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# Flash vacuum pyrolysis of 3-oxo-2-arylhydrazonopropanals and related derivatives

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**Abstract**—Flash vacuum pyrolysis (FVP) of 3-oxo-2-arylhydrazonopropanals at 500°C and 0.02 Torr yielded the corresponding derivatives of anilines, *N*-formylanilines, *N*-benzoylanilines and benzoylnitriles. Similar FVP of phenylhydrazonomalononitrile, phenylhydrazonoacetylacetone and phenylhydrazono ethyl cyanoacetate gave aniline in addition to *N*-cyanoaniline and 3,6-dicyano-1,4-diphenyl-1,2,4,5-tetrazine, acetanilide, *N*-methylacetanilide, pyruvonitrile and *N*-phenylurethane. 

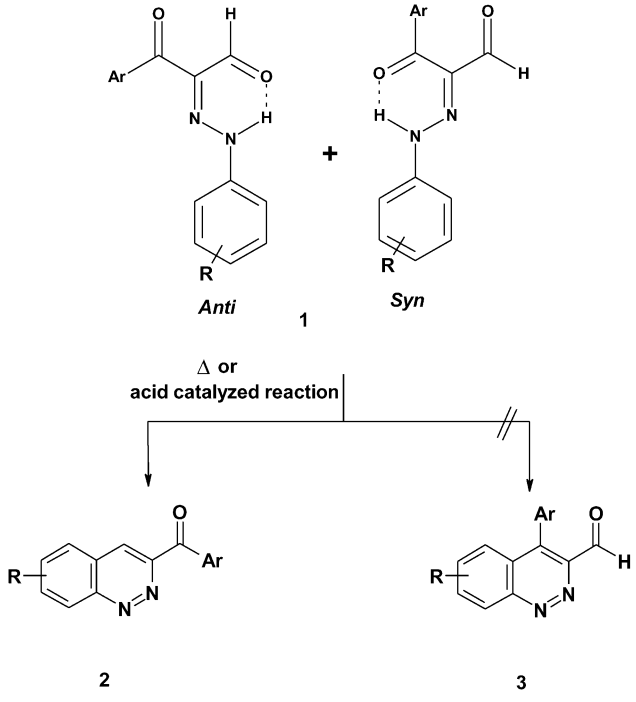
## 1. Introduction

We recently reported efficient procedures for the synthesis of 3-acylcinnolines starting with 3-oxo-3-aryl-2-arylhydrazonopropanals **1**. Thus, compounds **1** underwent preferential cyclization in acid medium to give only the corresponding 3-acylcinnolines **2** but none of expected isomeric 3-arylcinnoline-4-caroboxyaldehydes **3** (Scheme 1).[1] We have also, reported the results of our synthetic and kinetic studies on the gas phase thermal cyclization of compounds **1** into **2**.[2] Moreover, cyclization of (arylhydrazono)acetonitriles under Friedel–Crafts conditions has been earlier reported towards the preparation of substituted cinnoline derivatives.[3] In the present work, we describe our results on the utility of flash vacuum pyrolysis (FVP) as a possible technique for cyclizing these hydrazones into the corresponding cinnoline derivatives.

## 2. Results and discussion

FVP of compounds **1** gave an interesting series of compounds, none of which are the anticipated cinnoline derivatives. Scheme 2 illustrates the different products obtained upon FVP of **1** at 500°C and 0.02 Torr. These products (Table 1) were identified as arylamines **4**, formanilides **5**, benzanilides **6**, and arylglyoxylonitriles **7**.

The formation of **4**–**7** from **1** could be accounted for as illustrated in Scheme 3. Thus, the initial step involves intramolecular cyclization of *anti 1* into the diazacyclobutene zwitter ion **8** (route a), which then fragments into aroylglyoxylonitriles **7** and formanilides **5**. The latter undergo decarbonylation into the corresponding arylamines **4**. However, FVP of formanilide and acetanilide under the same conditions gave only pure recovered starting materials. It seems therefore that formation of arylamines most probably comes from homolysis of the N–N bond (route b) to the aminyl radical (**A**) followed by hydrogen atom abstraction. This homolysis would provide an alternative route to the nitrile **7** by consolidation of the resulting iminyl radical (**B**). Another reasonable route (route c) to the




**Scheme 1.**

*Keywords*: arylhydrazones; arylamines; anilides; acylnitriles; 1,2,4,5-tetrazine.

