Gas-phase pyrolysis of N-alkoxyphthalimides to functionally substituted aldehydes: kinetic and mechanistic study

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Abstract

Flash vacuum Pyrolysis (FVP) of primary N-alkoxyphthalimides at 400-500 °C and 0.02 Torr gave functionally substituted aldehydes. A mechanism of this pyrolytic transformation was proposed based on the kinetic data and product analysis.

Keywords: FVP, N-alkoxyphthalimides, aldehydes, kinetics, reaction mechanism

Introduction

Substituted aldehydes and ketones are important intermediates in pharmaceutical and cosmetic industries,¹⁻³ While synthetic approaches to simple aldehydes are well established,⁴ synthetic approaches to functionally substituted ones are not. FVP has been used in straightforward synthesis of many organic compounds which are not readily obtainable from reactions in solution. We have combined mechanistic and kinetic investigations to probe the gas-phase pyrolytic reaction in the synthesis of a wide rang of organic compounds.⁵⁻⁸ In this work we wish to report further application of FVP in organic synthesis by describing a possible route for conversion of alkyl halides via their corresponding N-alkoxyphthalimides to functionally substituted aldehydes.

Results and Discussion

Synthesis

N-Hydroxyphthalimide **1** was reacted with alkyl halides **2a-n** to produce the corresponding *N*-alkoxyphthalimides **3a-n**, some of which are new compounds.

Pyrolysates and mechanism of pyrolytic reactions

Reaction products from FVP of N-alkoxyphthalimides **3a-n** were obtained at 400-500 °C and 0.02 Torr and were characterized as the corresponding functionally substituted aldehydes **5a-n** and phthalimide **6** (Scheme 1).



Scheme 1

Table 1	Products	of FVP	of 3a-n,	and %	yield
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Cpd	R	% Yie	ld (FVP)	Temp. ⁰C
		5a-n	6	
3a	CH ₃ CO	14	60	400
b	C ₆ H ₅ CO	46	46	400
с	CH ₃ COCH ₂	18	67	400
d		13	49	500
e	Me N—CO Me	14	45	500
f	C ₂ H ₅ OCO	22	57	400
g	NC	12	74	400
h	p-CH ₃ C ₆ H ₄	28	61	500
i	p-NCC ₆ H ₄	32	60	500
j	p-ClC ₆ H ₄	27	63	500
k	C_6H_5	38	50	500
l	<i>p</i> -CH ₃ OC ₆ H ₄ CO	49	50	400
m	p-ClC ₆ H ₄ CO	38	52	400
n	<i>p</i> -O ₂ NC ₆ H ₄ CO	32	58	500

The pyrolysates were qualitatively analyzed by HPLC, yields of each products was calculated by ¹H NMR (Table 1). The possible mechanistic route for the formation of **5** and **6** involves semiconcerted six-membered transition state **4**, it is to be noted that substituted aldehydes **5a-n** and phthalimide **6** are the only identifiable products isolated from this pyrolytic reaction. We have extended this approach for the synthesize of functionally substituted aldehydes, so *N*-acyloxymethoxyphthalimide **3a,b** and **1** were converted to phenylhydrazones **7a-c** this accomplished by the reaction with phenylhydrazones **9a-c** and phthalimide **6**. Increasing the pyrolysis temperature to 500 °C led to decomposition of compounds **9a-c** yielding aniline, and the corresponding nitriles. This pyrolytic reaction provides new access for the synthesis of aldehydes **9a-c.** The literature shows only two synthetic methods to prepare **9a**.⁹



Scheme 2

Table 2.	Products of FV	'P of 7a-c	and %	yields	
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Cpd	R	% yield (FVP)		Temp. °C
		6	9a-c	
7a	CH ₃	55	45	400
b	C_6H_5	55	38	400
c	p-CH ₃ OC ₆ H ₂	57	40	400

Kinetic studies

In the static reactor system, each substrate behaved well kinetically and gave excellent and reproducible first-order rate coefficients with linearity up to 95% reaction and with no deviation in the Arrhenius plots. Since six fold changes in the amount of substrate used per kinetic run

gave no significant change in rate coefficient, these reactions were deemed to be first-order process. The homogeneity of the reaction was tested by comparing the kinetic rate using an empty reaction vessel with that of similar vessel packed with glass helices, this increase in the surface to volume of approximate nine fold has not affected the kinetic rate. The kinetic data of the pyrolytic gas-phase elimination reaction of the N-alkoxyphthalimides under study are given in (Table 2). Each rate constant at any given temperature represents an average of two values obtained in two separate kinetic runs conducted at the same temperature. The agreement among the values at the rate constants in each run is within $\pm 2\%$. Each kinetic run was monitored until 90-95% of the reaction was completed. Arrhenius plots were linear over the studied temperature and reaction range.

