5	7.00 d, 2H *J*=8.5	2.23 s, 3H

a) δ ($CDCl_3$) in ppm, *J* in Hz; b) coupling constants with H_f (*J*=4.7 Hz) and H_g (*J*=1.5 Hz); c) coupling constants with H_e (*J*=4.7 Hz) or H_h (*J*=1.2 Hz); d) broadened signal due to the additional coupling with H_f (*J*=1.2 Hz); e) broadened signal due to the additional coupling with H_a; f) 6H signal for both methyl groups with the same δ value.

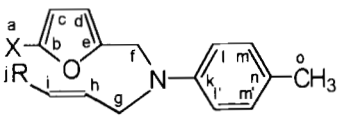
Table 3. ^{1}H NMR spectra[a] of *N*-2-furfuryl-*N*-2-isopentenyl- *p*-toluidine and 5-substituted 2-furfuryl derivatives



Compd.	a	b	c	d	e	f	h	h'	i, i'	j, j'	k
4a X=H	7.32 dd, 1H *J'*=1.8 *J''*=0.9	6.25 dd, 1H *J*=3.2 *J'*=1.8	6.10 dd, 1H *J*=3.2 *J''*=0.9	4.37 s, 2H	3.86 d, 2H *J*=6.2	5.22 t[b], 1H *J*=6.2	1.67 s, 3H	1.70 d, 3H *J*=1.2	6.76 d, 2H *J*=8.5	7.04 d, 2H *J*=8.5	2.23 s, 3H
4b X=CH_3	2.24 s, 3H[c]	5.84 dd, 1H *J*=2.9 *J*=0.9	5.98 d, 1H *J=2.9*	4.31 s, 2H	3.88 d, 2H *J=6.2*	5.23 t[b], 1H *J=6.2*	1.68 s, 3H	1.77 d, 3H *J=1.2*	6.71 d, 2H *J=8.5*	7.00 d, 2H *J=8.5*	2.24 s, 3H[c]
4c X=I		6.40 d, 1H *J*=3.2	6.01 d, 1H *J*=3.2	4.38 s, 2H	3.88 d, 2H *J*=6.5	5.21 t[b], 1H *J*=6.5	1.70 s, 3H	1.72 d, 3H *J*=1.2	6.72 d, 2H *J*=8.5	7.00 d, 2H *J*=8.5	2.23 s, 3H
4d X=NO_2		7.22 d, 1H *J*=3.5	6.32 d, 1H *J*=3.5	4.47 s, 2H	3.93 d, 2H *J*=6.5	5.23 t[b], 1H *J*=6.5	1.69 s, 3H	1.73 d, 3H *J*=1.2	6.67 d, 2H *J*=8.5	7.03 d, 2H *J*=8.5	2.25 s, 3H
4e X=OCH_3	3.76 s, 3H	4.99 d, 1H *J*=3.2	5.97 d, 1H *J*=3.2	4.24 s, 2H	3.87 d, 2H	5.21 t[b], 1H	1.69 s, 3H[c]	1.69 s, 3H[c]	6.70 d, 2H *J*=8.5	6.99 d, 2H *J*=8.5	2.22 s, 3H

a) δ ($CDCl_3$) in ppm, *J* in Hz ; b) broadened signal due to the additional coupling with H_h (*J*=1.2 Hz) and $H_{h'}$ (1.5 Hz); c) 6H signal for both methyl groups with the same chemical shift.

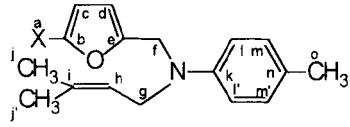
Table 4. ^{13}C NMR spectra[a] of *N*-allyl-*N*-2-furfuryl-*p*-toluidine[b] and new tertiary amines **3a - 3e**



