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Montmorillonite K-10 as a catalyst in the synthesis of 5, 5-disubstituted hydantoins under ultrasound irradiation

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Abstract. The rapid and highly efficient synthesis of 5,5-disubstituted hydantoins achieved by three-component condensation of corresponding ketones and aldehydes, potassium cyanide and ammonium carbonate in an additional reaction under ultrasound irradiation by using montmorillonite K-10 as a heterogenous catalyst. Utilizing ultrasound irradiation and montmorillonite in this method has several benefits, for example short reaction time, high yield and use of recyclable catalyst.

Keywords. Ultrasound irradiation; 5,5-disubstituted hydantoin; montmorillonite K-10; Bucherer–Bergs reaction.

1. Introduction

Hydantoins (2,4-imidazolidine-diones) are an important class of heterocycles.[1] Hydantoin nucleus is a common 5-membered ring containing a reactive cyclic urea core.[2] Imidazolidine-diones are a class of bioactive molecules that have broad medicinal,[3] antiulcers,[4] anticonvulsants,[5] anti-tumour,[6] antiarrhythmic,[7] anticancer,[8] antimicrobial,[9] antidiabetic,[10] and agrochemical (herbicidal and fungicidal) applications.[11]

Hydantoin derivatives are synthetically valuable, for e.g., as precursors to amino acid and pyruvic acid derivatives.[12,13] Several methods are used for synthesis of 5,5-disubstituted hydantoins.[14–17] The Bucherer–Bergs synthesis is most commonly used for preparation of these heterocycles. It is multi-component reaction that yields hydantoins from the reaction of ketone (or aldehyde) with cyanide, ammonia and carbon dioxide or ammonium carbonate.[18] This reaction used in the preparation of 5,5-disubstituted hydantoin derivatives suffers from drawbacks such as low yield and long reaction time.

Consequently, it is desirable to develop an efficient and simple method to synthesize 5,5-disubstituted hydantoins. Catalysts are very useful in achieving this goal. In recent years, there has been considerable growth of interest in the catalysis of organic reactions by clays. Clays as heterogenous catalysts are helpful to the synthetic chemist in a big way. By-products can be avoided or minimized by these solid acids. Using montmorillonite K-10 as an economically solid catalyst has several advantages such as ease of handling, being inexpensive and mild reaction conditions.[19–21]

On the other hand, use of ultrasound irradiation for the optimization and acceleration of organic reactions has rapidly increased.[22–24] The combined use of ultrasound reduced the reaction time significantly. High local temperature and pressure produced by cavitation lead to a diverse set of applications of ultrasound such as accelerating the rate of reaction, changing the reaction pathway, enhancing chemical reactivity and important uses in synthetic organic compounds.[25,26]

This prompted us to study the possibility of preparation of 5,5-disubstituted hydantions using the Bucherer–Bergs method involving montmorillonite K-10 catalysis and utilizing ultrasound irradiation.

2. Experimental

2.1 *Materials and instruments*

In a typical procedure, chemicals were purchased from Merck chemical company. ^{1}NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX-400 Avance Spectrometer. Tetramethyl silane (TMS) was used as an internal reference. IR spectra were obtained on a Magna-550 Nicolet instrument. Vibrational transition frequencies were reported

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as wave numbers (cm^{-1}), and band intensities designated as weak (w), medium (m) and strong (s). Sonication was performed in a UP 400 S ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly into the reaction mixture. The operating frequency was 50 KHz and the output power was 0–400 W through manual adjustment. UV spectra were recorded on a Hitachi 200-20 spectrometer using spectrophotometric grade ethanol (Baker). Melting points were obtained with a micro melting point apparatus (Electrothermal, MK3) and are uncorrected. The characteristics of montmorillonite K-10 are: surface area = 220–270 $m^2\ g^{-1}$, bulk density = 300–370 g l^{-1}, specific gravity = 2.5 g ml, refractive index = 1.51, crystal system, monoclinic.