Molecular reactivity

According to the pyrolysate of the pyrolytic reaction of the *N*-alkoxyphthalimides **3a-n** which eliminates to aldehydes **5a-n** and phthalimide **6**, a mechanistic pathway has been suggested as shown in (scheme 1), this involves a semiconcerted process with six-membered transition state 4, accordingly this reaction should be aided by greater electron- withdrawal from R, since this will increase the acidity of the hydrogen atom involved in the transition state which will facilitate the C-H^{*} bond breaking. Rate coefficients presented in Table 2 shows that the most reactive N-alkoxyphthalimides is **3a** (R = -COCH₃) with rate coefficient of 4.62 s⁻¹ at 500 K. This is 5.8 x 10^6 fold more reactive than the least reactive alkoxyphthalimide **3k** (R = C₆H₅). The analysis of the relative contribution to molecular reactivity from the polarization of the C-H^{*} bond involved in the transition state explains this dramatic drop in the reactivity of the pyrolytic elimination of aldehyde between **3a** and **3k**, this attributed to the big difference in the acidity of the hydrogen atom of the two compounds.

The acidity of this hydrogen atom [H^{*}] in substrates **3a-k** increases from $X = RCO > CN \cong CO_2R \cong CONR_2 > Ar$ in parallel comparison with the acidity of the following carbon acids.¹⁰ (Scheme 3)

$$\begin{array}{c} O \\ RC - CH_3 > NC - CH_3 \cong ROC - CH_3 \cong R_2N - C - CH_3 > Ar \\ R = CH_3, Ph \\ pKa \cong 19\text{-}20 \\ pKa \cong 25\text{-}30 \\ pKa \cong 40 \end{array}$$

Scheme 3

			\wedge			
				N—0		
				X		
Cpd.	R	T/K	10 ⁴ k /s ⁻¹	log A /s ⁻¹	Ea / k J mol ⁻¹	K500K/s ⁻¹
3a	CH ₃ CO	382.95	0.174	18.3 ± 0.69	351.2 ± 13.2	4.62
		388.95	0.419			
		394.85	1.124			
		400.55	1.649			
		406.55	3.816			
		412.55	7.343			
		424.25	35.73			
3 b	C ₆ H ₅ CO	359.75	1.015	$11.6~\pm~0.47$	$222.3~\pm~9.00$	2.36
		369.75	2.720			
		379.75	5.705			
		389.75	15.50			
		399.75	38.29			
3c	CH ₃ COCH ₂	359.65	0.893	$7.91~\pm~0.43$	151.5 ± 8.23	2.12×10^{-1}
		369.65	1.878			
		379.55	4.598			
		389.55	8.517			
		399.55	13.20			
		409.55	26.32			
3d	oN−co	462.25	0.293	16.7 ± 0.20	188.1 ± 1.82	1.21×10^{-3}
		472.15	0.876			
		481.95	2.227			
		491.75	5.346			
		502.00	14.55			
		511.85	34.83			
3e	Me N—CO	499.25	4.363	$3.38~\pm~0.04$	64.46 ± 0.37	4.46×10^{-4}
	Me					
		525.15	9.445			
		536.85	12.82			
		548.95	17.74			
		561.05	24.25			
3f	C ₂ H ₅ OCO	508.25	3.228	$9.47~\pm~0.13$	$181.3~\pm~2.49$	1.78×10^{-4}
		518.25	5.371			

Table 3. Rate coefficient (k/s⁻¹) and Arrhenius parameters of compounds 3a-k

Table 3. Continued

Cpd.	R	T/K	104k /s-1	log A /s-1	Ea / k J mol-1	K500K/s-1
		528.25	7.250			
		538.25	14.39			
		548.25	30.55			
3g	NC	509.45	1.542	$10.7~\pm~0.62$	$205.5~\pm~11.9$	6.17×10^{-5}
		519.45	2.502			
		529.45	4.018			
		539.45	6.014			
		549.45	14.43			
		559.45	22.41			
		569.45	46.98			
3h	p-CH ₃ C ₆ H ₄	550.85	0.923	$9.84~\pm~0.58$	$146.3~\pm~6.43$	3.63×10^{-6}
		562.75	2.020			
		574.95	3.615			
		586.75	5.782			
		598.55	10.89			
		610.65	24.39			
3i	p-NCC ₆ H ₄	544.95	0.727	$11.3~\pm~0.47$	160.6 ± 5.16	$2.97 imes 10^{-6}$
		555.05	1.456			
		565.15	2.637			
		574.85	4.101			
		585.05	7.129			
		594.65	13.83			
		604.75	27.05			
3j	p-ClC ₆ H ₄	554.05	0.680	$12.2~\pm~0.07$	$174.1~\pm~0.83$	1.12×10^{-6}
		565.95	1.462			
		578.05	3.167			
		589.95	6.581			
		601.75	13.49			
		614.05	26.97			
3k	C_6H_5	548.30	0.428	$12.9~\pm~0.50$	$182.0~\pm~5.53$	7.95×10^{-7}
		556.85	0.563			
		569.95	1.701			
		582.85	4.359			
		595.65	9.065			
		608.75	21.21			
		618.45	32.05			

