Proton and Carbon NMR Spectra and Stereochemical Assignments for 3,5-Disubstituted Nortricyclenes

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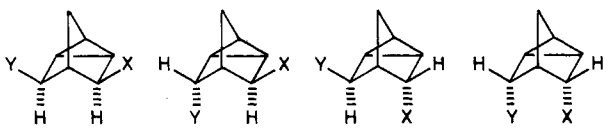
Received March 27, 1987

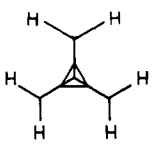
Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra of over 80 substituted nortricyclenes (including newly prepared stereoisomers) have been analyzed, leading to an empirical method for calculating the proton chemical shifts for endo-3 protons of *exo*-5- and *endo*-5,*exo*-3-disubstituted nortricyclenes. This calculation method has been used to establish the stereochemistry of other 3,5-disubstituted compounds of previously unknown or incorrectly assigned structures. Although the size of the data base for ^{13}C shifts is smaller, it does appear that γ-gauche and related effects are clearly insufficient to explain these shift changes.

The use of norbornadiene as a substrate for determining mechanisms for A_DE addition reactions has been well documented.[1-7] Combining those observations with new studies has lead to important mechanistic conclusions such as the concept of stereochemical control of product configuration in ion-pair processes[7,8] and the interesting occurrence of endo attack in norbornane-related systems.[9,10] In a related area, products of electrophilic addition to norbornadiene have been related to the products of electrophilic cleavage of carbon–carbon single bonds in strained quadricyclene systems.[11-14]

Correct stereochemical assignments for the configuration at positions 3 and 5 of 3,5-disubstituted nortricyclenes **1–4**



1 **2** **3** **4**



4a

are crucial to establishing the course of the aforementioned mechanisms. There has been a difference of opinion about the configurations of such compounds based on NMR data (cf. ref 2 and 7). The C_{3v} symmetry, **4a**, of the nortricyclene skeleton precludes the use of vicinal coupling constants, ^3J, between protons to determine exo and endo configuration, a use which has been very successful in norbornanes. Unambiguous structural assignments have been made by X-ray analysis[15,16] and by refined NMR techniques involving ^3J (proton–carbon) coupling constants.[17] Such methods are, however, time consuming and development of a simple NMR method is still desirable.

The purpose of this paper is to summarize NMR data for 3-substituted and 3,5-disubstituted nortricyclenes and to use these data to produce a simple equation for empirically predicting chemical shifts in these systems. These predictions would be very useful for establishing stereochemical assignments. Since NMR data for certain functional groups were not available, we have prepared some nortricyclene derivatives to fill these gaps.

Results and Discussion

Synthesis of Substituted Nortricyclenes. Since literature characterizations of certain simple nitro- and arylthio-substituted nortricyclenes are apparently not available, whereas a number of reports of electrophilic addition of NO_2^+ and ArS^+ species have been published,[8,18,19] we have prepared some model compounds.

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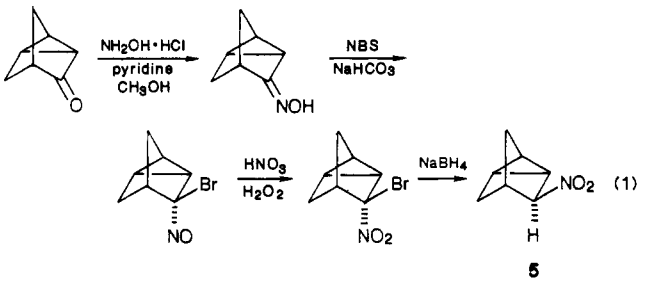
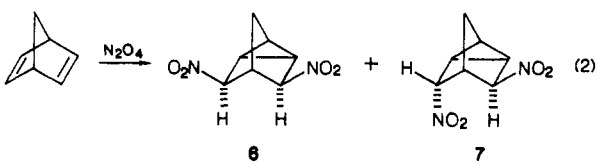
Nortricyclanone was converted to 3-nitronortricyclene (5) in a four-step sequence (eq 1). Epimeric 3,5-dinitronor-



(1)

tricyclenes, 6 and 7, were prepared by addition of N_2O_4 to norbornadiene (eq 2). The configurations of 6 and 7

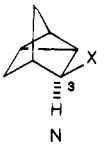


(2)

follow from the number of signals at lower field in the ^1H NMR spectra: exo,exo isomer 6 reveals its plane of symmetry by displaying only one H–C–NO_2 signal, while exo,endo isomer 7 shows two signals in this region. Isomeric 3,5-bis(phenylthio)nortricyclenes, 8 and 9, were prepared by photochemical addition of diphenyl disulfide to norbornadiene (eq 3).