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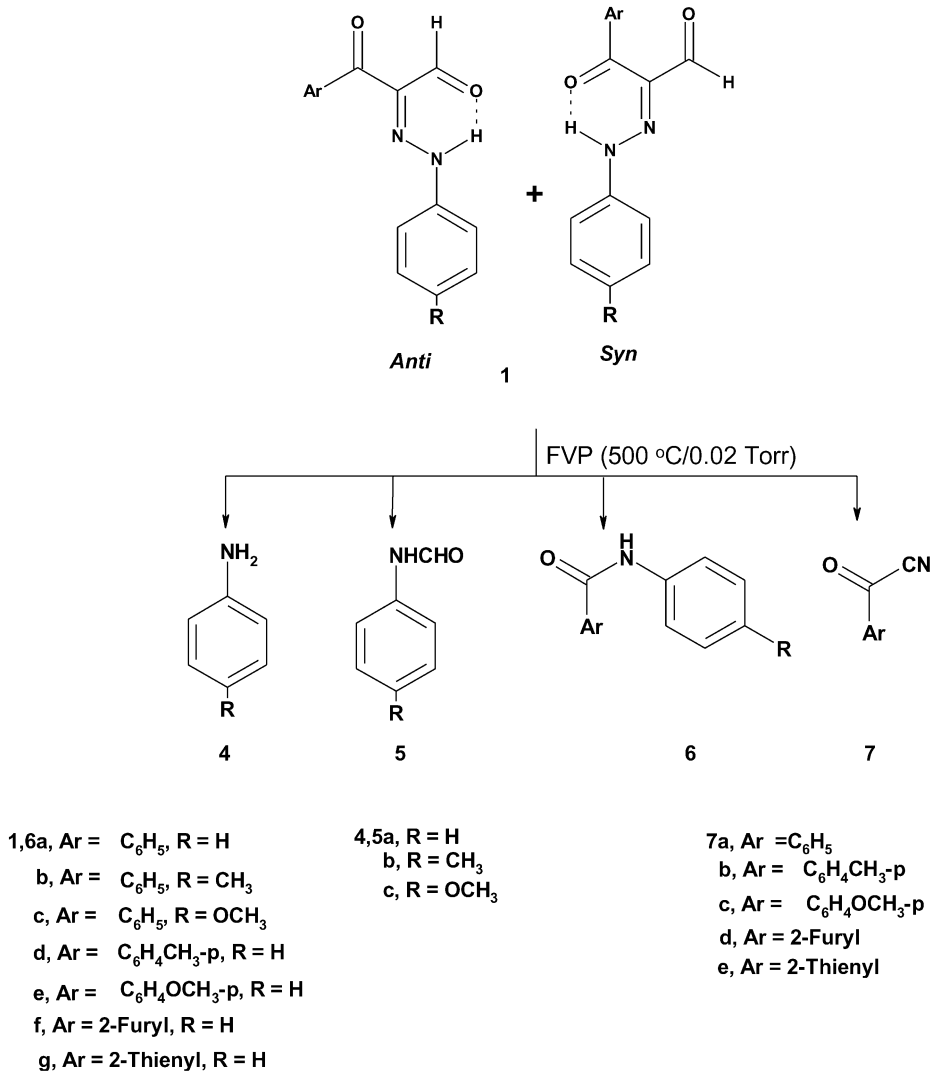