Each compound of (3a-k) has a constant factor difference than the above CH^{*} acids which is the *N*-oxyphthalimido group. The latter group should increase the acidity of the above carbon acids by a constant value. In absence of pKa value for our investigated compounds, we have correlated rate coefficient (at 500K) of the gase-phase pyrolysis of **3a-k** with the pKa of the above carbon acids (Table 3). The higher rate of pyrolysis of the amide **3d** over **3e** could be attributed to the less steric influence and the more inductive effect of the oxygen atom of the morpholide moiety in the former. The reaction pathway suggested to account for product formation is well rationalized by the kinetic investigation of these compounds.

Table 4. Rate coefficients of gas-phase pyrolysis of compounds **3a-k** at 500 K and pKa value of the corresponding carbon acids

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Cod.	R	рКа	k500K
3 a	CH ₃ CO	10.20	4.62
3 b	C ₆ H ₅ CO	19-20	2.36
3d			1.21x10 ⁻³
3e	N N	≅ 25-30	4.46x10 ⁻⁴
3f	C ₂ H ₅ OCO		1.78x10 ⁻⁴
3g	NC		6.17x10 ⁻⁵
3h	p-CH ₃ C ₆ H ₄		3.63x10 ⁻⁶
3i	p-NCC ₆ H ₄	≅ 40	2.97x10 ⁻⁶
3j	p-ClC ₆ H ₄		1.12×10^{-6}
3k	C_6H_5		7.95x10 ⁻⁷

Conclusions

The present work describes a functional group transformation of alkyl halides via their corresponding *N*-alkoxyphthalimide to the corresponding aldehydes. It also provides a new access to functionally substituted aldehydes. Product analysis suggests a mechanistic pathway involves a six-membered transition states, kinetic data supports well this mechanism.

Experimental Section

General. All melting points are uncorrected. ¹H and ¹³C NMR spectra were recorded on a Bruker DPX 400 MHz super-conducting NMR spectrometer. Mass spectra were measured on VG Autospec-Q (high resolution, high performance, tri-sector GC/MS/MS) and with LCMS using Agilent 1100 series LC/MSD with an API-ES/APCI ionization mode. Microanalysis was performed on a LECO CH NS-932 Elemental Analyzer. The HPLC analysis was performed using a Metrohm HPLC (pump model 7091C and SHIMADZU SPD-10 UV/VIS detector), and Suppelco ABZ⁺ chromatography column (2.5 cm length and 4.6 mm ID, for 5 µm sample). The reactor used for kinetic and product analysis is a Chemical Data System (CDS) custom-made pyrolyzer consisting of an insulated aluminum-alloy block fitted with a platinum resistance thermocouple connected to a Comark microprocessor thermometer for reactor temperature readout, accurate to < 0.5 °C. The alloy was chosen for its high thermal conductivity and low temperature gradient, and may be heated for up to 530 °C. The temperature of the reactor is controlled by means of a Eurotherm 093 precision temperature regulator to provide 0.1 °C incremental changes. The reaction tubes were Pyrex: 8 cm long for kinetic runs, and 12 cm for product analysis; with internal and outer diameters 1.5 cm and 1.7 cm, respectively, for both tubes.

Kinetic runs and data analysis

Stock solution (7 mL) was prepared by dissolving 5-10 mg of the substrate in acetonitrile to give a concentration of 1×10^3 - 2×10^3 ppm. An internal standard was then added, the amount of which was adjusted to give the desired peak area ratio of substrate to standard (2.5 : 1). The solvent and standard were selected to be stable under the conditions of pyrolysis, and because they do not interact or react with either substrate or product. The internal standard used in the present study was chlorobenzene and 1,3-dichlorobenzene. Each mixture was filtered before use to ensure a homogeneous solution.

