Phase-Transfer Catalyzed Alkylation of Hydantoin

and 5-Methyl-5-Phenylhydantoin

TARIQ R. SOBAHI*, MOHAMED A. HASSAN,

HUISSEN A. MOUSTAFA and NAHED O. BAWAKED

Department of Chemistry, Faculty of Science, King Abdulaziz University,

Jeddah-21589, P.O.Box 80203, Saudi Arabia.

E-mail: drtariq_s@hotmail.com

ABSTRACT. PTC-alkylation of hydantoin (**1a**) and 5-methyl-5-phenylhydantoin (**1b**) by different organohalogen reagents at 25°C in the presence of tetrabutylammonium bromide as catalyst has been investigated either in the absence or presence of CS_2. This work is aiming to study the comparative reactivity of N- versus O- of hydantoins toward alkylation and cycloalkylation. In all cases N3 monoalkylation or N1 and N3 dialkylation are the main products. The structures of alkylhydantoins have been established by IR, NMR, mass spectral data and elemental analysis.

Keywords: Phase-transfer catalysis (PTC), alkylation, cycloalkylation, hydantoin, 5-methyl-5-phenylhydantoin, tetrabutylammonium bromide.

Introduction

Phase-transfer catalysis (PTC) is one of the promising methods in organic synthesis of specialty chemicals. In the last 20 years, a steadily increasing number of published papers and patents dealing with phase transfer catalysis topics and their applications. PTC is not merely important for substitution reactions but, nowadays, it is being extensively applied in polymer chemistry, heterocyclic chemistry, organometallic, agrochemicals, dyes, flavors, perfumes and pharmaceutical manufacture[1-3].

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The technique of PTC has, extensively, been applied in the organic synthesis via substitution, displacement, condensation, elimination, redox, polymerization and Ylide-mediated reactions. The most advantages of using PTC technique to synthesize organic chemicals, are the enhancement of the reaction rate, carrying out the reaction at moderate conditions, obtaining high selectivity of the main product with high conversion of the reactants[4,5].

In continuation of our current research in the field of organic synthesis of some heterocyclic compounds via phase transfer catalysis conditions (PTC)[6-10], we are aiming here to study the reactivity of N- *vs* O- alkylations of hydantoin (**1a**) and 5-methyl-5-phenylhydantoin (**1b**) in absence or presence of carbon disulphide.

Hydantoins are very important class of organic compounds with numerous pharmaceutical applications[11,12]. They have a wide biological activities such as integrins and kinases inhibitors[13,14], anti-convulsants & anti-epileptics[15], fungicides & herbicides[16], anti-bacterial & anti-mycobacterial[17] and potent activity against the herpes simplex virus (HSV)[18], human immunodeficiency virus (HIV)[19] and the leukemia subpanel[20].

Experimental

All melting points reported are uncorrected. IR (KBr) spectra were recorded using Perkin Elmer's spectrum RXIFT-IR spectrophotometer (v in cm^{-1}). The NMR spectra were recorded on Bruker Avance DPx400 spectrometer, using CDCl$_3$ as solvent and TMS as internal standard (chemical shifts in δ values in ppm). Elemental analysis was preformed on Prekin Elmer 2400, series II microanalyzer. The mass spectra were recorded by Shimadzu

GC-17A gas chromatograph QP-5000 mass spectrometer. Hydantoins (**1a,b**) are Aldrich products and they are used without any further purifications.

General procedure of PTC-alkylation of Hydantoins (1a,b):

a) In the absence of carbon disulphide.

In a 100 ml conical flask , fitted with rubber stopper, a suspension of hydantoins (**1a,b**) (0.01 mol), anhydrous potassium carbonate (0.02 mol, 2.76 g) and tetrabutylammonium bromide (TBAB, 0.003 mol, 0.9 g) in tetrahydrofuran (THF, 100 ml) were stirred at 25°C for 30 min, then the organohalogen compound (alkylating agents) (0.03 mol for monohalogen compounds, and 0.01 mol for dihalogen reagents), namely, ethyl bromide, n-propyl bromide, n-butyl bromide, allyl bromide, benzyl bromide, ethyl bromoacetate, 1,2-dibromoethane or 1,3-dibromopropane was added. The reaction mixture was efficiently stirred at room temperature. The progress of the reaction was monitored by TLC during the entire reaction period. After the completion of the reaction, the organic layer was separated by filtration and the organic solvent was evaporated and the residue was crystallized from the proper solvent or separated by column chromatography using silica gel (80-120 mesh) and diethyl ether/petroleum ether (2:1) as eluent to separate the products from the unreacted hydantoins. On the other hand, the K_2CO_3 precipitate was dissolved in water (100 ml) and acidified by dilute HCl (10 %) to separate any acidic products, if any, which no acidic products were isolated by all alkylating agents. The results are listed in **Table 1**.

