Phase-Transfer Catalyzed Alkylation of Hydantoin and 5-Methyl-5-Phenylhydantoin

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Abstract. PTC-alkylation of hydantoin (**1a**) and 5-methyl-5-phenyl-hydantoin (**1b**) by different organohalogen reagents at 25ºC 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 DP × 400 spectrometer, using CDCl$_3$ as solvent and TMS as internal standard (chemical shifts in δ values in ppm). Elemental analysis was performed on Perkin Elmer 2400, series II micro-analyzer. 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 25ºC 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, but 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) fitted 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 25ºC. 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 separate the products from the unreacted hydantoins. The solid residue was crystallized from appropriate solvent. The results are listed in Table 1.

Results and Discussion

The approach reported here is an extension and continuation of our interest in alkylation of some heterocycles under 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 25ºC.
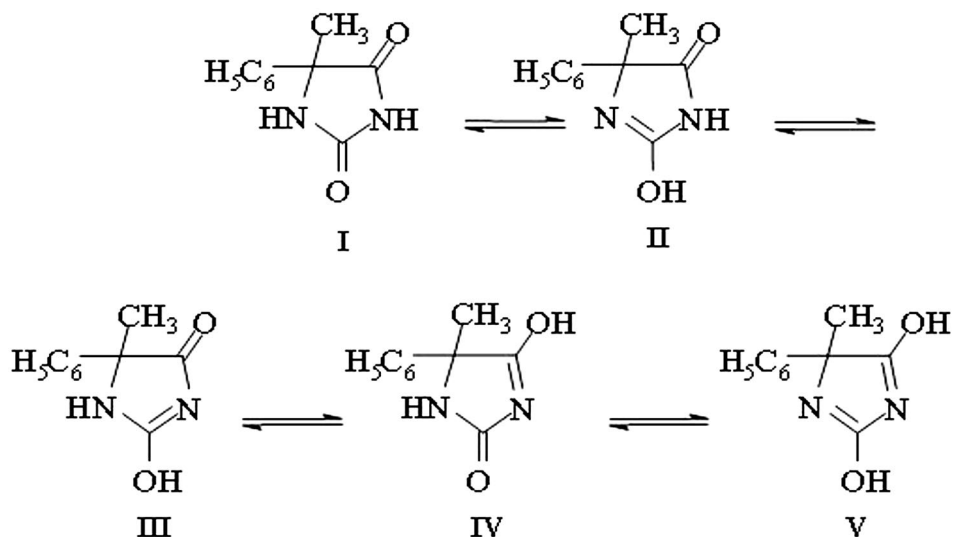
On the other hand, we are aiming to synthesize new hydantoin derivatives which might have an expected biological activity in addition to the well known biological, pharmacological and medicinal applications of hydantoins[11-20].

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

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

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

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 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_2CO_3) as liquid/solid phases and in the presence of tetrabutylammonium bromide as catalyst at 25ºC 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**) 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-dioxoimidazoliden-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 dial-

kylation (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).