The ratio of the amount of substrate with respect to the internal standard was calculated from the ratio of the substrate peak area to the peak area of the internal standard. The kinetic rate was obtained by tracing the rate of disappearance of the substrate with respect to the internal standard as follows: An aliquot part (0.2 mL) of each solution containing the substrate and the internal standard was pipetted into the pyrolysis tube, which was then cooled in liquid nitrogen and sealed at reduced pressure (0.28 mbar). The tube was then placed in the pyrolyzer for 6 minutes under non-thermal conditions (ambient temperature). A sample was then analyzed using HPLC with UV/VIS detector at wavelength, $\lambda = 256$ nm to calculate the standardization value (A_o). Several HPLC measurements were obtained with an accuracy $\geq 2\%$. The temperature of the pyrolysis block was then raised until ca 10% pyrolysis of the substrate was deemed to occur over 600 s interval. This process was repeated after each ca 10 °C rise in the reaction temperature until > 95% reaction was achieved. The relative ratios of the sample and the internal standard (A) at each reaction temperature was calculated for a minimum of two kinetic runs made at each of

these temperatures that were in agreement to within $\pm 2\%$ in order to ensure reproducible values of (A). Treatment of the kinetic data has been detailed elsewhere.⁵

N-Alkoxyphthalimides 3a-n. General procedure

To a mixture of *N*-hydroxyphthalimide **1** (1.63 gm, 10 mmol), anhydrous potassium carbonate (0.5 gm) in dry DMSO (20 mL) was added the appropriate alkyl halides **2a-n** (10 mmol). The reaction mixture was stirred at room temoerature over night, and then ice water (50 mL) was added. The precipitate was then collected and crystallized from the proper solvent.

N-(2-Oxopropoxy)phthalimide (3a). Colorless crystals from ethanol, mp 123-124 °C (lit.¹¹ mp 120-122 °C) yield (68%). MS: m/z = 219 (M⁺, 60%), 174 (45%), 161 (100%), 147 (70%). ¹H NMR (DMSO-d₆) δ 7.88 (s, 4H), 4.88 (s, 2H, CH₂), 2.22 (s, 3H, CH₃). ¹³C NMR (DMSO-d₆) δ 203.2, 163.2, 135.4, 129.1, 123.8, 81.3, 27.2.

3.3.2 *N*-(**2-Oxo-2-phenylethoxy)phthalimide (3b).** White crystals from ethanol, yield (74%), mp 134-136 °C (lit.¹² mp 135-136 °C). MS: m/z = 281 (M⁺,10%), 250 (20%), 222 (40%), 147 (50%), 105 (100%). ¹H NMR (CDCl₃) δ 7.97 (d, 2H, *J* 7.8 Hz), 7.84-7.81 (m, 2H), 7.76-7.73 (m, 2H), 7.60 (t, 1H, *J* 7.4 Hz), 7.48 (t, 2H, *J* 7.6 Hz), 5.44 (s, 2H, CH₂). ¹³C NMR (DMSO-d₆) δ 198.2, 168.2, 140.3, 139.7, 139.5, 134.4, 134.1, 133.4, 128.8, 84.1.

3.3.3 2-(3-Oxobutoxy)phthalimide (3c). White crystals from pet. Ether (60-80), yield (43%), mp 104-105 °C. MS: m/z = 233 (M⁺, 30%), 147 (100%). IR (KBr) 3069, 3008, 2970, 1727, 1630, 1373, 1184, 1130, 1032, 877, 703. ¹H NMR (CDCl₃) δ 7.87-7.84 (m, 2H), 7.79-7.76 (m, 2H), 4.52 (t, 2H, *J* 6.2 Hz), 2.98 (t, 2H, *J* 6.2 Hz), 2.28 (s, 3H, CH₃). ¹³C NMR (CDCl₃) δ 205.3, 163.6, 134.5, 128.7, 123.6, 72.8, 42.0, 30.3. Anal. Calcd for C₁₂H₁₁NO₄ (233.2): C 61.80; H 4.75; N 6.01. Found: C 61.75; H 4.66; N 6.08.

N-(2-Morpholinyl-2-oxoethoxy)phthalimide (3d). White crystals from ethyl acetate/petrolum ether (60-80), yield (58%), mp 176-178 °C. LCMS: m/z = 291 (M + 1). IR (KBr) 3029, 2996, 2855, 1792, 1745, 1652, 1484, 1445, 1391, 1245, 1118, 1112, 1002, 696. ¹H NMR (CDCl₃) δ 7.87-7.7.84 (m, 2H), 7.79-7.77 (m, 2H), 4.85 (s, 2H, CH₂), 3.86-3.84 (m, 2H), 3.79-3.76 (m, 4H), 3.67-3.65 (m, 2H). ¹³C NMR (CDCl₃) δ 164.3, 163.0, 134.8, 128.7, 123.8, 75.8, 66.6, 66.5, 46.4, 42.3. Anal. Calcd for C₁₄H₁₄N₂O₅ (290.3): C 57.93; H 4.86; N 9.65. Found: C 57.72; H 4.86; N 9.55. ¹³