2.2 *General procedure for the synthesis of hydantoin derivatives involving montmorillonite K-10 under ultrasonic irradiation*

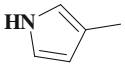
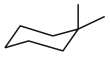
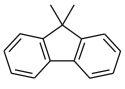
To a solution of 1 mmol of aldehyde or ketone, 1.3 mmol potassium cyanide, 6 mmol ammonium carbonate in 5 mL EtOH and 5 mL of H_2O, 100 mg montmorillonite K-10 was added and the mixture was exposed to ultrasonic irradiation at 45°C for the period as indicated in table 1. Progress of the reaction was monitored by TLC (petroleum ether: ethyl acetate, 1:1.2 v/v). The catalyst was removed by filtration and washed with pentane. Then, the reaction mixture was neutralized with diluted hydrochloric acid and filtered. The solid product obtained was washed with water and recrystallized from ethanol. Pure product was obtained in good yield (scheme 1). The structure of these compounds has been investigated using different methods of spectroscopy and spectrometry: UV, ^{1}H NMR, ^{13}C NMR, IR.

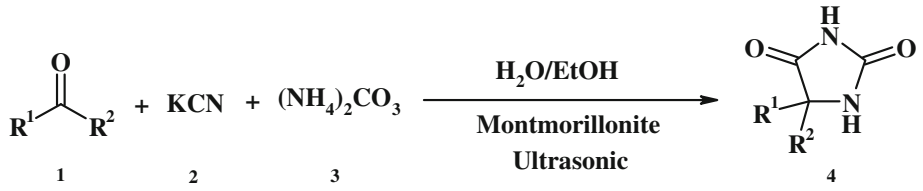
2.3 *Spectral data of 5,5-disubstituted hydantoins*

2.3a *5-Phenyl imidazolidine-2,4-dione ($C_9H_8N_2O_2$, **4a**)*: White powdery crystals; UV (CH_3OH) λ_{max}: 284 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.79 (s, 1H, N_3–H), 8.41(s, 1H, N_1–H), 7.31 (t, J = 6.8 Hz, 1H), 7.35 (d, J = 6.89 Hz, 2H), 7.40 (t, J = 6.89 Hz, 2H), 5.16 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 173.77 (C_4 = O), 157.67 (C_2 = O), 136.49 (C), 129.09 (2CH), 128.77 (2CH), 127.11 (CH), 62.26 (C_{spiro}); IR (KBr cm^{-1}) $\bar{\nu}$: 3500 (N–H, s), 3300 (N–H, s), 3150 (=C–H), 3024 (=C–H), 1745 (C = O), 1720 (C = O), 1450 (C = C), 1420 (N–H, b).

2.3b *5-(4-Methylphenyl)-imidazolidine-2,4-dione ($C_{10}H_{10}N_2O_2$, **4b**)*: White crystal; UV (CH_3OH) λ_{max}: 276 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.74 (s,

Table 1. Montmorillonite K-10 catalysed synthesis of 5,5-disubstituted hydantoins under ultrasonic irradiation.

Entry	R^1	R^2	Product	Time (min)/yield (%)	m.p.(°C) Rep.	m.p. (°C) Lit.
A	H	C_6H_5	**4a**	16/92	164–165	163 [12]
B	H	p-$CH_3C_6H_5$	**4b**	20/94	183–184	182.5 [27]
C	H	p-$OCH_3C_6H_5$	**4c**	26/88	193–197	–
D	H	o-$OCH_3C_6H_5$	**4d**	28/90	183–185	186–187 [27]
E	H	o-ClC_6H_5	**4e**	19/96	178–179	176 [27]
F	H		**4f**	18/94	259–262	258–261 [14]
G	H		**4g**	20/94	148–149	147 [27]
H	CH_3	i-Bu	**4h**	32/98	148–150	148 [27]
I	R=		**4i**	30/98	219–221	220 [12]
J	CH_3	C_6H_5	**4j**	30/87	197–199	195–196 [28]
K	CH_3	p-ClC_6H_4	**4k**	31/95	261–262	262–263 [29]
l	CH_3	m-$CH_3C_6H_4$	**4l**	50/97	180–182	175–180 [28]
M	CH_3	m-ClC_6H_4	**4m**	28/95	180–183	180–182 [28]
N	C_6H_5	C_6H_5	**4n**	72/86	295–296	297–298 [30]
O	R=		**4o**	82/85	300>	324–325 [27]



Scheme 1. Synthesis of hydantoin derivatives by using monmorillonite K-10 under ultrasonic irradiation.