b) In the presence of carbon disulphide:

In a round bottle flask (100 ml) filted with a water condenser, a suspension of hydantoins (**1a,b**) (0.01 mol), anhydrous K_2CO_3 (0.02 mol, 2.76

g), tetrabutylammonium bromide (TBAB, 0.003 mol, 0.90 g) and carbon disulphide (10 ml) in tetrahydrofuran (THF, 100ml) was added. The mixture was efficiently stirred at room temperature for 30 min, then the organohalogen reagents (0.05 mol) were added and the reaction mixture vigorously, stirred at 25°C. The progress of the reaction was monitored by TLC over the entire reaction period. After completion of the reaction, the organic layer was separated by filtration and the solvent was evaporated. The products were separated by column chromatography using silica gel (80-120 mesh) and diethyl ether/petroleum ether (2:1) as eluent to sparate the products from the unreacted hydantoins. The solid residue was crystallized from appropriate solvent. The results are listed in **Table 1**.

Table 1: The Physical data of alkylated products (2-4).

Compd No.	Reaction period t (h)	M. Formula (M. Wt.)	m.p.°C (colour)	Solvent[#] Cryston (Yield %)	Elemental analysis Calc./Found %		
					C	H	N
2a	7	$C_5H_8N_2O_2$ (128.13)	102-105 (white)	P.E.60-80. (73)	46.87 46.73	6.29 6.32	21.86 21.98
2b	6	$C_6H_{10}N_2O_2$ (142.16)	86-88 (white)	P.E.60-80. (67)	50.69 50.55	7.09 6.90	19.71 19.88
2c	9	$C_7H_{12}N_2O_2$ (156.18)	97-99 (white)	P.E.60-80. (65)	53.83 53.57	7.74 7.76	17.94 18.08
2d	24	$C_6H_8N_2O_2$ (140.14)	75-77 (white)	P.E.60-80. (45)	51.42 51.27	5.75 5.71	19.99 19.92
2e	2	$C_{10}H_{10}N_2O_2$ (190.20)	137 (white)	P.E./ B (61)	63.15 62.88	5.30 5.35	14.73 14.88
2f	7	$C_5H_7N_2O_2Br$ (207.03)	136-138 (white)	P.E. / B (80)	29.01 28.68	3.41 3.39	13.53 13.45
2g	7	$C_6H_9N_2O_2Br$ (221.06)	118-120 (white)	P.E.80-100 (91)	32.60 32.47	4.10 4.14	12.67 12.76
2h	24	$C_{11}H_{16}N_2O_6$ (272.26)	Oil (yellow)	Ether/P.E.(1:1) (68)	48.53 48.38	5.93 5.87	10.29 10.38
2i	1	$C_{12}H_{14}N_2O_2$ (218.25)	109	P.E./B (68)	66.04 65.83	6.47 6.39	12.84 12.96
2j	0.5	$C_{13}H_{16}N_2O_2$ (232.28)	100	P.E. (65)	67.22 66.83	6.94 6.83	12.06 12.18
2k	0.5	$C_{14}H_{18}N_2O_2$ (246.31)	91	P.E. (61)	68.27 68.05	7.37 7.34	11.37 11.35

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|							
2l	3	$C_{13}H_{14}N_2O_2$	76-8	P.E.	67.81	6.13	12.17
		(230.27)		(68)	67.71	6.16	12.23
2m	10	$C_{12}H_{13}N_2O_2Br$	261	E	48.50	4.41	9.43
		(297.15)		(31.1)	48.41	4.37	9.52
2n	5	$C_{13}H_{15}N_2O_2Br$	115	P.E.	50.18	4.86	9.00
		(311.18)		(58)	50.02	4.84	9.17
2o	2	$C_{24}H_{22}N_2O_2$	115	E	77.81	5.99	7.56
		(370.45)		(90)	77.69	5.97	7.63
2p	3	$C_{18}H_{22}N_2O_6$	oil	E/P.E.	59.66	6.12	7.73
		(362.38)		(eluent)(75)	59.52	6.13	7.82
3	3	$C_{13}H_{14}N_2O_2$	119-21	P.E./B	67.81	6.13	12.17
		(230.27)		(60)	67.67	6.15	12.27
4a	2	$C_{16}H_{28}N_2O_2S_2$	74-76	P.E.	55.78	8.19	8.13
		(344.54)	(yellow)	(32)	55.64	8.21	8.21
4b	24	$C_{16}H_{20}N_2O_2S_2$	86-88	Ether/P.E.(1:2)	57.11	5.99	8.33
		(336.48)	(yellow)	(38)	56.95	5.97	8.40
4c	24	$C_{16}H_{22}N_2O_8S_2$	Oil	Ether/P.E.(1:1)	44.23	5.10	6.45
		(434.49)	(yellow)	(59)	44.07	5.13	6.53

P.E. = petroleum ether, E = ethanol, B = benzene

Results and Discussion

The approach reported here is an extension and continuation of our interest in alkylation of some heterocycles uender phase-transfer catalysis (PTC) conditions[6-10]. This work is aiming to study the Phase-transfer catalyzed alkylation of hydantoin (1a) and 5-methyl-5-phenylhydantoin (1b) and the comparative reactivity towards N- *vs* O- upon treatment with different organohalogen reagents in liquid/solid in the presence of tetrabutylammonium bromide (TBAB) as a catalyst in the absence or presence of CS_2 at 25 °C.