N-(*N*,*N*-Dimethylcarboxamidomethoxy)phthalimide (3e). White crystals from ethyl acetate/pet. ether (60-80), yield (58%), mp 157-158 °C (lit.¹⁴ mp 155-157 °C). LCMS: m/z = 249 (M + 1). IR (KBr). 3029, 2935, 1724, 1649, 1381, 1186, 1133, 1183, 1017, 993, 874, 699. ¹H NMR (CDCl₃) δ 7.86-7.82 (m, 2H), 7.78-7.75 (m, 2H), 4.86 (s, 2H, CH₂), 3.25 (s, 3H, CH₃), 3.00 (s, 3H, CH₃).¹³C NMR (CDCl₃) δ 165.7, 163.1, 134.8, 128.8, 123.7, 75.7, 37.2, 35.6. Anal. Calcd for C₁₂H₁₂N₂O₄ (248.2): C 58.06; H 4.87; N 11.28. Found: C 58.00; H 4.86; N 11.19.

N-Ethoxycarbonylmethoxyphthalimide (3f). White crystals from ethanol, yield (75%), mp 97-98 °C (lit.¹⁵ mp 95-97 °C). ¹H NMR (CDCl₃) δ 7.89-7.85 (m, 2H), 7.83-7.80 (m, 2H), 4.83 (s, 2H), 4.29 (q, 2H, *J* 7.2 Hz), 1.32 (t, 3H, *J* 7.2 Hz). *N*-Cyanomethoxyphthalimide (3g). White crystals from ethanol, mp 155-156 °C, yield (64%). MS: m/z = 202 (M⁺, 30%), 146 (15%), 132 (70%), 104 (100%). IR (KBr) 3076, 3022, 2980, 2228, 1771, 1740, 1462, 1417, 1356, 1322, 1183, 1127, 876, 706. ¹H NMR (DMSO-d₆) δ 7.93-7.89 (m, 4H), 5.24 (s, 2H, CH₂). ¹³C NMR (DMSO-d₆) δ 163.0, 135.6, 129.0, 124.1, 116.2, 63.2. Anal. Calcd for C₁₀H₆N₂O₃ (202.2): C 59.41; H 2.99; N 13.86. Found: C 59.38; H 2.86; N 13.79.

N-p-Methylbenzyloxyphthalimide (3h). White crystals from ethanol, yield (87%), mp 193-194 °C (lit.¹⁶ mp 194 °C). ¹H NMR (CDCl₃) δ 7.85-7.81 (m, 2H), 7.77-7.74 (m, 2H), 7.44 (d, 2H, *J* 7.8 Hz), 7.20 (d, 2H, *J* 7.8 Hz), 5.19 (s, 2H), 2.42 (s, 3H).

N-p-Cyanobenzyloxyphthalimide (3i). White crystals from ethanol, yield (81%), mp 202-204 °C (lit.¹⁷ mp 199-200 °C). ¹H NMR (DMSO-d₆) δ 7.90 (d, 2H, *J* 8.0 Hz), 7.88-7.84 (m, 4H), 7.75 (d, 2H, *J* 8.0 Hz), 5.28 (s, 2H).

N-p-Chlorobenzyloxyphthalimide (3j). White crystals from ethanol, yield (86%), mp 138-140 °C (lit.¹⁸ mp 137-138 °C). ¹H NMR (CDCl₃) δ 7.85-7.82 (m, 2H), 7.77-7.73 (m, 2H), 7.50 (d, 2H, *J* 8.3 Hz), 7.37 (d, 2H, *J* 8.3 Hz), 5.20 (s, 2H, CH₂). ¹³C NMR (CDCl₃) δ 163.3, 135.3, 134.5, 132.0, 131.0, 128.6, 128.5, 123.4, 78.8.

N-Benzyloxyphthalimide (3k). White crystals from ethanol, yield (81%), mp 143-144 °C (lit.¹⁹ mp 142-143 °C). ¹H NMR (CDCl₃) δ 7.85-7.81 (m, 2H), 7.78-7.75 (m, 2H), 7.58-7.55 (m, 2H), 7.41-7.38 (m, 3H), 5.24 (s, 2H). ¹³C NMR (CDCl₃) δ 163.3, 134.3, 133.4, 129.7, 129.2, 128.6, 128.4, 123.5, 79.7.