^{13}C	**3**[b] X=H, R=H	**3a** X=H, R=CH_3	**3b**[c] X=CH_3, R=CH_3	**3c** X=I, R=CH_3	**3d** X=NO_2, R=CH_3	**3e** X=OCH_3, R=CH_3
e	152,7(s)	152.9(s)	150.7(s)	158.5(s)	151.4(s)	142.4(s)
k	146,5(s)	146.7(s)	146.4(s)	146.3(s)	145.6(s)	146.7(s)
b	141,7(d)	141.5(d)	150.6(s)	85.8(s)	157.3(s)	160.8(s)
m	129,6(d)	129.6(d)	129.2(d)	129.6(d)	129.5(d)	129.5(d)
h[d]	134,1(d)	127.4(d)	126.9(d)	127.7(d)	125.9(d)	127.4(d)
i[d]	116,2(t)	127.0(d)	126.6(d)	126.5(d)	128.4(d)	126.8(d)
n	126,1(s)	126.0(s)	125.4(s)	126.8(s)	126.9(s)	125.9(s)
l	113,3(d)	113.5(d)	113.6(d)	113.3(d)	113.3(d)	113.4(d)
c	110,2(d)	110.1(d)	105.8(d)	120.8(d)	112.4(d)	79.7(d)
d	107,2(d)	107.1(d)	107.9(d)	110.2(d)	110.3(d)	108.4(d)
g	53,1(t)	52.4(t)	51.9(t)	58.5(t)	52.8(t)	52.2(t)
f	47,5(t)	47.4(t)	47.1(t)	47.5(t)	47.5(t)	47.2(t)
o	20,2(q)	20.2(q)	19.9(q)	20.2(q)	19.9(q)	20.2(q)
j		17.6(q)	17.3(q)	17.7(q)	17.4(q)	17.7(q)
a			13.1(q)			57.7(q)

a) $\delta_{(CDCl_3)}$ in ppm; b) prepared by reported[8] procedure for comparison of NMR data; c) signals for carbon b and e are interchangeable; d) interchangeable δ values in compounds **3a-3e.**

Table 5. ^{13}C NMR spectra[a] of *N*-2-furfuryl-*N*-2-isopentenyl-*p*-toluidine (**4**) and 5-substituted 2-furfuryl derivatives (**4b-4e**)



^{13}C	**4a** X=H	**4b**[b] X=CH_3	**4c**[c] X=I	**4d**[d] X=NO_2	**4e** X=OCH_3
e	153.0(s)	151.0(s)	158.6(s)	151.1(s)	142.3(s)
k	146.8(s)	146.8(s)	146.5(s)	145.7(s)	146.6(s)
b	141.5(d)	150.8(s)	85.8(s)	157.5(s)	160.7(s)
m	129.6(d)	129.4(d)	129.6(d)	129.6(d)	129.3(d)
h	121.5(d)	121.3(d)	121.1(d)	120.2(d)	121.3(d)
i	134.5(s)	134.1(s)	134.8(s)	135.6(s)	134.0(s)
n	126.1(s)	125.9(s)	126.4(s)	127.0s)	125.7(s)
l	113.8(d)	113.6(d)	113.7(d)	113.6(d)	113.5(d)
c	110.2(d)	105.8(d)	120.8(d)	112.5(d)	79.5(d)
d	107.1(d)	107.7(d)	110.2(d)	110.3(d)	108.1(d)
g	48.4(t)	48.2(t)	48.5(t)	48.9(t)	48.0(t)
f	47.7(t)	47.6(t)	47.8(t)	47.7(t)	47.3(t)
o	20.2(q)	20.0(q)	20.3(q)	19.9(q)	20.0(q)
j	17.9(q)	17.7(q)	18.0(q)	17.7(q)	17.7(q)
j'	25.5(q)	25.5(q)	25.8(q)	25.5(q)	25.5(q)
a		13.4(q)			57.2(q)

a) δ ($CDCl_3$) in ppm; b) signals for b and e are interchangeable; c) signals for c and h are interchangeable; d) signals for c and d are interchangeable.

purifications. All secondary amines, except **1e**[15] were prepared by sodium borohydride reduction of corresponding azomethynes similarly to a reported procedure.[6,8] Melting points were determined on an Original Kofler Mikroheiztisch apparatus (Reichert, Wien) and are not corrected.

N-(5-Methoxy-2-furfuryl)-p-toluidine (**1e**). The mixture of **1c** (4.7g, 15 mmol) in methanol and sodium methoxide (8.1g, 50 mmol) in the presence of powdered cupric oxide (5.0g) was heated under reflux and stirring for 20 hrs. The product was purified by column chromatography on neutral alumina with hexane/ether (10:1) as the eluent. The light-yellow oil[16] (3.6g, 83%) is identical with the original sample[8] (TLC and spectroscopic evidence).