On the other hand, we are aiming to synthesis new hydantoin derivatives which might have an expected biological activity in addition to the well known biological, pharmacological and medicinal applications of hydantoins[11-20].

5-Methyl-5-phenylhydantoin (1b) may be existed in different tautomeric structures I-VII (Scheme 1).

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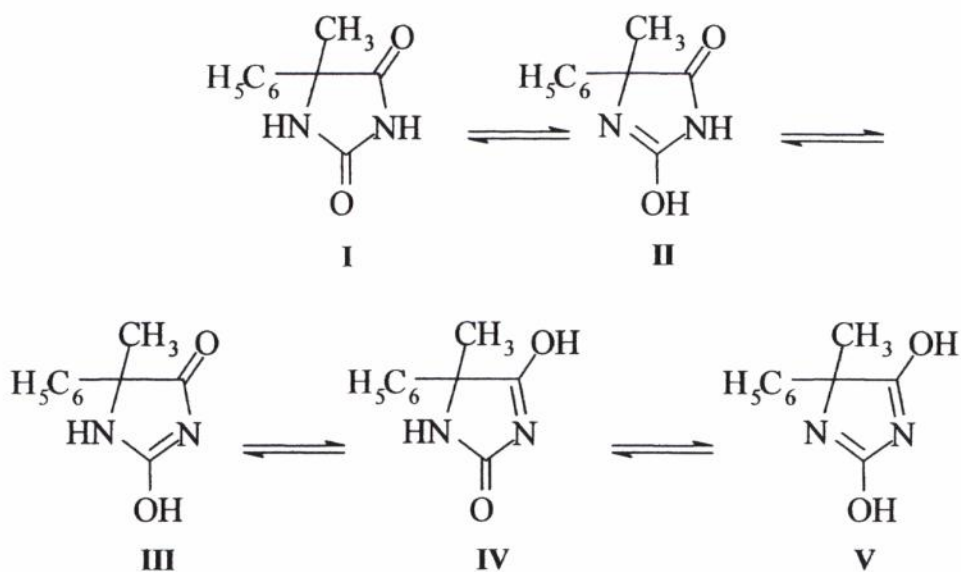
(Scheme 1)

The structure of hydantoin and 1-mono or 1,5-disubstituted hydantoins were investigated[21] by one and two dimensional ^1H and $^{13}CNMR$ techniques, which are proved the existence of hydantoins, predominantly, in the lactam form (**I**). Also, the IR spectrum of hydantoin (**1a**) displayed an absorption bands at v (in cm^{-1}): 1706 (C=O), 1774 (C=O), 2765 (CH), 3062 (CH), 3146 (NH) and 3258 (NH), while the ^1HNMR (pyridine-d_5) displayed signals at δ (in ppm): 5.28 (s, 2H, C$\underline{H}_2$), 10.00 (s, 1H, N1-$\underline{H}$) and 13.53 (s, 1H, N3-$\underline{H}$).

Treatment of hydantoins (**1a,b**) with ethyl bromide, n-propyl bromide, n-butyl bromide, allyl bromide, benzyl bromide (1:3 molar ratio), 1,2-dibromoethane and 1,3-dibromopropane (1:1 molar ratio) in tetrahydrofuran (THF) and anhydrous potassium carbonate (K$_2$CO$_3$) as liquid/solid phases and in the presence of tetrabutylammonium bromide as catalyst at 25°C and absence of CS$_2$ with efficient stirring gives after a short reaction period (t), a promising yield of 3-alkylhydantions (3-alkylimidozolidine-2,4-diones) (**2a-g**)

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or 3-alkyl-5-methyl-5-phenyl- hydantion (**2i-n**) in good yield, respectively (**Scheme 2**). The alkylation occurs, exclusively, at nitrogen in position-3 (N3) to give the mono-alkylated product (**2a-g & 2i-n**), (**Scheme 2**), except hydantoin (**1a**) was alkylated by ethyl bromoacetate to give diethyl 2,2`(2,4-dioxoimidazoli- den-1,3-diyl) diacetate (**2h**) as pale yellow oil via N1 and N3 dialkylation, while 5-methyl-5-phenylhydantoin (**1b**) was alkylated by benzyl bromide or ethyl bromoacetate as a highly reactive organohalogen reagent afforded, 1,3-dibenzyl-5-methyl-5-phenylhydantoin (**2o**) or diethyl 2,2`(5-methyl-5-phenyl-2,4-dioxoimidazoliden-1,3-diyl) diacetate (**2p**) via N1, N3 simultaneous dialkylation (**Scheme 2**). Meanwhile, treatment of 5-methyl-5-phenyl- hydantoin (**1b**) with 1,3-dibromopropane (2:1 molar ratio) under the same PTC reaction conditions underwent cycloalkylation via N1 and N3, simultaneous dialkylation to give, 7-methyl-7-phenyl-1,5-diazabicyclo[3.2.1] octane-6,8-dione (**3**), (**Scheme 2**).