1H, N_3–H), 8.35 (s, 1H, N_1–H), 7.19 (s, 4H), 5.09 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 174.82 (C = O), 157.97 (C = O), 138.01 (C), 133.57 (2CH), 129.64 (2CH), 127.08 (C), 61.46 (C–H), 21.15 (C–H); IR (KBr cm^{-1}) $\bar{\nu}$: 3524 (N–H, s), 3426 (N–H, s), 3050 (=C–H), 2970 (C–H), 1777 (C = O), 1755 (C = O), 1500 (C = C), 1448 (N–H, b).

2.3c *5-(4-Methoxyphenyl)-imidazolidine-2,4-dione* ($C_{10}H_{10}N_2O_3$, ***4c***): White needles; UV (CH_3OH) λ_{max}: 280 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.3 (s, 1H, N_3–H), 8.34 (s, 1H, N_1–H), 7.21 (d, J = 7.7 Hz, 2H), 6.94 (d, J = 7.7 Hz, 2H), 5.08 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 166.71 (C = O), 160.04 (C = O), 158.37 (C), 127.12 (2CH), 120.03 (2CH), 113.63 (C), 61.04 (C_{spiro}), 55.20 (C–H); IR (KBr cm^{-1}) $\bar{\nu}$: 3350 (N–H, m), 3215 (N–H, s), 1779 (C = O, s), 1732 (C = O, s), 1610 (C = C, w), 1515 (C = C, w), 1246 (C–O, m).

2.3d *5-2-Methoxyphenyl)-imidazolidine-2,4-dione* ($C_{10}H_{10}N_2O_3$, ***4d***): White needles; UV (CH_3OH)λ_{max}: 274 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.40 (s, 1H, N_3–H), 7.99 (s, 1H, N_1–H), 7.30 (d, J = 7.00 Hz, 1H), 7.08–6.92 (m, 2H), 6.85 (d, J = 7.00 Hz, 1H), 4.85 (s, 1H), 4.01 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 166.01 (C = O), 161.12 (C = O), 157.62 (C), 128.13 (2CH), 119.11 (2CH), 114.02 (C), 62.01 (C_{spiro}), 54.17 (C–H); IR (KBr cm^{-1}) $\bar{\nu}$: 3348 (N–H, m), 3217 (N–H, s), 1780 (C = O, s), 1729 (C = O, s), 1612 (C = C, w), 1518 (C = C, w), 1250 (C–O, m).

2.3e *5-(2-Chlorophenyl)-imidazolidine-2,4-dione* ($C_9H_7N_2O_2Cl$, ***4e***): White needles; UV (CH_3OH) λ_{max}: 275 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.70 (s, 1H, N_3–H), 8.03 (s, 1H, N_1–H), 7.90 (d, J = 6.98 Hz, 1H), 7.71 (t, J = 6.98 Hz, 1H), 7.35–7.36 (m, 2H), 5.13 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 168.71 (C = O), 151.04 (C = O), 158.37 (C), 127.12 (2CH), 120.03 (2CH), 113.63 (C), 61.04 (C_{spiro}); IR (KBr cm^{-1}) $\bar{\nu}$: 3350 (N–H, m), 3215 (N–H, s), 1779 (C = O, s), 1732 (C = O, s), 1613 (C = C, w), 1514 (C = C, w).

2.3f *5-(3-Pyrrolyl)-imidazolidine-2,4-dione* ($C_7H_6N_3O_2$, ***4f***): White needles; UV (CH_3OH) λ_{max}: 280 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 12.02 (s, 1H, N_3–H), 10.58 (s, 1H, N_1–H), 8.06 (s, 1H), 7.59 (s, 1H), 7.09 (s, 1H), 4.99 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 167.01 (C = O), 159.21 (C = O), 130.99 (CH), 122.27 (1CH), 118.07 (2CH), 113.70 (C), 62.00 (C_{spiro}); IR (KBr cm^{-1}) $\bar{\nu}$: 3400 (N–H, s), 3351 (N–H, m), 3219 (N–H, s), 1780 (C = O, s), 1735 (C = O, s), 1612 (C = C, w), 1517 (C = C, w).