N-(2-Oxo-2-*p*-methoxyphenylethoxy)phthalimide (3l). White crystals from ethanol, yield (80%), mp 148-150 °C. LCMS: m/z = 312 (M + 1). ¹H NMR (CDCl₃) δ 8.00 (dd, 2H, *J* 8.4, 1.6 Hz), 7.87-7.82 (m, 2H), 7.78-7.73 (m, 2H), 6.96 (dd, 2H, *J* 8.4, 1.6 Hz), 5.39 (s, 2H), 3.90 (s, 3H). ¹³C NMR (CDCl₃) δ 190.7, 164.2, 163.0, 134.4, 129.7, 128.9, 127.6, 123.7, 114.2, 78.5, 55.5. Anal. Calcd for C₁₇H₁₃NO₅ (311.3): C 65.59; H 4.21; N 4.50. Found: C 65.48; H 4.16; N 4.49.

N-(2-Oxo-2-*p*-chlorophenylethoxy)phthalimide (3m). White crystals from ethanol, yield (83%), mp 164-165 °C. (Lit.²⁰ mp 162-163 °C). LCMS: m/z = 318 (M + 3), 316 (M + 1). ¹H NMR (CDCl₃) δ 8.01 (dd, 2H, *J* 8.4, 1.6 Hz), 7.89-7.86 (m, 2H), 7.81-7.78 (m, 2H), 7.51 (dd, 2H, *J* 8.4, 1.6 Hz), 5.37 (s, 2H). ¹³C NMR (CDCl₃) δ 191.3, 163.0, 140.4, 134.5, 132.5, 129.4, 129.0, 128.5, 123.5, 78.4.

N-(2-Oxo-2-*p*-nitrophenylethoxy)phthalimide (3n). Colorless crystals from ethanol, yield (88%), mp 180-82 °C (Lit.²⁰ mp. 178-180 °C). LCMS: m/z = 327 (M + 1). ¹H NMR (CDCl₃) δ 8.39 (d, 2H, *J* 8.8 Hz), 8.28 (d, 2H, *J* 8.8 Hz), 7.90-7.886 (m, 2H), 7.83-7.79 (m, 2H), 5.41 (s, 2H). ¹³C NMR (DMSO_{d6}) δ 192.3, 162.6, 150.2, 139.0, 134.9, 129.6, 128.6, 123.9, 123.3, 78.9.

Synthesis of compounds 7a-c. General procedure

To a mixture of compounds **3a,b,l** (10 mmol), phenylhydrazine (10 mmol) in ethanol (20 mL) was heated for 30 minutes and then ice water (50 mL) was added to the reaction mixture. The yellow precipitate so formed was then collected and crystallized from ethanol to give **7a-c**.

2-(2-Phenylhydrazinopropoxy)isoindole-1,3-dione (7a). Yellow crystals from ethanol, mp 135-136 °C yield (70%). LCMS: *m/z* = 310 (M + 1). MS: *m/z* = 309 (M⁺, 60%), 174 (45%), 161 (100%), 147 (70%). IR (KBr) 3334, 3052, 2915, 1726, 1601, 1494, 1369, 1242, 1123, 974, 876, 749, 695. ¹H NMR (CDCl₃) δ 7.79-7.76 (m, 2H), 7.71-7.67 (m, 2H), 7.25 (br, 1H), 7.13 (t, 2H, *J* 7.6 Hz), 6.89 (d, 2H, *J* 7.8 Hz), 6.79 (t, 1H, *J* 7.4 Hz), 4.76 (s, 2H, CH₂), 2.15 (s, 3H, CH₃).¹³C NMR (CDCl₃) δ 167.9, 142.5, 142.3, 134.4, 132.6, 129.1, 123.6, 123.0, 114.4, 68.9, 13.1. Anal. Calcd for C₁₇H₁₅N₃O₃ (309.3): C 66.01; H 4.89; N 13.58. Found: C 66.00; H 4.86; N 13.49.

2-(2-Phenyl-2-phenylhydrazinoethoxy)isoindole-1,3-dione (7b). Yellow crystals from ethanol, mp 165-166 °C yield (78%). LCMS: m/z = 372 (M + 1). MS: m/z = 371 (M⁺, 60%), 209 (75%), 103 (100%). IR (KBr) 3303, 3036, 1785, 1729, 1600, 1492, 1256, 1182, 1136, 974, 878, 754, 696. ¹H NMR (DMSO-d₆) δ 10.06 (s, 1H, NH), 7.96-7.93 (m, 2H), 7.91-7.88 (m, 2H), 7.81 (d, 2H, *J* 8.4 Hz), 7.44 (t, 2H, *J* 8.0 Hz), 7.36-7.32 (m, 5H), 6.91-6.87 (m, 1H), 5.39 (s, 2H). ¹³C NMR (CDCl₃) δ 163.5, 144.7, 137.2, 135.2, 135.0, 129.2, 128.6, 127.8, 125.0, 123.5, 122.9, 120.3, 112.9, 69.2. Anal. Calcd for C₂₂H₁₇N₃O₃ (371.4): C 71.15; H 4.61; N 11.31. Found: C 71.08; H 4.46; N 11.29.