(Scheme 2)
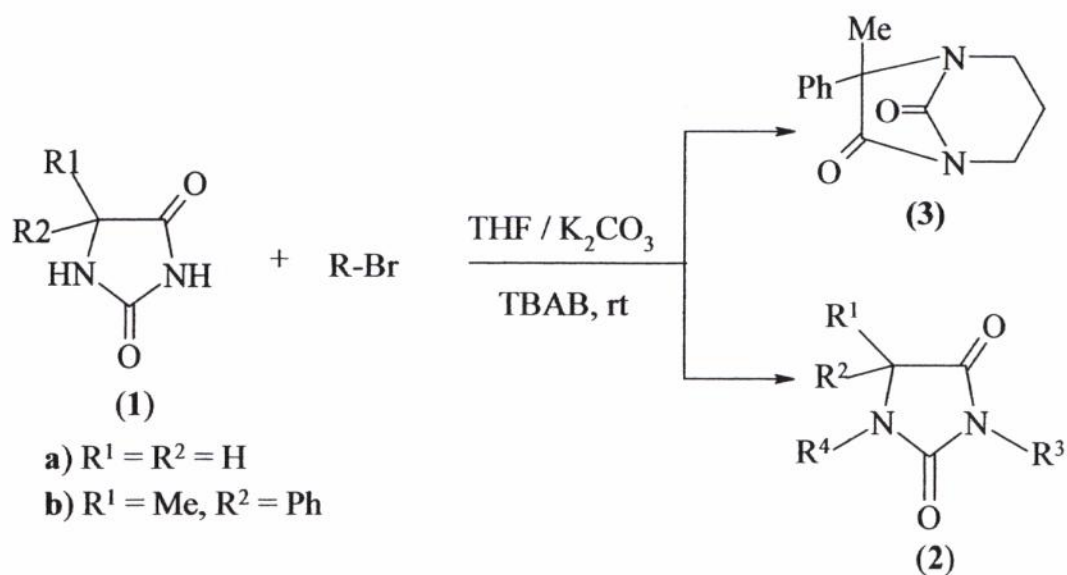
2	R^1	R^2	R^3	R^4
a	H	H	C$_2$H$_5$	H
b	H	H	n-C$_3$H$_7$	H
c	H	H	n-C$_4$H$_9$	H
d	H	H	CH$_2$CH=CH$_2$	H
e	H	H	C$_6$H$_5$CH$_2$	H
f	H	H	(CH$_2$)$_2$Br	H
g	H	H	(CH$_2$)$_3$Br	H
h	H	H	CH$_2$CO$_2$Et	CH$_2$CO$_2$Et
i	Me	Ph	C$_2$H$_5$	H
j	Me	Ph	n-C$_3$H$_7$	H
k	Me	Ph	n-C$_4$H$_9$	H
l	Me	Ph	CH$_2$CH=CH$_2$	H
m	Me	Ph	(CH$_2$)$_2$Br	H
n	Me	Ph	(CH$_2$)$_3$Br	H
o	Me	Ph	C$_6$H$_5$CH$_2$	C$_6$H$_5$CH$_2$
p	Me	Ph	CH$_2$CO$_2$Et	CH$_2$CO$_2$Et

The structure of mono and dialkylated hydantoins (2a-g and 3) have been established by spectral data (Table 2) and elemental analysis (Table 1).

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Table 2: Spectral data of alkylated hydantoins (**2, 3**).