**Scheme 2.**

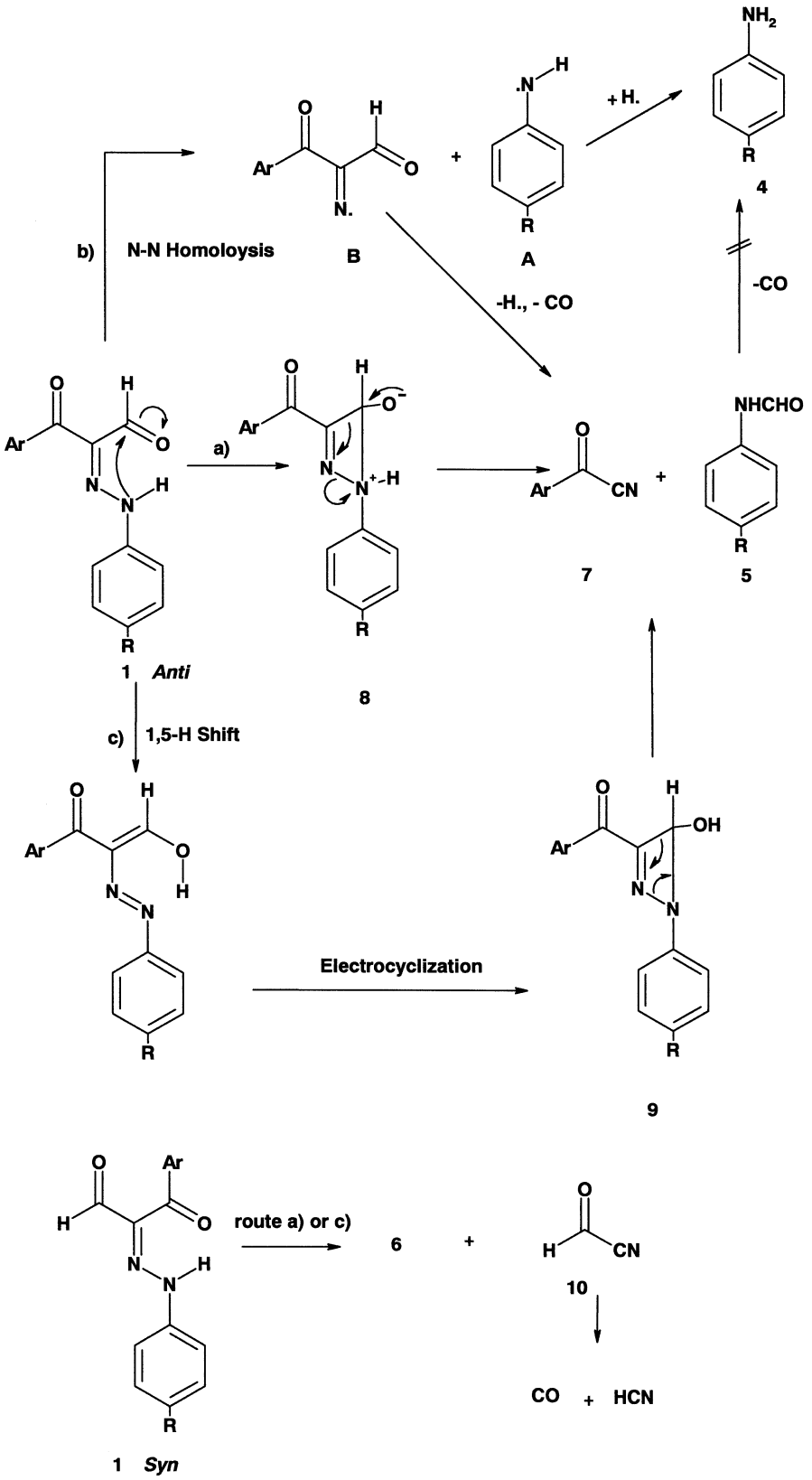
formation of **5** and **7** involves initial 1,5-H shift to generate the hydroxy-azo tautomer of **1** followed by electrocyclization to the corresponding diazetine **9** which is the possible immediate precursor of the nitrile **7** and amides **5** (this mechanism would be in line with reported thermal behavior of 2-azadienes).[19] The pyrolysis products of *N*-methylpyruvaldehyde phenylhydrazone **18**, further support route a where 1,5-H shift is not possible. Similar mechanistic pathways account for the conversion of *syn* **1** into the corresponding benzanilide derivatives **6** and formyl cyanide **10**. The latter is presumably decomposed into CO and HCN.