2-(2-*p***-Methoxyphenyl-2-phenylhydrazinoethoxy)isoindole-1,3-dione (7c).** Yellow crystals from ethanol, mp 168-170 °C yield (68%). LCMS: m/z = 402 (M + 1). MS: m/z = 401 (M⁺, 60%), 174 (45%), 161 (100%), 147 (70%). IR (KBr) 3281, 3029, 2953, 1784, 1732, 1494, 1354, 1255, 1160, 977, 829, 698. ¹H NMR (CDCl₃) δ 9.92 (s, 1H, NH), 7.97-7.94 (m, 2H), 7.92-7.89 (m, 2H), 7.76 (d, 2H, *J* 8.4 Hz), 7.33-7.30 (m, 4H) 7.01 (d, 2H, *J* 8.4 Hz), 6.89-6.86 (m, 1H), 5.35 (s, 2H), 3.79 (s, 3H). ¹³C NMR (CDCl₃) δ 163.9, 159.7, 145.4, 135.0, 135.5, 130.2, 129.7, 129.1, 127.0, 124.0, 120.5, 114.5, 113.3, 69.9, 55.7. Anal. Calcd for C₂₃H₁₉N₃O₄ (401.4): C 68.82; H 4.77; N 10.47. Found: C 68.78; H 4.76; N 10.39.

Product analysis

Flash vacuum pyrolysis

The apparatus used was similar to the one which has been described in our recent publication.⁶ The sample was volatilized from a tube in a Buchi Kugelrohr oven through a 30 x 2.5 cm horizontal fused quartz tube. This was heated externally by a Carbolite Eurotherm tube furnace MTF-12/38A to a temperature of 500 °C, the temperature being monitored by 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 to be =10 ms. The different zones of the product collected in the U-shaped trap were analyzed by ¹H, ¹³C NMR, IR and GC-MS. Relative and percent yields were determined from NMR.

Pyrolysis products

2-Oxopropanal (5a). MS: m/z = 72 (M⁺, 20%). ¹H NMR (CDCl₃) δ 9.22 (s, 1H), 2.44 (s, 3H, CH₃).²¹

Phenylglyoxal (5b). Mp 90-91 °C (lit.²² mp 90-91 °C). ¹H NMR (CDCl₃) δ 9.69 (s, 1H), 8.21 (d, 2H, *J* 7.6 Hz), 7.66 (t, 1H, *J* 7.6 Hz), 7.52 (d, 2H, *J* 7.6 Hz).

3-Oxobutanal (5c). MS: $m/z = 86 (M^+, 20\%)$. ¹H NMR (CDCl₃) δ 9.82 (s, 1H), 4.52 (s, 2H, CH₂), 2.32 (s, 3H, CH₃).²³

Morpholino-4-yl-oxoacetaldehyde (5d). MS: m/z = 143 (M⁺, 40%), 114 (100%). ¹H NMR (CDCl₃) δ 9.48 (s, 1H), 3.58-3.55 (m, 4H), 3.42-3.39 (m, 4H).²⁴

N,*N*-Dimethylglyoxylamide (5e). MS: m/z = 101 (M⁺, 30%), 45 (60%). ¹H NMR (CDCl₃) δ 9.51 (s, 1H), 3.20 (s, 3H, CH₃), 3.06 (s, 3H, CH₃).²⁵

Ethyl glyoxalate (5f). LCMS: m/z = 102 (M + 1). ¹H NMR (CDCl₃) δ 9.42 (s, 1H), 4.40 (q, 2H, *J* 6.8 Hz), 1.38 (t, 3H, *J* 6.8 Hz).²⁶

Glyoxylonitrile (5g). MS: $m/z = 55 \text{ (M}^+, 80\%)$. ¹H NMR (CDCl₃) δ 9.32 (s, 1H). IR (KBr) 2252 (CN), 1737 (CO).²⁷

p-Methylbenzaldehyde (5h). ¹H NMR (CDCl₃) δ 9.99 (s, 1H), 7.80 (d, 2H, *J* 8.0 Hz), 7.35 (d, 2H, *J* 8.0 Hz), 2.40 (s, 3H).^{28a}

p-Cyanobenzaldehyde (5i). ¹H NMR (CDCl₃) δ 10.12 (s, 1H), 8.02 (d, 2H, *J* 8.4 Hz), 7.87 (d, 2H, *J* 8.4 Hz).²⁹

p-Chlorobenzaldehyde (5j). ¹H NMR (CDCl₃) δ 10.01 (s, 1H), 7.89 (d, 2H, *J* 8.4 Hz), 7.54 (d, 2H, *J* 8.4 Hz).^{28b}