Compd No.	IR (ν in cm^{-1})			^{1}H-NMR CDCl$_3$ / δ (ppm)	^{13}C-NMR δ (ppm)	MS (abundance%)
	C=O	CH	NH,OH			
2a	1710	2832 2982	3224	1.23 (t, 3H, C<u>H</u>$_3$), 3.58 (q, 2H, C<u>H</u>$_2$ of C$_2$H$_5$), 3.98 (s, 2H, C5-<u>H</u>$_2$), 6.44 (b, 1H, N<u>H</u>).	12.7 (CH$_3$), 33.6 (CH$_2$,C$_2$H$_5$), 46.4 (C5), 158.6 (C4), 171.3 (C2).	128 (67, M$^+$), 113 (15, M-(NH or CH$_3$), 100 (21, M-CO or M-C$_2$H$_4$), 85 [58, M-(CO+ NH) or(NH+ C$_2$H$_4$)], 72 [35, M-(CO+ C$_2$H$_4$)], 56(100, N$_2$CO).
2b	1699 1776	2875 2965	3249	1.14 (t, 3H, C<u>H</u>$_3$), 1.86 (m,2H, C<u>H</u>$_2$-Me), 3.69 (t, 2H, N-C<u>H</u>$_2$), 4.19 (s, 2H, C5-<u>H</u>$_2$), 6.90 (b, 1H, N<u>H</u>).	10.5 (CH$_3$), 20.8 (Me-CH$_2$), 40.2 (N-CH$_2$), 46.4 (C5), 158.9 (C4), 171.47 (C2).	142 (27, M$^{+\cdot}$), 101(5l, M-C$_3$H$_6$), 85 (36, M-NC$_3$H$_7$) and 56 (100, N$_2$CO).
2c	1689 1772	2868 2949	3246	0.94 (t, 3H, C<u>H</u>$_3$), 1.35 (m,2H, C<u>H</u>$_2$), 1.60 (m, 2H, C<u>H</u>$_2$), 3.51 (t, 2H, N-C<u>H</u>$_2$), 3.98 (s, 2H, C5-<u>H</u>$_2$) 6.94 (b, 1H, N<u>H</u>).	12.9 (CH$_3$), 20.3(CH$_2$), 30.7 (CH$_2$), 39.4 (CH$_2$) 46.4 (C5), 159.1 (C4), 171.6 (C2).	156 (26, M$^{+\cdot}$), 127 (8, M-HCO), 114 (37, M-HNCO), 101 (86, M-C$_4$H$_8$), 85 (36, M-NC$_4$H$_9$), 56 (100, N$_2$CO).
2d	1714 1768	2848 3005	3239	4.00 (s, 2H, C5-<u>H</u>$_2$), 4.13 (d, 2H, N-C<u>H</u>$_2$), 5.19 (dxd, 2H, C<u>H</u>$_2$=), 5.81 (m, 1H, -C<u>H</u>=), 5.90 (b, 1H, N<u>H</u>).	....	140 (33, M$^{+\cdot}$), 112 (17, M-CO), 97 (9, M-C$_3$H$_6$), 83 (10, M-C$_3$H$_6$NCO), 70 (20, M-C$_3$H$_6$N$_2$CO), 56 (100, N$_2$CO).
2e	1717 1769	2855 2978 3111	3240	4.01 (s, 2H, C5-<u>H</u>$_2$), 4.71 (s, 2H, N-C<u>H</u>$_2$), 6.53 (s, 1H, N<u>H</u>), 7.31-7.45 (m, 5H, ph-<u>H</u>).	42.4 (N-CH$_2$), 47.3 (C5), 127.4, 128.1, 129.0, 129.5, 129.7 (Ph-<u>C</u>H), 136.0 (Ph-C), 158.6 (C4), 171.4 (C2).	190 (81, M$^{+\cdot}$), 161 (40, M-HCO), 132 (13,M-2x HCO), 118 (21, MHN(CO)$_2$),104 (100, M-C$_6$H$_5$), 91(97, C$_7$H$_7^+$), 77 (52, C$_6$H$_5^{+\cdot}$), 65 (59) , 56 (56, N$_2$CO).
2f	1706 1770	2818 2978	3259	3.57 (t, 2H, Br-C<u>H</u>$_2$), 3.94 (t, 2H, N-C<u>H</u>$_2$), 4.03 (s, 2H, C5-<u>H</u>$_2$), 6.16 (b, 1H, N<u>H</u>).	....	206 (10, M$^{+\cdot}$), 127 (100, M-Br), 79 & 81(15,Br), 85 [23, M-(N-C$_2$H$_4$Br)],56 (72,N$_2$CO).
2g	1696 1758	2877 2940	3272	2.21 (m, 2H, C2-<u>H</u>$_2$,propyl), 3.41 (t, 2H, Br-C<u>H</u>$_2$), 3.68 (t, 2H, N-C<u>H</u>$_2$), 3.99 (s, 2H, C5-<u>H</u>$_2$), 5.48 (b, 1H, N<u>H</u>).	....	220 (3.6,M$^+$), 141 (82.0,M-Br), 114 (26.9,M-CH$_2$=CH-Br) 79 & 81(18,Br),85 [40.1,M-(M-C$_3$H$_6$Br)] , 56 (100,N$_2$CO).
2h	1724	2985	......	1.29, 1.30 (2xt, 6H, 2xC<u>H</u>$_3$ ester), 4.12 (s, 2H, N1-C<u>H</u>$_2$), 4.18 (s, 2H, C5-<u>H</u>$_2$), 4.23, 4.24 (2xq, 4H, 2xO-C<u>H</u>$_2$-), 4.26 (s, 2H, N3-C<u>H</u>$_2$).	....	....
2i	1703 1765	2985	3332	1.19 (t, 3H, CH$_3$ of ethyl), 1.82 (s, 3H, CH$_3$), 3.54 (q, 2H, CH$_2$ of ethyl), 7.03 (b, IH, NH), 7.27-7.52 (m, 5H, Ph-H).	13.2 (CH$_3$, ethyl), 23.8 (5-CH$_3$), 33.8 (CH$_2$, ethyl), 63.5 (C5), 124.3 – 129.6 (Ph-<u>C</u>H), 138.8 (Ph-<u>C</u>), 157.1 (C4), 175.3 (C2).	218 (11, M$^{+\cdot}$), 203 (52, M-CH$_3$ or M-NH), 119 (35), 104 (100, C$_6$H$_5$C≡N$^+$H), 77 (50, C$_6$H$_5^{+\cdot}$), 56 (16, N$_2$CO), 51 (42).