2.3g *5-(2-Furyl)-imidazolidine-2,4-dione* ($C_7H_6N_2O_3$, ***4g***): White needles; UV (CH_3OH) λ_{max}: 273 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.40 (s, 1H, N_3–H), 9.61 (s, 1H, N_1–H), 7.61 (s, 1H), 6.85 (d, J = 3.2 Hz, 1H), 5.97 (d, J = 3.2, 1H), 4.71 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 167.61 (C = O), 162.13 (C = O), 142.19 (C), 118.02 (1CH), 117.16 (1CH), 114.05 (1CH), 62.17 (C_{spiro}); IR (KBr cm^{-1}) $\bar{\nu}$: 3400 (N–H, m), 3217 (N–H, s), 1781 (C = O, s), 1742 (C = O, s), 1623 (C = C, w), 1512 (C = C, w).

2.3h *5-Isobutyl-5-methyl-imidazolidine-2,4-dione* ($C_8H_{14}N_2O_2$, ***4h***): White needles; UV (CH_3OH) λ_{max}: 312 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.52 (s, 1H, N_3–H), 7.89 (s, 1H, N_1–H), 1.57–1.51 (m, 2H), 1.46–1.42 (m, 1H), 1.20 (s, 3H), 0.87–0.86 (d, J = 5 Hz, 3H), 0.79–0.77 (d, J = 5 Hz, 3H); ^{13}C NMR(DMSO-d_6, 100 MHz) δ: 166.46 (C = O), 158.47 (C = O), 67.16 (C_{spiro}), 46.67 (C–H), 23.99 (C–H), 22.17 (C–H), 20.92 (C–H).; IR (KBr cm^{-1}) $\bar{\nu}$: 3197 (N–H, s), 3117 (N–H, s), 2981 (C–H), 2971 (C–H), 1771 (C = O), 1720 (C = O), 1403 (N–H, b), 1195.

2.3i *1,3-Diazaspiro[4,5]decane-2,4-dione* ($C_8H_{12}N_2O_2$, ***4i***): White needles; UV (CH_3OH) λ_{max}: 348 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.47 (s, 1H, N_3–H), 8.38 (s, 1H, N_1–H), 1.62–1.45 (m, 9H), 1.21–1.27 (m, 1H).; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 179.61 (C = O), 157.51 (C = O), 62.89 (C_{spiro}), 39.76 ($2CH_2$), 25.33 ($2CH_2$), 21.71 (CH_2); IR (KBr cm^{-1}) $\bar{\nu}$: 3250 (N–H,), 3199 (N–H, s), 3069 (=C–H, s), 2936 (C–H, s), 1776

(C = O, m), 1734 (C = O, s), 1456 (N–H, b, s), 1411 (s), 1292 (m), 1228 (m), 1072 (m), 942 (m), 780 (m), 753 (m).

2.3j *5-Methyl-5-phenyl-imidazolidine-2,4-dione ($C_{10}H_{10}N_2O_2$, **4j**)*: White needles; UV (CH_3OH) λ_{max}: 252 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.75 (s, 1H, N_3–H), 8.62 (s, 1H, N_1–H), 7.47–7.45 (d, J = 6 Hz, 2H), 7.40–7.36 (t, J = 6 Hz, 2H), 7.32–7.31 (t, J = 6 Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 166.16 (C = O), 157.41 (C = O), 127.41 (C), 127.38 (2CH), 126.79 (2CH), 123.70 (2CH), 71.22 (C_{spiro}), 22.14 (C–H); IR (KBr cm^{-1}) $\bar{\nu}$: 3282 (N–H, s), 3208 (N–H, s), 3064 (=C–H, m), 2989 (C–H, m), 1731 (C = O, s), 1726 (C = O, s), 787 (=C–H, b), 482 (w).

2.3k *5-(4-Chlorophenyl)-5-methyl-imidazolidine-2,4-dione ($C_{10}H_9ClN_2O_2$, **4k**)*: White needles; UV (CH_3OH) λ_{max}: 272 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.6 (s, 1H, N_3–H), 8.64 (s, 1H, N_1–H), 7.49 (d, J = 8.3, 2H), 7.47 (d, J = 8.3, 2H), 1.63 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 177.14 (C = O), 156.69 (C = O), 139.39 (C), 133.16 (C), 128.89 (2CH), 127.77 (2CH), 64.06 (C_{spiro}), 25.51 (CH_3); IR (KBr cm^{-1}) $\bar{\nu}$: 3274 (N–H, s), 3209 (N–H, s), 1778 (C = O, m), 1725 (C = O, s), 1489 (C = C, w), 1447 (C = C, w), 1401 (N–H, b, m).