General procedure for the preparation of tertiary amines **3a-e** *and* **4a-e:** To an appropriate, freshly recrystallized or rechromatographed secondary amine (0.01 mole) a slight surplus of *trans*-2-butenyl or 2-isopentenyl bromide (0.011 mole) was added under stirring and cooling in an ice bath. The reaction mixture was kept at 10-15° C over night. The crude hydrobromide of the tertiary amine was treated with 5% aqueous sodium hydroxide. The organic material was extracted with ether. The etheral extracts were dried over anhydrous magnesium sulphate and solvent evaporated. The oily residue was purified by column chromatography on silica gel (**3a-c** and **4a-c**) or alumina (**3d**, **3e**, **4d** and **4e**) using petroleum ether/ether (10:1) as the eluent. Pure tertiary amines were obtained as light-yellow oils. Analytically pure compounds were obtained by repeated column chromatography.

In the first few fractions the colourless oily material (comp. **5**, R_f = 0.72); ^{1}H NMR ($CDCl_3$): δ 1.66 (s, 6H), 2.22 (s, 3H), 3.76-3.80 (m, 4H), 5.44-5.57 (m, 4H), 6.61 (d, 2H) and 6.99 (d, 2H, J=8.5Hz) has been obtained during purification of **3e**. In the last several chromatographic fractions of **4c** the colourless crystalline compound **6** (R_f =0.36) has been isolated. M.p. 80-82° C; ^{1}H NMR ($CDCl_3$): δ

2.24 (s, 3H), 4.45 (s, 4H), 6.05 (d, 2H) and 6.42 (d, 2H, J=3.2 Hz), 6.74 (d, 2H) and 7.08 (d, 2H, J=8.5 Hz); MS: m/z 519 (M^+, 5%), 394 (36), 207(84), 179(100), 91(49), 81(37).

Acknowledgement:

We thank the Ministry of Science and Technology of the Republic of Croatia, for partial support through the grant 1.07.039.

References:

1. In the course of the experiments concerning the IMDA reaction of tertiary amines with furan as the diene and allyl group as the dienophyle[2-8] we noticed that the kinetics of this reaction depended on the electronic and/or steric effects of the substituents in the furanic diene.[4,8] The examples extensively studied were the amines with unsubstituted allyl group as a dienophyle. The exception was cyclohexenyl group but in this case[7] the furanic diene was unsubstituted.

2. Bilović, D.; Stojanac, Ž. and Hahn, V. *Tetrahedron Lett.* **1964**, 2071.

3. Bilović, D. and Hahn, V. *Croat. Chem. Acta* **1967**, *39*, 189.

4. Klepo, Ž. and Jakopčić, K. *Croat. Chem. Acta* **1975**, *47*, 45.

5. Mintas, M.; Klepo, Ž. and Jakopčić, K. *Org. Mass Spectrom.* **1979**, *14*, 254.

6. Klepo, Ž. and Jakopčić, K. *J. Chem. Eng. Data* **1985**, *30*, 237.

7. Mance, A. D. and Jakopčić, K. *Vestn. Slov. Kem. Druš.* **1986**, *33*, 287.

8. Klepo, Ž. and Jakopčić, K. *J. Heterocyclic Chem.* **1987**, *24*, 1787.

9. If a substantial excess of alkyl halide was used the products of undesirable alkyl exchange reaction predominated.

10. Dean, F. M. and Sargent, M. V. *"Furans and their Benzo Derivatives: (i) Structure"*, Part 3.10. in Katritzky, A. R. and Rees C. W. (eds.): *"Comprehensive Heterocyclic Chemistry"*, Pergamon Press, Oxford **1984**, Vol. 4, p. 531.

11. Pretsch, E.; Clerc, T.; Seibl, J. and Simon, W. *"Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden"*, Springer Verlag, Berlin, **1981**.

12. Kalinowski, H.-O.; Berger, S. and S. Braun, S. *"^{13}C-NMR-Spektroskopie"*, Georg Thieme Verlag, Stuttgart-New York, **1984**.

13. Katritzky, A. R.; Paluchowska, M. H. and Gallos, J. K. *J. Heterocyclic Chem.* **1989**, *26*, 421.

14. Dötz, K. H.; Noack, R.; Harms, K. and Müller, G. *Tetrahedron,* **1990,** *46,* 1235.

15. We found the exchange of 5-iodine with 5-methoxy substituent (**1c** into **1e**) superior to reported procedure.[6, 8]

16. The explosive thermal decomposition prevented purification by distillation.

(Received in The Netherlands 12 September 1995)