**Table 1.** Yields of FVP products of **1a**–**g**

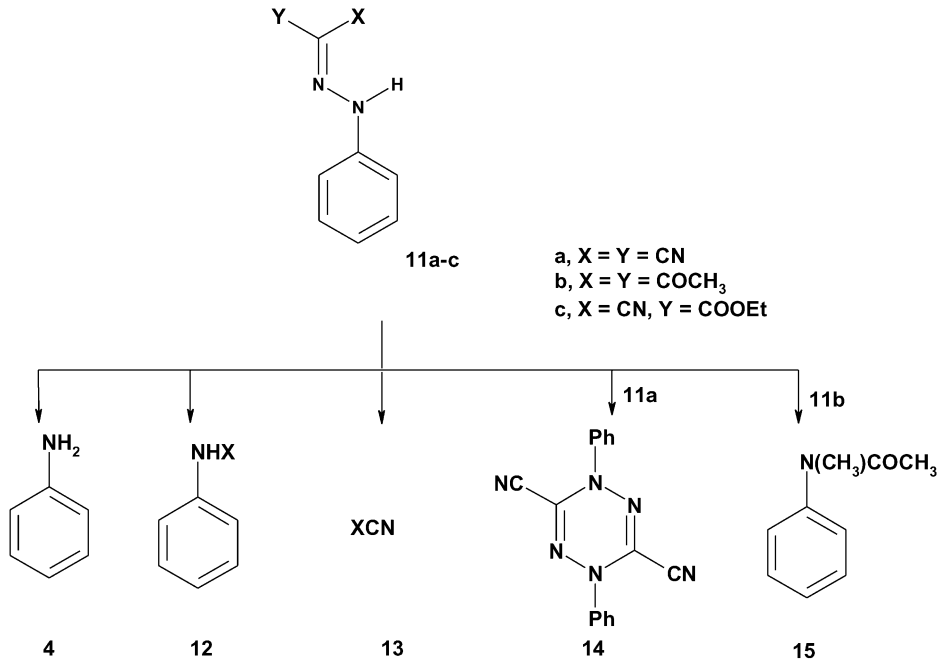
| Substrate | Products (yield %) | | | |
|---|---|---|---|---|
| **1a** | **4a** (20)[4] | **5a** (13)[5] | **6a** (15)[6] | **7a** (49)[7] |
| **1b** | **4b** (10)[8] | **5b** (11)[9] | **6b** (20)[10] | **7a** (27)[7] |
| **1c** | **4c** (15)[11] | **5c** (15)[12] | **6c** (5)[10] | **7a** (33)[7] |
| **1d** | **4a** (22)[4] | **5a** (18)[5] | **6d** (11)[10] | **7b** (34)[13] |
| **1e** | **4a** (50)[4] | **5a** (10)[5] | **6e** (10)[10] | **7c** (51)[14] |
| **1f** | **4a** (12)[4] | **5a** (10)[5] | **6f** (20)[15] | **7d** (50)[16] |
| **1g** | **4a** (40)[4] | **5a** (22)[5] | **6g** (20)[17] | **7e** (60)[18] |

This proposed mechanism could be substantiated by the percent yields of the obtained products **4**, **5**, **7** relative to **6** which is consistent with the percent (ca. 80:20) of *anti* and *syn* compositions of **1**.[1] However, since *E*-*Z*-isomerization of double-bonded groups is well known under FVP, so this correlation with the *syn*–*anti* composition is likely to be coincidental.

Similarly, FVP of the hydrazones **11a**–**c** gave the products **4**, **12**–**15** outlined in Scheme 4. Also, in these cases none of expected cinnoline derivatives[3] were detected. Thus, **11a** gave mainly aniline (40%), *N*-cyanoaniline[20] (**12**, X=CN, 20%) and 3,6-dicyano-1,4-diphenyl-1,2,4,5-tetrazine[21] (**14**, 5%). Compound **11b** gave aniline (10%), *N*-methylaniline[22] (5%), pyruvonitrile[23] (**13**, X=$COCH_3$, 15%), acetanilide[24] (**12**, X=$COCH_3$, 10%) and *N*-methylacetanilide[25] (**15**, 20%). Compound **11c** gave *N*-cyanoaniline (**12**, X=CN, 30%), *N*-phenylurethane[26] (**12**, X=COOEt, 35%), ethyl cyanoformate[23] (**13**, X=COOEt, 54%). The formation of these products seems to follow the same mechanistic pathways as that proposed for the FVP of compounds **1**. The formation of 3,6-dicyano-1,4-diphenyl-1,2,4,5-tetrazine **14** from **11a** presumably takes place via the initial elimination


b) N-N Homoloysis
B
A
+H.
4
-CO
-H., - CO
a)
7
5
1 Anti
8
c) 1,5-H Shift
Electrocyclization
9
route a) or c)
6
10
CO + HCN
1 Syn