2.3l *5-Methyl-5-(3-methylphenyl)-imidazolidine-2,4-dione ($C_{11}H_{12}N_2O_2$, **4l**)*: White powdery; UV (CH_3OH) λ_{max}: 268 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.73 (s, 1H, N_3–H), 8.56 (s, 1H, N_1–H), 7.42–7.25 (s, 3H), 7.12 (s, 1H), 2.30 (s, 3H), 1.87–1.61 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 166.16 (C = O), 157.41 (C = O), 137.99 (C), 131.30 (CH), 128.16 (CH), 127.31 (CH), 126.73 (CH), 123.32 (C), 72.43 (C_{spiro}), 22.14 (CH_3), 20.84 (CH_3); IR (KBr cm^{-1}) $\bar{\nu}$: 3290 (N–H, s), 3211 (N–H, s), 3050 (=C–H, m), 2972 (C–H, m), 1798 (C = O, m), 1730 (C = O, s), 1018 (m), 762 (=C–H, b).

2.3m *5-(3-Chlorophenyl)-5-methyl imidazolidine-2,4-dione ($C_{10}H_9N_2O_2Cl$, **4m**)*: White crystal; UV (CH_3OH) λ_{max}: 270 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.86 (s, 1H, N_3–H), 7.99 (s, 1H, N_1–H), 7.54–7.47 (m, 2H), 7.18 (d, J = 6.5, 1H), 7.01 (t, J = 6.5, 1H), 2.09 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 176.4 (C = O), 158.2 (C = O), 156.3 (C), 139.0 (CH), 132.8 (CH), 128.5 (CH), 127.4 (CH), 126.2 (C), 63.7 (C_{spiro}), 25.1 (CH_3); IR (KBr cm^{-1}) $\bar{\nu}$: 3285 (N–H, s), 3214 (N–H, s), 3042 (=C–H, m), 2800 (C–H, m), 1763 (C = O, m), 1716 (C = O, s), 823 (m).

2.3n *5,5-Diphenylhydantoin ($C_{15}H_{12}N_2O_2$, **4n**)*: White needles; UV (CH_3OH) λ_{max}: 276 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.1 (s, 1H, N_3–H), 9.33 (s, 1H, N_1–H), 7.36 (m, 10H); ^{13}CNMR (DMSO-d_6, 100 MHz) δ: 175.26 (C = O), 156.43 (C = O), 140.39 (2C), 128.96 (2CH), 128.48 (4CH), 127.04 (4CH), 70.66 (C_{spiro}); IR (KBr cm^{-1}) $\bar{\nu}$: 3270 (N–H, s), 3200 (N–H, s), 1770 (C = O, m), 1730 (C = O, s), 1710 (C_4 = O_{asym}, s), 1400 (N–H, b), 760 (=C–H, b), 740 (=C–H).

2.3o *Spiro[fluorene-9,4-imidazolidine]-2,4-dione ($C_{15}H_{10}N_2O_2$, **4o**)*: Yellow powdery; UV (CH_3OH) λ_{max}: 250 nm; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.1 (s, 1H, N_3–H), 9.33 (s, 1H, N_1–H), 7.89–7.85 (t, J = 6.7 Hz, 2H), 7.50–7.45 (m, 4H), 7.37–7.34 (t, J = 6.7, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 175.26 (C_4 = O), 156.43 (C_2 = O), 140.39 (2C), 128.96 (2C), 128.48 (4CH), 127.04 (4CH), 70.66 (C_{spiro}), IR (KBr cm^{-1}) $\bar{\nu}$: 3270 (N–H, s), 3200 (N–H, s), 1770 (C = O, m), 1730 (C_4 = O, s), 1400 (N–H, b, w), 760 (=C–H, b), 740 (=C–H, w).