	IR			^1H NMR	^{13}C NMR	Mass
2j	1702 1771	2874 2964	3256	0.87 (t, 3H, CH$_3$ of propyl), 1.63 (m, 2H, CH$_2$), 1.83 (s, 3H, 5-CH$_3$), 3.47 (t, 2H, -N-CH$_2$), 6.65 (b, IH, NH), 7.26-7.52 (m, 5H, Ph-H).	....	232 (13, M$^{+\cdot}$), 217 (47, M-CH$_3$ or M-NH), 132 (15) , 119 (34, C$_6$H$_5$(CH$_3$)C=NH), 104 (100, C$_6$H$_5$C≡NH), 9 (14, C$_6$H$_5$N$^{+\cdot}$) , 77 (47, C$_6$H$_5^{\cdot}$), 51 (16).
2k	1705 1774	2869 2953	3258	0.89 (t, 3H, CH$_3$ of butyl), 1.27 (m, 2H, CH$_2$), 1.55 (m, 2H, CH$_2$), 1.81 (s, 3H, C5-CH$_3$), 3.48 (t, 2H, N-CH$_2$), 7.3-7.53 (m, 6H, Ph-H + NH).	12.95 (CH$_3$) , 19.8 (CH$_2$), 23.82 (5-CH$_3$), 29.3 (CH$_2$), 39.2 (N-CH$_2$), 63.5 (C5), 124.3-129.6 (Ph-CH), 138.82 (Ph-C), 157.30 (C4), 175.5 (C2).	246 (18, M$^{+\cdot}$), 231 (46, M-CH$_3$ or M-NH), 119 (33, C$_6$H$_5$ (CH$_3$)C=NH), 104 (100, C$_6$H$_5$C≡NH), 91 (16, C$_6$H$_5$N$^{+\cdot}$) 77 (51, C$_6$H$_5^{\cdot}$), 57 (29, C$_4$H$_9^{+\cdot}$), 51 (32).
2l	1706 1774	2930 2996 3040	3362	1.88 (s, 3H, CH$_3$), 3.59 (t, 2H, CH$_2$-Br), 3.94 (t, 2H, N-CH$_2$), 6.51 (S, 1H, NH), 7.27-7.54 (m, 5H, Ph-H).	....	....
2m	1709 1769	2855 2978 3111	3240	4.01 (s, 2H, C5-H$_2$), 4.71 (s, 2H, N-CH$_2$), 6.53 (s, 1H, NH), 7.31-7.45 (m, 5H, ph-H).	....	....
2n	1706 1766	2839 2974	3254	1.85 (s, 3H, CH$_3$), 2.19 (m, 2H, C2-H$_2$ of propyl), 3.35 (t, 2H, CH$_2$-Br), 3.66 (t, 2H, N-CH$_2$), 6.73 (s, IH, NH), 7.28-7.53 (m, 5H, Ph-H).	26.8 (CH$_3$), 30.7 (C2-propyl), 32.9 (Br-C3, propyl), 40.7 (N-C1-propyl), 65.4 (C5), 126.0-131.5 (Ph-CH), 140.3 (Ph-C), 158.4 (C4), 176.93 (C2).	312 (24, M$^+$), 297 (43, M-CH$_3$ or M-NH), 231 (51, M-HBr), 146 (28, M-Br(CH$_2$)$_3$ NCO), 132 (28, C$_6$H$_5$(CH$_3$) C$_2$O), 119 (61, C$_6$H$_5$(CH$_3$) C=NH), 104 (100, C$_6$H$_5$C≡ NH), 79& 81 (12,Br),77(78, C$_6$H$_5^+$),51 (70).
2o	1706 1761	2933 3031	......	1.57 (s, 3H, CH$_3$), 3.77 (d, IH, N1-CH), 4.75 (q, 2H, N3-CH$_2$), 4.92 (d, IH, N1-CH), 7.16-7.40 (m, 15H, Ph-H).	23.6 (CH$_3$), 45.5 (N-CH$_2$), 69.3 (C5), 127.2 - 131.8 (Ph-CH), 137.8 (Ph-C-CH$_2$), 138.9 (Ph-C-C5) , 158.2 (C4), 176.51 (C2).	370 (12, M$^{+\cdot}$), 355 (2, M-CH$_3$), 146 (18, C$_6$H$_5$CHN$_2$CO), 132 (87, C$_6$H$_5$CH=N-CO$^+$), 91 (100, C$_7$H$_7^+$), 77 (28, C$_6$H$_5^+$), 65 (29), 51 (19).
2p	1723 1766	2980 3028	......	1.27 (txt, 6H, 2xCH$_3$, ester), 1.89 (s, 3H, C5-CH$_3$), 3.52 (d, IH, N1-CH), 4.18 (qxq, 4H,2x OCH$_2$, ester), 4.34 (q, 2H, N3-CH$_2$), 5.30 (s, IH, N1-CH), 7.27-7.42 (m, 5H, Ph-H).	14.5 (CH$_3$, ester), 23.9 (5-CH$_3$), 39.75 (N3-CH$_2$), 42.5 (N1-CH$_2$), 58.9 (CH$_2$, ester), 61.58 (CH$_2$, ester), 67.5 (C5), 125.5 - 129.9 (Ph-CH), 135.7 (Ph-C), 155.1 (C4), 166.9 (C=O, ester), 168.2 (C=O, ester), 174.2 (C2).	362 (6, M$^{+\cdot}$), 347 (11, M-CH$_3$), 289 (20, M-CO$_2$C$_2$H$_5$), 215 (12 M-2xCO$_2$C$_2$H$_5$), 187 (41, M-2xCH$_2$CO$_2$C$_2$ H$_5$), 132 (26, C$_6$H$_5$(CH$_3$)C$_2$O), 91 (100, C$_7$H$_7$), 84 (31), 56 (14).
3	1706 1771	2980 3098	....	1.82 (s, 3H, CH$_3$), 2.03 (m, 2H, C2-H$_2$, propyl), 3.51 (m, 4H, C1-H$_2$+C3-H$_2$, Propyl), 7.28-7.52 (m, 5H, ph-H).	24.4 (3-CH$_2$), 25.8 (CH$_3$), 35.8 (4-CH$_2$), 37.4(2-CH$_2$), 63.6 (C7), 124.5-129.7 (ph-CH), 138.6 (ph-C), 156.9 (N2C=O), 175.3 (C6).	....