The structure of mono and dialkylated hydantoins (**2a-g** and **3**) has been established by spectral data (Table 2) and elemental analysis (Table 1).
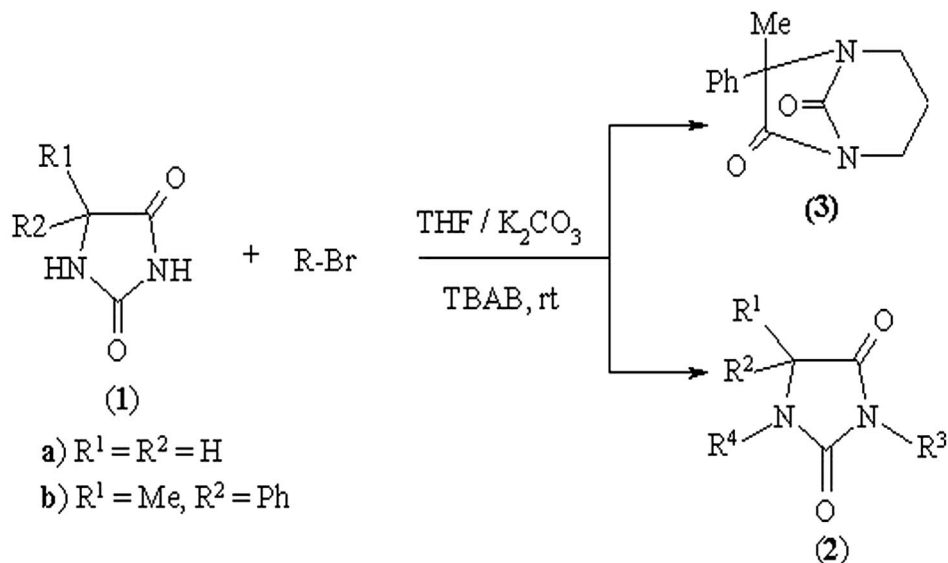
2	R^1	R^2	R^3	R^4
a	H	H	C_2H_5	H
b	H	H	$n\text{-}C_3H_7$	H
c	H	H	$n\text{-}C_4H_9$	H
d	H	H	$CH_2CH=CH_2$	H
e	H	H	$C_6H_5CH_2$	H
f	H	H	$(CH_2)_2Br$	H
g	H	H	$(CH_2)_3Br$	H
h	H	H	CH_2CO_2Et	CH_2CO_2Et
i	Me	Ph	C_2H_5	H
j	Me	Ph	$n\text{-}C_3H_7$	H
k	Me	Ph	$n\text{-}C_4H_9$	H
l	Me	Ph	$CH_2CH=CH_2$	H
m	Me	Ph	$(CH_2)_2Br$	H
n	Me	Ph	$(CH_2)_3Br$	H
o	Me	Ph	$C_6H_5CH_2$	$C_6H_5CH_2$
P	Me	Ph	CH_2CO_2Et	CH_2CO_2Et

Scheme 2

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

Compd. no.	IR (ν in cm^{-1}) C=O	CH	NH,OH	^{1}H-NMR CDCl$_3$ / δ (ppm)	^{13}C-NMR δ(ppm)	MS (abundance %)
2a	1710	2832 2982	3224	1.23 (t, 3H, C$\underline{H}_3$), 3.58 (q, 2H, C$\underline{H}_2$ of C$_2$H$_5$), 3.98 (s, 2H, C5-$\underline{H}_2$), 6.44 (b, 1H, N$\underline{H}$).	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$\underline{H}_3$), 1.86 (m, 2H, C$\underline{H}_2$-Me), 3.69 (t, 2H, N-C$\underline{H}_2$), 4.19 (s, 2H, C5-$\underline{H}_2$), 6.90 (b, 1H, N$\underline{H}$).	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$^+$), 101 (51, 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$\underline{H}_3$), 1.35 (m, 2H, C$\underline{H}_2$), 1.60 (m, 2H, C$\underline{H}_2$), 3.51 (t, 2H, N-C$\underline{H}_2$), 3.98 (s, 2H, C5-$\underline{H}_2$) 6.94 (b, 1H, N$\underline{H}$).	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$^+$), 127 (8, M-HCO), 114 (37, M-HNCO), 101 (86, M-C$_4$H$_8$), 85 (36, MNC$_4$H$_9$), 56 (100, N$_2$CO).
2d	1714 1768	2848 3005	3249	4.00 (s, 2H, C5-$\underline{H}_2$), 4.13 (d, 2H, N-C$\underline{H}_2$), 5.19 (d ×d, 2H, C$\underline{H}_2$=), 5.81 (m, 1H, -C$\underline{H}$=), 5.90 (B, 1H, N$\underline{H}$).	....	140 (33, M$^+$), 112 (17, MCO), 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-$\underline{H}_2$), 4.71 (s, 2H, N-C$\underline{H}_2$), 6.53 (s, 1H, N$\underline{H}$), 7.31-7.45 (m, 5H, ph-$\underline{H}$).	42.4 (N-CH$_2$), 47.3 (C5), 127.4, 128.1, 129.0, 129.5, 129.7 (Ph-$\underline{C}$H), 136.0 (Ph-C), 158.6 (C4), 171.4 (C2).	190 (81, M$^+$), 161(40, M-HCO), 132 (13, M-2×HCO), 118 (21, MHN (CO)$_2$), 104 (100, M-C$_6$H$_5$), 91 (97, C$_7$H$_7^+$), 77 (52, C$_6$H$_5^+$), 65 (59), 56 (56, N$_2$CO).