3. Result and discussion

In this study, we prepared hydantoin derivatives such as 5-phenyl hydantoin **(4a)**, 5-(4-methylphenyl) hydantoin **(4b)**, 5-(4-methoxyphenyl) hydantoin **(4c)**, 5-(2-methoxyphenyl) hydantoin **(4d)**, 5-(2-chlorophenyl) hydantoin **(4e)**, 5-(3-pyrrolyl) hydantoin **(4f)**, 5-(2-furryl) hydantoin **(4g)**, 5-isobutyl-5-methyl hydantoin **(4h)**, 1,3-diazaspiro[4,5]decane-2,4-dione **(4i)**, 5-methyl-5-phenyl hydantoin **(4j)**, 5-(4-chlorophenyl)-5-methyl hydantoin **(4k)**, 5-methyl-5-(3-methylphenyl) hydantoin **(4l)**, 5-(3-chlorophenyl)-5-methyl hydantoin **(4m)**, 5,5-diphenyl hydantoin **(4n)** and spiro[fluorene-9,4-imidazolidine]-2,4-dione **(4o)** through the Bucherer–Bergs synthesis in the presence of montmorillonite as a solid catalyst under ultrasound irradiation.

Initially, as shown in table 2, the effect of molar ratio of starting materials on the yield of reaction was studied by considering aldehyde (or ketone): KCN:$(NH_4)_2CO_3$ ratios and the yield increased from 72% to 98%, from 1:1:5 to 1:1.3:6. At aldehyde (or ketone):KCN:$(NH_4)_2CO_3$ ratio of 1:1.3:6, the best yield of 5-isobutyl-5-methyl hydantoin was achieved (table 2). Exceeding ratio of 1:1.3:6 reduced yield of product because of formation of side product.

Table 2. Effect of molar ratio of starting materials on the yield of reaction.[a]

Weight percentage of product (%)		Molar ratio of starting materials (mmol)		
Unreacted ketone	5-isobutyl-5-methyl hydantoin	Ketone	KCN	$(NH_4)_2CO_3$
28	72	1.0	1.0	5
2	98	1.0	1.3	6
24	84	1.0	1.5	6.2
23	77	1.0	1.7	6.4
25	75	1.0	2.0	6.6
31	69	1.0	2.1	6.8

[a]Under ultrasound irradiation

Table 3. Effect of polarity of solvent on the yield of reaction.

Solvent	Unreacted ketone	5-isobutyl-5-methyl-hydantoin (%)
Ethanol	10	90
Methanol	24	76
Methanol:H_2O	5	95
DMSO	47	53
Ethanol:H_2O	2	98
Dichloromethane	69	31

Next, we considered the effect of solvent on the yield of reaction. The results in table 3, show the highest yield of 5,5-disubstituted hydantoin achieved at EtOH to H_2O ratio of 1:1 (mL). When other solvents were used, no significant improvement in the yield was observed. In the ultrasound-assisted procedure, ethanol was chosen because of solvating power and H_2O was added for better solvation of KCN and $(NH_4)_2CO_3$.

Then, we focused on optimizing conditions for synthesis of hydantoin derivatives by using different amounts of clay to determine the effect of the amount of catalyst. The results show that 100 mg (0.12 mmol) is an optimal quantity of catalyst (table 4). The reaction yield with increasing amount of catalyst (0.22 mmol) was not substantially increased.

From the results, optimum reaction conditions were chosen: aldehyde or ketone derivatives (1 mmol), potassium cyanide (1.3 mmol), ammonium carbonate (6 mmol), montmorillonite (100 mg, 0.12 mmol), ethanol (10 mL) and H_2O (20 mL). Their yields varied from 82% to 98% depending on the nature of the R^1 and R^2 groups.