Scheme 3.




**Scheme 4.**

of HCN to give the intermediate nitrilium imine **16** which finally dimerizes into **14** (Scheme 5).

Also, the formation of *N*-methylacetanilide **15** from **11b** presumably takes place by first the methyl shift from the tautomer **17** to give **18** with extrusion of carbon monoxide, followed by the same mechanistic pathway (route b) proposed in Scheme 3 through the four-membered ring **19** which will fragment into **15** and HCN (Scheme 5). This presumption was substantiated by FVP of *N*-methylpyruvaldehyde phenylhydrazone **18** and pyruvaldehyde phenylhydrazone **20** at 500°C, 2 Torr. Compound **18** gave *N*-methylaniline[22] (25%), *N*,*N*-dimethylaniline[27] (50%), *N*-methylacetanilde (6%). Also, compound **20** gave *N*-methylaniline (33%), *N*-methylacetanilde (15%) and aniline (22%).

The present investigation illustrates the behavior of arylhydrazones under FVP conditions and their possible utility in some synthetic applications. Such synthetic applications are now under further investigation in our laboratory. Interestingly, all α-oxohydrazones fragment via the four-membered ring intermediates **8** or **9** and **14** to give the corresponding products. The present study also complements the previous studies concerning their cyclization in gas phase[2] and under acid catalyzed[1,3] conditions which led to the formation of the cinnoline derivatives.

## 3. Experimental

IR: (KBr) Shimadzu IR-740 spectrometer. $^{1}H$ and $^{13}C$ NMR: Bruker Avance 400 spectrometer. MS: GC/MS INCOS XL Finnigan MAT. Microanalysis: LECO CHNS-932. All FVP products were identified and analyzed by GC–MS, $^{1}H$, $^{13}C$ NMR, and IR spectra.

### 3.1. Flash vacuum pyrolysis of 1a–d, 11a,c, 18 and 20

The apparatus used was similar to the one, which has been described in literature.[28] The sample was volatilized from a tube in a Büchi Kugelrohr oven through a 30×2.5 $cm^2$ horizontal fused quartz tube. This was heated externally by a Carbolite Eurotherm tube furnace MTF-12/38A to a temperature of 500°C (700°C for **11a**), the temperature being monitored by a Pt/Pt–13%Rh thermocouple situated at the center of the furnace. The products were collected in a U-shaped trap cooled in liquid nitrogen. The whole system was maintained at a pressure of $10^{-2}$ Torr by an Edwards Model E2M5 high capacity rotary oil pump, the pressure being measured by a Pirani gauge situated between the cold trap and the pump. Under these conditions the contact time in the hot zone was estimated to be ≅10 ms. The different zones of the products collected in the U-shaped trap were analyzed by $^{1}H$, $^{13}C$ NMR, IR and GC–MS. Relative and percent yields were determined from $^{1}H$ NMR. Compounds obtained were identified by comparison of their $^{1}H$, $^{13}C$ NMR, IR with reported data (cf. Table 1).

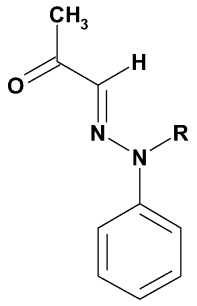
### 3.2. Spectral data of products

**3.2.1. Compounds 4a–c. 4a**, MS: $m/z$=93 ($M^+$); $^{1}H$ NMR ($CDCl_3$): $\delta$ 3.67 (s, 2H), 6.75 (d, $J$=7.6 Hz, 2H), 6.86 (t, $J$=7.6 Hz, 1H), 7.25 (t, $J$=7.6 Hz, 2H); $^{13}C$ NMR ($CDCl_3$): $\delta$ 146.4, 129.2, 118.4, 115.0.