Table 2. Contd.

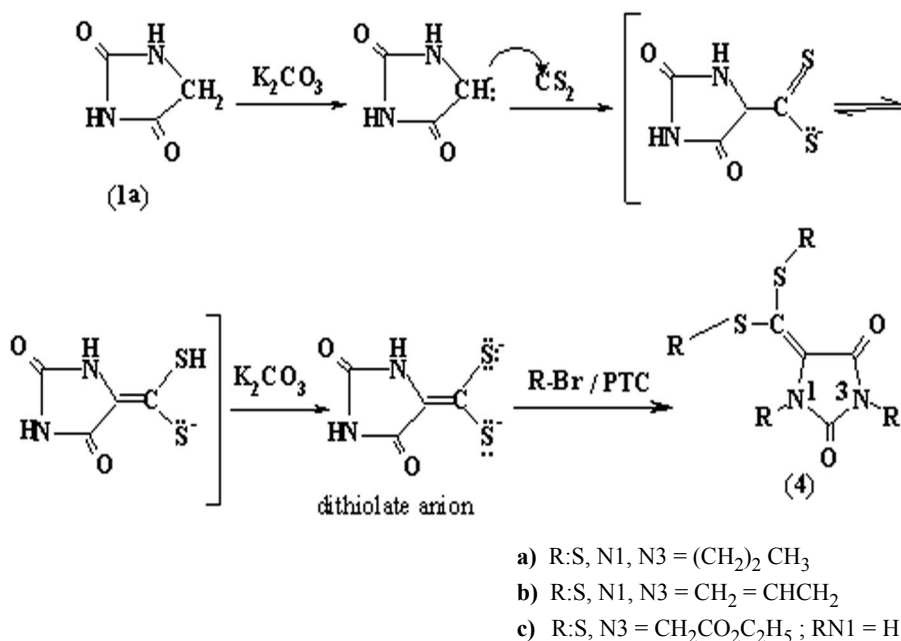| Compd. no.	IR (ν in cm⁻¹)			¹H-NMR CDCl₃ / δ(ppm)	¹³C-NMR δ(ppm)	MS (abundance %)
	C=O	CH	NH,OH			
2f	1706 1770	2818 2978	3259	3.57 (t, 2H, Br-C$\underline{H}_2$), 3.94 (t, 2H, N-C$\underline{H}_2$), 4.03 (s, 2H, C5 $\underline{H}_2$), 6.16 (b, 1H, N$\underline{H}$).	....	206 (10, M⁺), 127 (100, M-Br), 79 & 81 (15, Br), 85 [23, M-(N-C₂H₄Br)], 56 (72, N₂CO).
2g	1696 1758	2877 2940	3272	2.21 (m, 2H, C2-$\underline{H}_2$, propyl), 3.41 (t, 2H, Br-C$\underline{H}_2$), 3.68 (t, 2H, N-C$\underline{H}_2$), 3.99 (s, 2H, C5-$\underline{H}_2$), 5.48 (b, 1H, N$\underline{H}$).	....	220 (3.6, M⁺), 141 (82.0, M-Br), 114 (26.9, M-CH₂ = CH-Br) 79 & 81 (18, Br), 85 [40.1, M-(M-C₃H₆Br)], 56 (100, N₂CO).
2h	1724 1765	2985	......	1.29, 1.30 (2×t, 6H, 2×C$\underline{H}_3$ ester), 4.12 (s, 2H, N1-C$\underline{H}_2$), 4.18 (s, 2H, C5-$\underline{H}_2$), 4.23, 4.24 (2×q, 4H, 2×O-C$\underline{H}_2$), 4.26 (s, 2H, N3-C$\underline{H}_2$).	....	....
2i	1703 1765	2985	3332	1.19 (t, 3H, CH₃, of ethyl), 1.82 (s, 3H, CH₃), 3.54 (q. 2H CH₂ of ethyl), 7.03 (b, IH, NH), 7.27-7.52 (m, 5H, Ph-H).	13.2 (CH₃, ethyl), 23.8 (5-CH₃), 33.8 (CH₂, ethyl), 63.5 (C5), 124.3-129.6 (Ph-C$\underline{H}$), 138.8 (Ph-$\underline{C}$), 157.1 (C4), 175.3 (C2).	218 (11, M⁺), 203 (52, M-CH₃ or M-NH), 119 (35), 104 (100, C₆H₅C≡N⁺H), 77 (50, C₆H₅⁺), 56 (16, N₂CO), 51 (42).
2j	1702 1771	2874 2964	3256	0.87 (t, 3H, CH₃, of propyl) 1.63 (m, 2H, CH₂), 1.83 (s, 3H, 5-CH₃), 3.47 (t, 2H, -H-CH₂), 6.65 (b, 1H, NH), 7.26-7.52 (m, 5H, Ph-H).	....	232 (13, M⁺), 217 (47, M-CH₃ or M-NH), 132 (15), 119 (34, C₆H₅(CH₃) C=NH), 104 (100, C₆H₅C≡NH), 9 (14, C₆H₅N⁺), 77 (47, C₆H₅⁺), 51 (16).