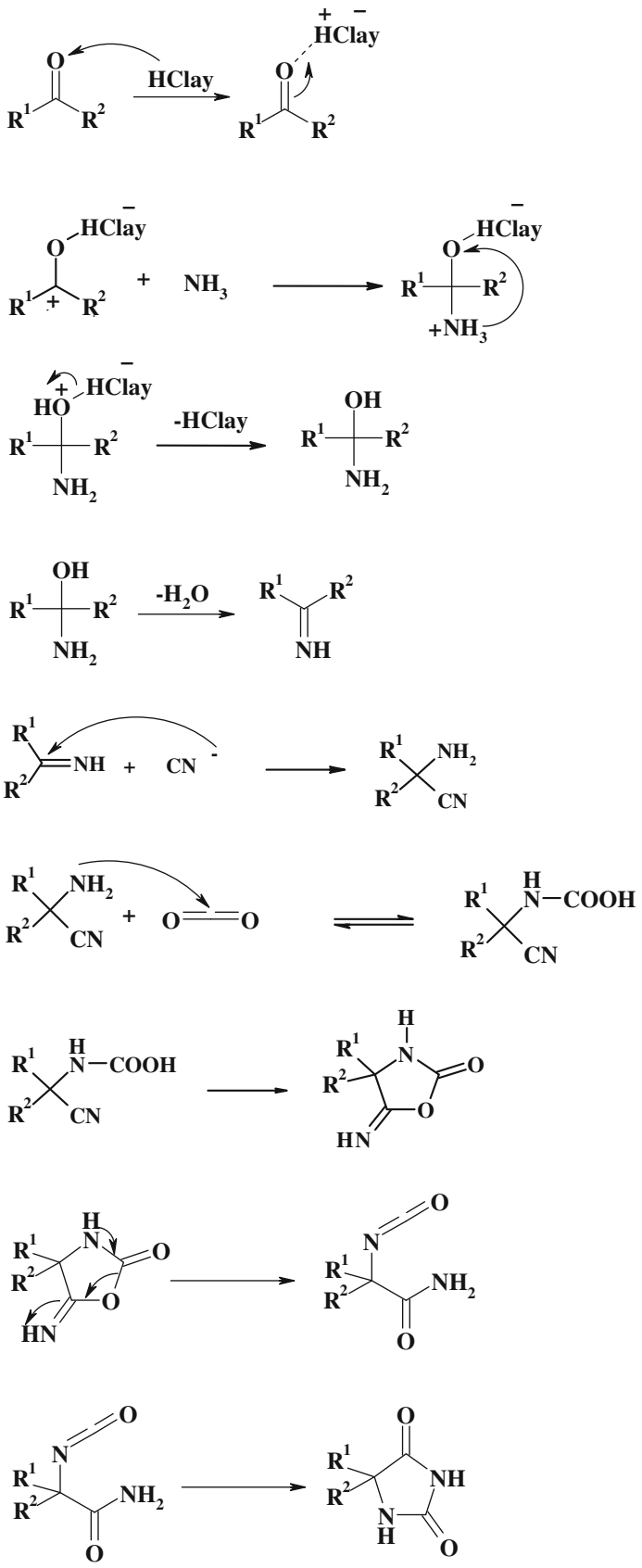
As shown in table 1, among the various carbonyl compounds it was concluded that more activity can be achieved by aldehydes. Aldehydes (table 1, entry A–G) have shorter reaction time. Also, it is observed that aldehydes (or ketones) containing electron-withdrawing groups were found to be more reactive and could react with KCN and ammonium carbonate rapidly. In contrast, ketones (or aldehydes) containing electron-donating groups have shown lower reactivity.[14] This shows that the electronic effects of substitutents have a significant effective on the reaction time. The best yield of hydantoins was achieved for dialkyl ketones (table 1, entries H and I). Finally, the structure of these compounds was investigated using melting point, UV, ^{1}H NMR, ^{13}C NMR and IR.

Table 4. Optimization amount of catalyst for synthesis of 5-isobutyl-5-methyl hydantoin under ultrasound irradiation.[a]

Entry	Clay (mmol)	Time (min)	Yield (%)[b]
A	0.0	48	73
B	0.09	42	87
C	0.13	37	91
D	0.18	32	98
E	0.22	32	98
F	0.25	32	98

[a]Ketone (1 mmol), KCN (1.3 mmol), $(NH_4)_2CO_3$ (6 mmol)
[b]Isolated yields

It is of interest to note that use of the montmorillonite K-10 as solid acid offers high yield of hydantoin derivatives compared to the conventional procedures, probably due to more number molecular interactions. Also, montmorillonite K-10 shows complexation with carbonyl compounds. Therefore, the electrophilic character of carbonyl groups and yield of reactions increase.



Scheme 2. Possible mechanism for the preparation of hydantoin derivatives.

A plausible mechanism for this reaction is shown in scheme 2.

4. Conclusion

A facile, one-pot procedure for the synthesis of 5,5-disubstituted hydantoins has been developed employing montmorillonite K-10 as a catalyst under ultrasound irradiation as energy source. The K-10 clay is inexpensive and a reusable catalyst. Absorption of ultrasound irradiation in conjunction with the use of montmorillonite provides shorter reaction time, milder reaction condition and higher yield.

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