**4b**, MS: $m/z$=107 ($M^+$); $^{13}C$ NMR ($CDCl_3$): $\delta$ 143.8, 129.7, 127.6, 115.2, 20.4.

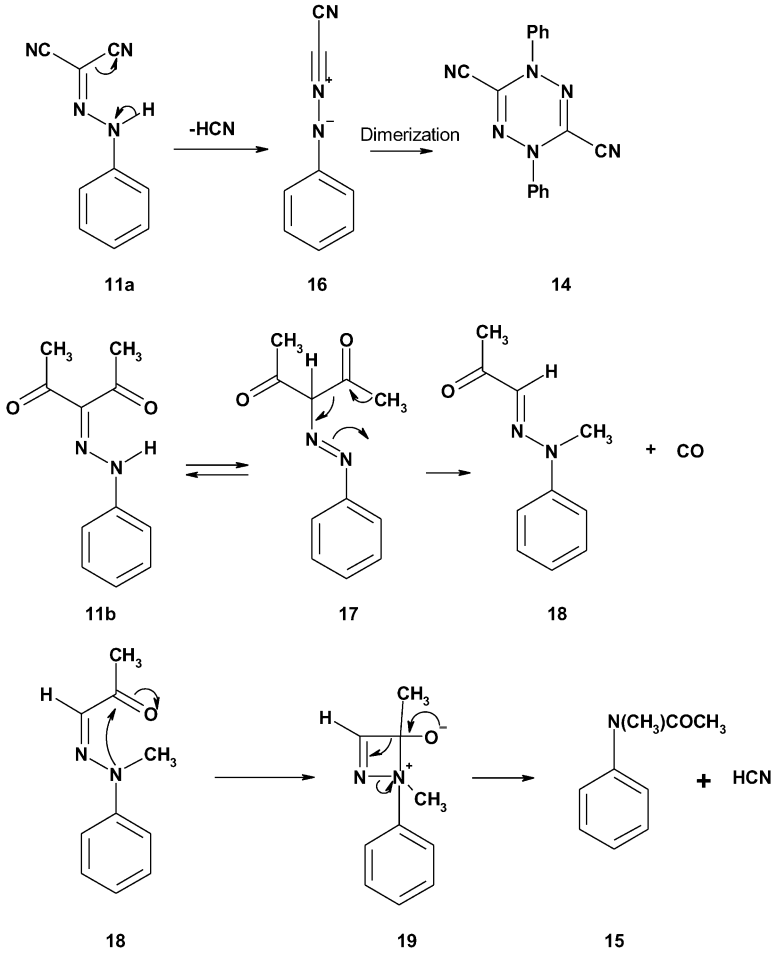
**4c**, MS: $m/z$=123 ($M^+$); $^{1}H$ NMR ($CDCl_3$): $\delta$ 2.8 (s, 2H), 3.7 (s, 3H), 6.68 (m, 2H), 6.79 (m, 2H); $^{13}C$ NMR ($CDCl_3$): $\delta$ 152.8, 139.9, 116.4, 114.8, 55.7.

**3.2.2. Compounds 5a–c. 5a**, MS: $m/z$=121 ($M^+$); IR



18, R = CH3

20, R = H




**Scheme 5.**

(KBr): 3275, 1695, 1601, 1543, 1443; $^{13}$C NMR ($CDCl_3$): $\delta$ 163.0, 159.6, 137.0, 136.8, 129.6, 128.8, 125.3, 124.5, 120.6, 118.6.

**5b**, MS: $m/z$=135 ($M^+$); $^{13}$C NMR ($CDCl_3$): $\delta$ 162.8, 159.0, 135.4, 134.7, 134.6, 134.4, 130.5, 129.8, 120.5, 119.5, 22.45, 22.37.

**5c**, MS: $m/z$=151 ($M^+$); IR (KBr): 3430, 1700; $^1$H NMR ($CDCl_3$): $\delta$ 3.75 (s, 3H), 7.20 (m, 4H), 7.90–8.20 (br s, 1H), 8.37 (m, 1H).

