^{1}H Nmr Stuctural Analysis of N_3'-Dialkylaminoethyl derivatives from Azabicyclospirohydantoins

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Based on the data from ^{1}H nmr spectra, the structure and spatial conformation of the N_3'-β-dimethyl and diethylaminoethyl derivatives from 3-alkyl-3-azabicyclo[3.2.1]octane-8-spiro-5'-hydantoins and 3-alkyl-3-azabicyclo[3.3.1]nonane-9-spiro-5'-hydantoins are established. The monosubstitution on the imide nitrogen atom has also been confirmed.

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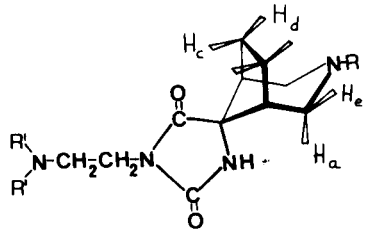
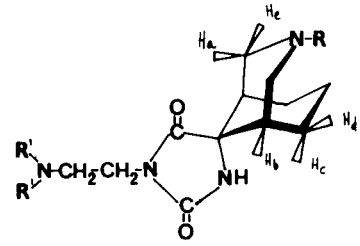
In previous papers the synthesis and structural analysis of two series of azabicyclospirohydantoins have been reported (1,2), now we wish to report the synthesis and structural analysis of the above mentioned compounds N_3'-substituted (Fig. 1).

Figure 1

N_3'-Dialkylaminoethyl derivatives from 3-alkyl-3-azabicyclo[3.2.1]octane-8-spiro-5'-hydantoins



N_3'-Dialkylaminoethyl derivatives from 3-alkyl-3-azabicyclo[3.3.1]nonane-9-spiro-5'-hydantoins



The chemical shifts and the coupling constants of the azabicyclospirohydantoins systems are similar to those previously described (1,2). The chair configuration of the piperidine ring is confirmed by the values of JH_a-H_b and JH_e-H_b of approximately 3 Hz in compounds **1-5**. In compounds **6-10**, JH_a-H_b has a value of about 3 Hz, and JH_e-H_b about 1 Hz, which implies that the piperidine ring is partially flattened. The geminal constants JH_a-H_e have a value of about 12 Hz.

Table 1

Chemical Shifts of Compounds **1-5** in Deuteriochloroform (δ values, TMS as Internal Reference)

									N-R		$(O=C)_2N$-CH_2-CH_2		R'-N-R'	
											α	β		
Compound	R	R'	H_a	H_e	H_b	H_c	H_d	H_α	H_β	H_α	H_β	H_α	H_β
1	CH_3	$(CH_2)_2$-$N(C_2H_5)_2$	2.44	2.66	2.04	2.23	1.85	2.33		3.56	2.6	2.52	0.98
2	C_2H_5	$(CH_2)_2$-$N(CH_3)_2$	2.46	2.7	2.04	2.2	1.84	2.52	1.04	3.56	2.6	2.23	
3	C_2H_5	$(CH_2)_2$-$N(C_2H_5)_2$	2.46	2.7	2.04	2.2	1.84	2.52	1.04	3.56	2.6	2.52	0.98
4	$CH(CH_3)_2$	$(CH_2)_2$-$N(CH_3)_2$	2.6	2.7	2.1	2.2	1.84	2.6	1.04	3.58	2.6	2.23	
5	$CH(CH_3)_2$	$(CH_2)_2$-$N(C_2H_5)_2$	2.6	2.7	2.04	2.2	1.86	2.6	1.08	3.56	2.6	2.56	0.98

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Table 2

Chemical Shifts of Compounds **6-10** in Deuteriochloroform (δ values, TMS as Internal Reference)

Compound	R	R′	H_a	H_e	H_b	H_c	H_d	H_f	N−R H_α	N−R H_β	$(O{=}C)_2N\text{-}CH_2\text{-}CH_2$ H_α	$(O{=}C)_2N\text{-}CH_2\text{-}CH_2$ H_β	R′-N-R′ H_α	R′-N-R′ H_β
6	CH_3	$-(CH_2)_2\text{-}N(CH_3)_2$	3.2	2.8	1.9	1.9	1.9	1.9	2.23		3.6	2.6	2.23	
7	CH_3	$-(CH_2)_2\text{-}N(C_2H_5)_2$	3.2	2.82	1.8	1.8	1.8	1.8	2.24		3.54	2.6	2.5	0.98
8	$CH(CH_3)_2$	$-(CH_2)_2\text{-}N(CH_3)_2$	3.4	2.7	1.8	1.8	1.8	1.8	2.6	1	3.52	2.6	2.24	
9	$CH(CH_3)_2$	$-(CH_2)_2\text{-}N(C_2H_5)_2$	3.4	2.72	1.8	1.8	1.8	1.8	2.6	1.02	3.54	2.6	2.56	0.98
10	$(CH_2)_3\text{-}CH_3$	$-(CH_2)_2\text{-}N(CH_3)_2$	3.14	2.76	1.8	1.8	1.8	1.8	2.5		3.6	2.6	2.23	