Benzaldehyde (5k). ¹H NMR (CDCl₃): δ 10.05 (s, 1H), 7.90 (d, 2H, *J* 7.6 Hz), 7.67 (t, 1H, *J* 7.4 Hz), 7.56 (t, 2H, *J* 7.5).^{26c}

p-Methoxyphenylglyoxal (51). Yellow oil. LCMS: m/z = 165 (M + 1). ¹H NMR (CDCl₃) δ 9.67 (s, 1H), 8.23 (dd, 2H, *J* 8.4, 1.6 Hz), 6.97 (dd, 2H, *J* 8.4, 1.6 Hz), 3.78 (s, 3H, OCH₃). ¹³C NMR (CDCl₃) δ 190.2, 187.1, 167.4, 131.0, 129.2, 114.7, 55.9.³⁰

p-Chlorophenylglyoxal (5m). Mp 42-44 °C (lit.³¹ mp 40-41 °C). LCMS: m/z = 171 (M + 3), 169 (M + 1). ¹H NMR (CDCl₃) δ 9.64 (s, 1H), 8.31 (d, 2H, *J* 8.4 Hz), 8.16 (d, 2H, *J* 8.4 Hz). ¹³C NMR (DMSO-d₆) δ 191.4, 189.3, 141.5, 131.3, 129.2, 129.1.

p-Nitrophenylglyoxal (5n) Yellow oil. LCMS: m/z = 180 (M + 1). ¹H NMR (CDCl₃) δ 9.68 (s, 1H), 8.39 (d, 2H, *J* 8.8 Hz), 8.06 (d, 2H, *J* 8.8 Hz). ¹³C NMR (CDCl₃) δ 191.4, 187.3, 154.5, 142.5, 130.6, 124.2.³⁰

Phthalimide (6). Mp 232-234 °C (lit.³² mp 232-235 °C). ¹H NMR (DMSO-d₆) δ 10.83 (s, 1H, NH), 7.90-7.87 (m, 4H). ¹³C NMR (DMSO-d₆) δ 167.9, 134.4, 132.6, 123.6.

2-Phenylhydrazonopropionaldehyde (9a). Mp.116-118 °C (lit.³³ mp115-116 °C). LCMS: m/z = 163 (M + 1). ¹H NMR (CDCl₃) δ 9.51 (s, 1H, CHO), 8.21 (br, 1H, NH), 7.37 (t, 2H, *J* 7.6 Hz), 7.30 (d, 2H, *J* 7.8 Hz), 7.07 (t, 1H, *J* 7.4 Hz), 2.01 (s, 3H). ¹³C NMR (CDCl₃) δ 190.8, 134.4, 129.5, 123.6, 123.0, 114.4, 14.7.

Phenyl-(phenyhydrazono)acetaldhyde (9b). Mp. 113-115 °C (lit.³³ mp. 115-116 °C). LCMS: m/z = 225 (M + 1). ¹H NMR (CDCl₃) δ 9.47 (s, 1H, CHO), 8.45 (br, 1H, NH), 7.26 (d, 2H, *J* 7.8

Hz), 7.16 (t, 2H, *J* 7.6 Hz), 6.95 (t, 1H, *J* 7.6 Hz), 6.84 (d, 2H, *J* 7.8 Hz), 6.78 (t, 1H, *J* 7.7 Hz), 7.70 (t, 2H, *J* 7.6 Hz).

p-Methoxyphenyl-(phenylhydrazono)acetaldhyde (9c). Yellow crystals, mp. 112-14 °C. LCMS: m/z = 255 (M + 1). ¹H NMR (CDCl₃) δ 9.46 (s, 1H, CHO), 7.49 (d, 2H, *J* 8.0 Hz), 7.16 (t, 2H, *J* 7.8 Hz), 7.15 (t, 1H, *J* 7.6 Hz), 6.85-6.83 (m, 4H), 3.77 (s, 3H). ¹³C NMR (CDCl₃) δ 193.2, 160.5, 142.3, 133.7, 131.6, 127.3, 125.9, 123.4, 112.9, 112.4, 53.2. Anal. Calcd for C₁₅H₁₄N₂O₂ (254.3): C 70.85; H 5.55; N 11.02. Found: C 70.78; H 5.46; N 11.00.

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