Table 2. Contd.

Compd. no.	IR (v in cm^{-1})			^{1}H-NMR CDCl$_3$ / δ (ppm)	^{13}C-NMR δ(ppm)	MS (abundance %)
	C=O	CH	NH,OH			
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$_2$), 6.35 (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$_5$), 57 (29, C$_4$H$_9$$^+$), 51 (32).
2l	1706 1774	2930 2996 3040	3362	1.88 (s, 3H, CH$_3$), 3.59 (t, 2H, CH$_2$-Br), 3.94 (t, 2H, N-CH$_2$), 6.51 (S, 1H, NH), 7.27-7.54 (m, 5H, Ph-H).	………	………
2m	1709 1769	2855 2978 3111	3240	4.01 (s, 2H, C5-H$_2$), 4.71 (s, 2H, N-CH$_2$), 6.53 (s, 1H, NH) 7.31-7.45 (m, 5H, ph-H).	………	………
2n	1706 1766	2839 2974	3254	1.85 (s, 3H, CH$_3$), 2.19 (m, 2H, C2-H$_2$ of propyl), 3.35 (t, 2H, CH$_2$-Br), 3.66 (t, 2H, N-CH$_2$), 6.73 (s, 1H, NH), 7.28-7.53 (m, 5H, Ph-H).	26.8 (CH$_3$), 30.7 (C2-propyl), 32.9 (Br-C3, propyl), 40.7 (N-Cl-propyl), 65.4 (C5), 126.0-131.5 (Ph-CH), 140.3 (Ph-C), 158.4 (C4), 176.93 (C2).	312 (24, M$^{+\cdot}$), 297 (43, M-CH$_3$ or M-NH), 231 (51, M-HBr), 146 (28, M-Br (CH$_2$)$_3$ NCO), 132 (28, C$_6$H$_5$ (CH$_3$) C$_2$O), 119 (61, C$_6$H$_5$(CH$_3$) C=NH), 104 (100, C$_6$H$_5$C≡NH), 79 & 81 (12, Br), 77 (78, C$_6$H$_5$$^+$), 51 (70).

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Table 2. Contd.