On the other hand alkylation of hydantoin (**1a**) by n-propyl bromide or allyl bromide (1:5 molar ratio, respectively) under the same PTC reaction conditions and in the presence of CS_2 with efficient stirring and TLC–reaction was monitoring by TLC afforded after 2h, 5-[bis(alkylthio) methylene]-1,3-dialkylimidazolidine-2,4-dione (**4a,b**) in 32% yield. There is no improvement of the yield of **4** even after 3 days reaction period. Meanwhile, alkylation of hydantoin (**1a**) by ethyl bromoacetate under the same PTC-reaction conditions and in the presence of CS_2 yielded diethyl 2,2`-[[3-(2-ethoxy-2-oxoethyl)-2,5-dioxoimidazolidin-4-ylidene]-methylene]bis (thio)] diacetate (**4c**) as yellow viscuss oil. The products **4** and the unreacted hydantoin (**1a**) were isolated by column chromatography using diethyl ether/petroleum ether (2:1) (**Scheme 3**).

The reaction proceeds with nucleopilic addition of the intermediate C5-carbonion on CS_2 to give the intermediate dithiolate anion which is dialkylated at N-1 and N-3 by n-propyl / or allyl bromide, while N-1 alkylation's, only, by ethyl bromoacetate (**Scheme 3**).