**3.2.3. Compounds 6a–g. 6a**, MS: $m/z$=197 ($M^+$); IR (KBr): 3327, 1635.

**6b**, MS: $m/z$=211 ($M^+$); IR (KBr): 3338, 1650.

**6c**, MS: $m/z$=227 ($M^+$); IR (KBr): 3284, 1645.

**6d**, MS: $m/z$=211 ($M^+$); IR (KBr): 3265, 1660.

**6e**, MS: $m/z$=227 ($M^+$); IR (KBr): 3350, 1650.

**6f**, MS: $m/z$=187 ($M^+$); IR (KBr): 1650; $^1$H NMR ($CDCl_3$): $\delta$ 6.56 (s, 1H), 7.2–7.66 (m, 6H), 8.06 (s, 1H), 9.70 (br s, 1H).

**6g**, MS: $m/z$=203 ($M^+$); IR (KBr) 3300, 1625; $^1$H NMR ($CDCl_3$): $\delta$ 7.00–7.7 (m, 7H), 7.9 (m, 1H), 10.10 (br s, 1H).

**3.2.4. Compounds 7a–e. 7a**, MS: $m/z$=131 ($M^+$); IR (KBr): 2230, 1680; $^1$H NMR ($CDCl_3$): $\delta$, 7.25–7.83 (m, 3H), 8.00–8.67 (m, 2H).

**7b**, MS: $m/z$=145 ($M^+$); IR (KBr): 2225, 1670.

**7c**, MS: $m/z$=161 ($M^+$); IR (KBr): 2220, 1675.

**7d**, MS: $m/z$=121 ($M^+$); IR (KBr): 2231, 1664.

**7e**, MS: $m/z$=137 ($M^+$); IR (KBr): 2220, 1648; $^1$H NMR ($CDCl_3$): $\delta$ 7.34 (m, 1H), 7.93–8.22 (m, 2H).

**3.2.5. Compounds 12–15. 12** (X=CN), MS: $m/z$=118 ($M^+$); $^{13}$C NMR ($CDCl_3$): $\delta$ 139.8, 130.8, 123.9, 116.3, 111.6.

**12** (X=COMe), MS: $m/z$=135 ($M^+$); IR (KBr): 3280, 1740; $^{13}$C NMR ($CDCl_3$): $\delta$ 169.5, 138.2, 128.7, 124.1, 120.4, 24.1.

**12** (X=COOEt), MS: $m/z$=165 ($M^+$); IR (KBr): 3330, 1720; $^{13}$C NMR ($CDCl_3$): $\delta$ 153.5, 137.7, 128.5, 122.9, 118.5, 60.9, 14.5.

**13** (X=COMe), MS: $m/z$=69 ($M^+$); IR (KBr): 2220, 1730; $^1$H NMR ($CDCl_3$): $\delta$ 2.25 (s).

**13** (X=COOEt), MS: $m/z$=99 ($M^+$); IR (neat): 2993, 2247, 1752; $^1$H NMR ($CDCl_3$): $\delta$ 1.39 (t, $J$=7.1 Hz, 3H), 4.41 (q, $J$=7.1 Hz, 2H); $^{13}$C NMR ($CDCl_3$): $\delta$ 144.6, 109.8, 65.2, 14.0.

**14**, MS: $m/z$=286 ($M^+$); IR (KBr): 2241; $^1$H NMR (DMSO-$d_6$): $\delta$, 7.29–7.42 (m, 10H).

**15**, MS: $m/z$=149 ($M^+$); IR (KBr): 3040, 2930, 1655; $^1$H NMR ($CDCl_3$): $\delta$ 1.87 (s, 3H), 3.27 (s, 3H), 7.20 (m, 2H), 7.30–7.37 (m, 1H), 7.39–7.46 (m, 2H); $^{13}$C NMR ($CDCl_3$): $\delta$ 170.5, 144.6, 129.7, 127.7, 127.1, 37.1, 22.4.