Table 3

Coupling Constants of Compounds **1-5** in Deuteriochloroform
(Hz Values, TMS as Internal Reference)

Compound	N-R H_α-H_β	$O{=}C\text{-}N(C{=}O)\text{-}CH_2CH_2$- H_α-H_β	$N\text{-}(CH_2CH_3)_2$ H_α-H_β
1		7	7
2	7	7	
3	7	7	7.5
4	6.2	7	
5	6	7	7

Table 4

Coupling Constants of Compounds **6-10** in Deuteriochloroform
(Hz Values, TMS as Internal Reference)

Compound	N-R H_α-H_β	N-R H_γ-H_δ	$O=C-N(C=O)-CH_2CH_2-$ H_α-H_β	$N-(CH_2CH_3)_2$ H_α-H_β
6			6	
7			7	7
8	6		7	
9	6		7	7
10	7	7	7	

Table 5

N_3'-Dialkylaminoethyl derivatives from 3-Alkyl-3-azabicyclo[3.2.1]octane-8-spiro-5'-hydantoins and 3-Alkyl-3-azabicyclo[3.3.1]nonane-9-spiro-5'-hydantoins

Compound	M.p.°C	Ir (C=O)(cm^{-1}) (a)	Ms m/e	Yield % (b)	Formula	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	120	1760, 1700	308	77	$C_{16}H_{28}O_2N_4$	62.31	9.15	18.16	62.35	9.13	18.18
2	132	1760, 1695	294	55	$C_{15}H_{26}O_2N_4$	61.20	8.90	19.03	61.24	8.93	19.07
3	105	1760, 1695	322	68	$C_{17}H_{30}O_2N_4$	63.32	9.37	17.37	63.37	9.41	17.38
4	170	1760, 1690	308	76	$C_{16}H_{28}O_2N_4$	62.31	9.15	18.16	62.35	9.14	18.18
5	160	1760, 1690	336	67	$C_{18}H_{32}O_2N_4$	64.25	9.58	16.65	64.30	9.60	16.63
6	165	1760, 1701	294	61	$C_{15}H_{26}O_2N_4$	61.20	8.90	19.03	61.21	8.95	18.99
7	128	1765, 1700	322	68	$C_{17}H_{30}O_2N_4$	63.32	9.37	17.37	63.38	9.42	17.33
8	101	1763, 1706	322	62	$C_{17}H_{30}O_2N_4$	63.32	9.37	17.37	63.28	9.35	17.39
9	105	1770, 1710	350	69	$C_{19}H_{34}O_2N_4$	65.10	9.77	15.98	65.15	9.69	15.96
10	91	1770, 1710	336	56	$C_{18}H_{32}O_2N_4$	64.25	9.58	16.65	64.25	9.62	16.61

(a) Potassium bromide. (b) From ethanol.

The substitution of the N_3'-hydrogen atom, implies a greater acidity for the N_1'-H hydrogen atom, because of the negative charge on the N_1'-nitrogen atom is delocalized on the adjacent carbonyl group, so the signal corresponding to N_1'-H in the compounds N_3'-substituted appears at approximately 8 ppm. Furthermore, the N_3'-H substitution is confirmed by the fact that the band due to the N_3'-H stretching vibration about 3020 cm^{-1} (3) disappears in all the cases.

EXPERIMENTAL

All melting points were taken in open capillary tubes and are uncorrected. Infrared spectra were determined using a Perkin Elmer 577 spectrophotometer. The ^1H nmr spectra have been recorded using a Variant XL 100 spectrometer. The mass spectra were determined on a Hitachi Perkin-Elmer RMU-6M spectrometer.

N_3'-Dialkylaminoethyl-3-alkyl-3-azabicyclo[3.2.1]octane-8-spiro-5'-hydantoins and N_3'-dialkylaminoethyl-3-alkyl-3-azabicyclo[3.3.1]nonane-9-spiro-5'-hydantoins.

A solution of 0.005 mole of the suitable spirohydantoin (1,2) in 3 ml. of ethanol was added to 5 ml. of 1 *N* aqueous sodium hydroxide, the mixture was refluxed about 15 minutes and the solution was allowed to cool to room temperature. To this solution was added a solution of 0.00682 mole of 2-β-dialkylaminoethyl chloride, hydrochloride in 1.7 ml. of aqueous sodium hydroxide. The mixture was refluxed about 2 hours and allowed to cool to room temperature. The resulting precipitate was washed with water and recrystallized. The newly synthesized spirohydantoins are described in Table 5.

REFERENCES AND NOTES

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(3) T. H. Elliot and P. N. Natarajan, *P. Pharm Pharmacol.*, **19**, 209 (1967).