a) R:S, N1, N3 = $(CH_2)_2CH_3$
b) R:S, N1, N3 = $CH_2=CHCH_2$
c) R:S, N3 = $CH_2CO_2C_2H_5$; RN1 = H
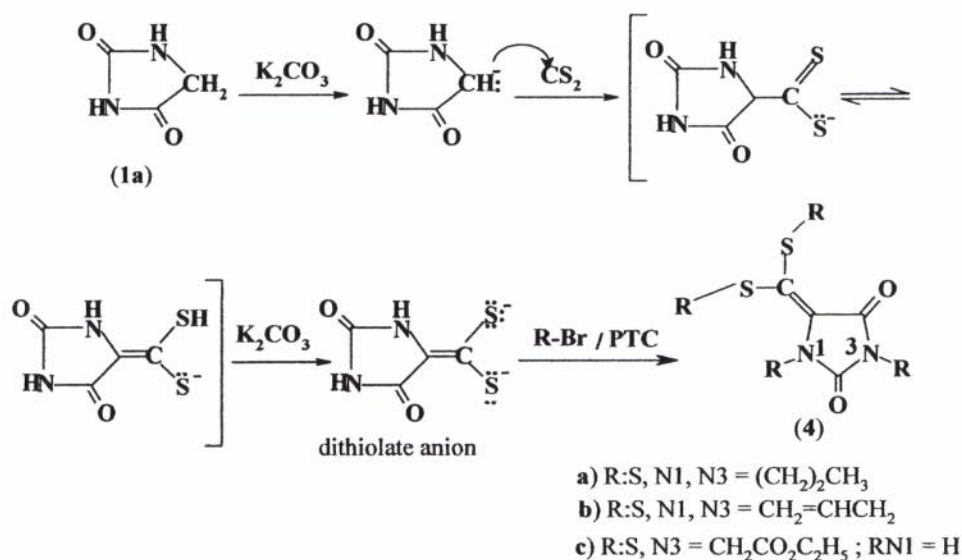
(**Scheme 3**)

The structure of alkylatedhydantoins (**4a-c**) has been established by spectral data (**Table 3**) and elemental analysis (**Table 1**).

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Table 3: Spectral data of compounds of alkylatedhydantoin (4a-c).

Compd No.	IR (ν in cm^{-1})			^{1}H-NMR CDCl$_3$ / δ (ppm)	MS (abundance%)
	C=O	CH	NH		
4a	1713 1787	2872 2959	......	0.76 (t, 3H, C$\underline{H}_3$), 0.9(t,3H,C$\underline{H}_3$),1.0(t, 3H, C$\underline{H}_3$), 1.04 (t, 3H, C$\underline{H}_3$), 1.45 (m, 2H, C$\underline{H}_2$), 1.73 (m, 6H, 3xC$\underline{H}_2$), 2.91 (t, 2H, S-C$\underline{H}_2$), 3.05 (t, 2H, S-C$\underline{H}_2$), 3.34 (t, 2H, N-CH$_2$), 3.86 (t, 2H, N-C$\underline{H}_2$).	345 (2, M$^{+\cdot}$), 260 (13, M-2xC$_3$H$_7$), 226 (16), 218 (45, M-3xC$_3$H$_7$), 189 (16), 175(10), 144 (16), 56 (100,N$_2$CO).
4b	1720 1793	2857 2983 3082	......	3.60 (d, 2H, S-C$\underline{H}_2$), 3.69 (d, 2H, S-C$\underline{H}_2$), 3.98 (d, 2H, N1-C$\underline{H}_2$), 4.53 (d, 2H, N3-C$\underline{H}_2$), 5.04-5.36 (m, 8H, 4x C$\underline{H}_2$=), 5.63 (m, 1H,-C$\underline{H}$=), 5.86 (m, 2H, 2xC$\underline{H}$=), 5.95 (m, 1H, -CH=).	....
4c	1722 1783	2982	3255	1.29 (t, 9H, 3xC$\underline{H}_3$), 4.08 (s, 4H, 2xS-C$\underline{H}_2$), 4.22 (q, 6H, 3xO-C$\underline{H}_2$) 4.37 (s, 2H, N3-C$\underline{H}_2$), 5.79 (b, 1H, N1-$\underline{H}$).	....

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ألكلة هيدانتوين و 5-مثيل-5-فنيل هيدانتوين
تحت ظروف حفز الأنتقال الصنفى

طارق رشاد سبحي* ، محمد علي حسن ، حسين أحمد مصطفى ، ناهد عمر باواكد

قسم الكيمياء ، كلية العلوم ، جامعة الملك عبد العزيز

ص.ب. ٨٠٢٠٣ ـ جدة ٢١٥٨٩ ـ المملكة العربية السعودية

المستخلص.   تم ألكلة كل من هيدانتوين (1a) و 5-مثيل-5-فنيل هيدانتوين (1b) فى وجود أو غياب ثانى كبريتيد الكربون تحت ظروف حفز الإنتقال الصنفى وذلك بإستخدام بعض الكواشف العضوية الهالوجينية عند درجة حرارة الغرفة وفى وجود بروميد رباعى بيوتيل أمونيوم كحافز. ويهدف البحث فى دراسة مقارنة لدرجة نشاط ألكلة N- أو O- للهيدانتوينات. أثبتت الدراسة فى جميع الحالات أنه تتم الألكلة الأحادية فى N3 بينما تتم الألكلة الثنائية أو المتحولة على كل من N1 و N3. وتم إثبات تراكيب النواتج من مشتقات ألكيل هيدانتوين بإستخدام الوسائل الطيفية المختلفة مثل طيف الأشعة تحت الحمراء وطيف الرنين النووي المغناطيسى وطيف الكتلة وكذلك التحاليل الدقيقة للعناصر.