**3.2.6. *N*-Methylaniline.** MS: $m/z$=107 ($M^+$); $^{13}$C NMR ($CDCl_3$): $\delta$ 149.3, 129.1, 117.1, 112.3, 30.6.

**3.2.7. *N*,*N*-Dimethylaniline.** MS: $m/z$=121 ($M^+$); $^{13}$C NMR ($CDCl_3$): $\delta$ 150.6, 129.0, 116.6, 112.6, 40.5.

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## References

1. Al-Awadi, N. A.; Elnagdi, M. H.; Ibrahim, Y. A.; Kaul, K.; Kumar, A. *Tetrahedron* **2001**, *57*, 1609–1614.
2. Kumar, A.; Al-Awadi, N. A.; Elnagdi, M. H.; Ibrahim, Y. A.; Kaul, K. *Int. J. Chem. Kinet.* **2001**, *33*, 402–406.
3. Gewald, K.; Calderon, O.; Schafer, H.; Hain, U. *Liebigs Ann. Chem.* **1984**, 1390–1394.
4. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 696, FT-NMR Aldrich Catalog 1(2), 451A, FT-IR 1(1), 1189A.
5. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 4265, FT-NMR Aldrich Catalog 1(2), 1359A, FT-IR 1(2), 355A.
6. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 1088, FT-NMR Aldrich Catalog 1(2), 1402B, FT-IR 1(2), 375C.
7. *Beil. 10*, 659, NMR Aldrich Catalog II(2), 403B, FT-IR 1(2), 428A.
8. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 6974, FT-NMR Aldrich Catalog 1(2), 473A, FT-IR 1(1), 1202B.
9. Villineuve, G. B.; Chan, T. H. *Tetrahedron Lett.* **1997**, *38* (37), 6489–6492.
10. Yuzuri, T.; Suezawa, H.; Hirota, M. *Bull. Chem. Soc. Jpn* **1994**, *67*, 1664–1673.
11. *Beil. 13*, 435, NMR Aldrich Catalog II(1), 1013B, IR III, 724E.
12. Nunno, L. D.; Scilimati, A. *Tetrahedron* **1986**, *42* (14), 3913–3920.
13. Murahashi, S.-I.; Naota, T. *Synthesis* **1993**, 433–440.
14. Harle, H.; Jochims, J. C. *Chem. Ber.* **1986**, 1400–1412.
15. Toda, F.; Miyamoto, H.; Kanemoto, K.; Tanaka, K.; Takahashi, Y.; Takenaka, Y. *J. Org. Chem.* **1999**, *64*, 2096–2102.
16. Tanaka, M. *Tetrahedron Lett.* **1980**, *21*, 2959–2962.
17. Papadopoulos, E. P. *J. Org. Chem.* **1974**, 2540–2542.
18. Tanaka, M. *Bull. Chem. Soc. Jpn* **1981**, 637–638.
19. Blake, A. J.; McNab, H.; Murray, M. E. A. *J. Chem. Soc. Perkin Trans. I* **1989**, 589–595 and references cited therein.
20. Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1980**, *45*, 114–122.
21. Abdel-Khalik, M. M.; El-Nagdi, M. H.; Agamy, S. M. *Synthesis* **2000**, *8*, 1166–1169.
22. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 6098, FT-NMR Aldrich Catalog 1(2), 452A, FT-IR 1(1), 1189C.
23. Compared with IR and NMR spectra measured for pure sample purchased from Aldrich Chemical Company.
24. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 47, FT-NMR Aldrich Catalog 1(2), 1360B, FT-IR 1(2), 356B.
25. Paredes, R.; Bastos, H.; Montoya, R.; Chavez, A. L. *Tetrahedron* **1988**, 6821–6830.
26. Baudin, J.-B.; Julia, S. A.; Ruel, O. *Tetrahedron* **1987**, *43* (5), 881–889.
27. *The Merck Index*, 12th ed.; Windholz, M., Ed.; Merck and Co Inc: Rahway, NJ; p 3284, FT-NMR Aldrich Catalog 1(2), 454C, FT-IR 1(1), 1191B.
28. Sharp, J. T.; Gosney, I.; Rowley, A. G. *Practical Organic Chemistry*; Chapman & Hall: London, 1989; p 51.