Compd. no.	IR (ν in cm⁻¹)			¹H-NMR CDCl₃ / δ (ppm)	¹³C-NMR δ(ppm)	MS (abundance %)
	C =O	CH	NH,OH			
2o	1706 1761	2933 3031	…….	1.57 (s, 3H, CH₃), 3.77 (d, 1H, N1-CH), 4.75 (q, 2H, N3-CH₂), 4.92 (d, lH, N1-CH), 7.16-7.40 (m, 15H, Ph-H).	23.6 (CH₃), 45.5 (N-CH₂), 69.3 (C5), 127.2-131.8 (Ph-CH), 137.8 (Ph-C-CH₂), 138.9 (Ph-C-C5), 158.2 (C4), 176.51 (C2)	370 (12, M⁺), 355 (2, M-CH₃), 146 (18, C₆H₅CHN₂CO), 132 (87, C₆H₅CH=N-CO⁺), 91 (100, C₇H₇⁺), 77 (28, C₆H₅⁺), 65 (29), 51 (19)
2p	1723 1766	2980 3028	…….	1.27 (t×t, 6H, 2 × CH₃, ester), 1.89 (s, 3H, C5-CH₃), 3.52 (d, 1H, N1-CH), 4.18 (q ×q, 4H, 2 × OCH₂, ester) 4.34 (q, 2H, N3-CH₂), 5.30 (s, 1H, N1-CH), 7-27-7.42 (m, 5H, Ph-H).	14.5 (CH₃, ester), 23.9 (5-CH₃), 39.75 (N3-CH₂), 42.5 (N1-CH₂), 58.9 (CH₂, ester), 61.58 (CH₂, 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⁺), 347 (11,M-CH₃), 289 (20, M-CO₂C₂H₅), 215 (12 M-2×CO₂C₂H₅), 187 (41, M-2 ×CH₂CO₂C₂H₅), 132 (26, C₆H₅CO₂C₂H₅), 91 (100, C₆H₅(CH₃)C₂O), 91 (100, C₇H₇), 84 (31), 56 (14).
3	1706 1771	2980 3098	…….	1.82 (s, 3H, CH₃), 2.03 (m, 2H, C2-H₂, propyl), 3.51 (m, 4H, C1-H₂+C3-H₂, propyl), 7.28-7.52 (m, 5H, ph-H).	24.4 (3-CH₂), 25.8 (CH₃), 35.8 (4-CH₂), 37.4 (2-CH₂), 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 monitored by TLC, this 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 viscous 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 = $(CH_2)_2 CH_3$
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).

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

Compd. no.	IR (v 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, $3 \times$ C$\underline{H}_2$), 2.91 (t, 2H, S-C$\underline{H}_2$), 3.05 (t, 2H, S-C$\underline{H}_2$), 3.34 (t, 2H, N-C$\underline{H}_2$), 3.86 (t, 2H, N-C$\underline{H}_2$).	345 (2, M$^{+\cdot}$), 260 (13, M-2 $\times$ C$_3$H$_7$), 226 (16), 218 (45, M-3 $\times$ C$_3$H$_7$), 18 (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, $4 \times$ C$\underline{H}_2$=), 5.63 (m, 1H,-C$\underline{H}$=), 5.86 (m, 2H, $2 \times$C$\underline{H}$=), 5.95-(m, 1H, -CH=).	....
4c	1722 1783	2982	3255	1.29 (t, 9H, $3 \times$ C$\underline{H}_3$), 4.08 (s, 4H, 2 $\times$ S-C$\underline{H}_2$), 4.22 (q, 6H, $3 \times$O-C$\underline{H}_2$) 4.37 (s, 2H, N3-C$\underline{H}_2$), 5.79 (b, 1H, N1-$\underline{H}$).	....

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ألْكَلَة هـيدانتوين و ٥-مثيل-٥-فنيل هيدانتوين تحت ظروف حفز الانتقال الصنفي

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المستخلص. تـم ألْكلة كـل من هـيدانتوين (1a) و ٥-مثيل-٥-فنيل هيدانتوين (1b) في وجود أو غياب ثاني كبريتيد الكربون تحت ظروف حفـز الانتقـال الصنفى ، وذلك باستـخدام بعض الكواشف العضـوية الهالوجينية عند درجة حرارة الغرفة وفي وجود بروميد رباعي بيوتيل أمونيوم كحافز . ويهدف البحث في دراسة مقارنة لدرجة نشاط ألْكلة N- أو -O للهيدانتـوينات. أثبتت الدراسة - في جـميع الحـالات - أنه تتم الألْكلة الأحادية في N3 ، بينما تتم الألْكلة الثنائية أو المتحولقة على كل من N1 و N3. وتم إثبات تراكيب النواتج من مشتقـات ألكيل هيدانتوين باستخدام الوسائل الطيفية المختلفة ، مثل طيف الأشعـة تحت الحمراء ، وطيف الرنين النووي المغنـاطيسي ، وطيف الكتلة ، وكـذلك التـحـاليل الدقيقة للعناصر .