^1H NMR Data for Substituted Nortricyclenes. Chemical shifts of 3-substituted nortricyclenes are pre-

Table I. Chemical Shifts of the 3-H Protons of Monosubstituted Nortricyclenes



entry	subst	shift	ref	average shift
1	F	4.58	20	4.63 ± 0.32
2		4.68	21	
3		(5.05)	22, 23	
4	Cl	3.88	24	
5		3.87	25	
6		3.83	26	3.85 ± 0.03
7		3.81	27	
8		3.87	28	
9	Br	3.88	29	3.91 ± 0.12
10		3.94	30	
11	I	3.80	31	3.79 ± 0.06
12		3.78	32	
13	OCH_3	3.39	33	3.39 ± 0.03
14		3.40	34	
15	OH	3.80	29	
16	$O(C{=}O)CH_3$	4.56	35	
17		4.67	34	
18		4.56	36	4.62 ± 0.05
19		4.64	37a	
20		4.64	37a	
21	$O(C{=}O)Ph$	4.90	37a	
22	CCl_3	2.72	24	
23	SCH_2Ph	1.74	38	
24	$S(O)CH_2Ph$	2.66	39	
25	SPh	3.14	24	
26	$2\text{-}CH_3C_6H_4$	3.10	40	
27	$2,4,6\text{-}(CH_3)_3C_6H_2$	2.80	41	
28	$4\text{-}ClC_6H_4S$	3.06	41	
29	$2\text{-}NO_2C_6H_4S$	3.24	42	
30	$2,4\text{-}(NO_2)_2C_6H_3S$	3.25	43	3.28 ± 0.16
31		3.30	44	
32	$S(C{=}O)CH_3$	3.40	45	
33	SCN	3.28	46	
34	NCS	3.62	46	
35	$NH(C{=}O)CH_3$	3.80	47	3.82 ± 0.09
36		3.83	48	
37	ONO_2	4.77	49	
38	NO_2	4.40	37a	
39		4.41	37a	4.41 ± 0.01
40		4.41	37b	

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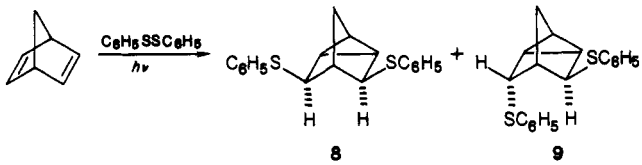

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(3)

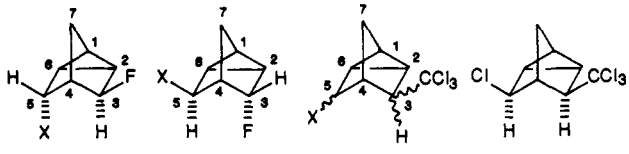
sented in Table I and analogous data for 3,5-exo,exo-disubstituted nortricyclenes 1 are presented in Table II. Comparison of various published NMR data usually reveals variations in chemical shifts for a given proton in the 0.1–0.15-ppm range. Reproducibility of chemical shifts for the compounds determined in our laboratories are in the range ±0.04 ppm, despite variations in sample concentrations and spectrometers used.

In 1969 Coulson suggested two empirical generalizations for nearest neighbor deshielding effects in 3,5-disubstituted nortricyclenes:[33] (i) The 3-H chemical shift is not significantly affected by 5-exo substituents (i.e., non-nearest-neighbor effects are minor). (ii) Endo substitution at C-5 shifts endo-3 protons downfield.

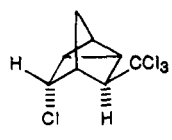
The validity of the first generalization can be tested by comparing Tables I and II. For a number of substituents this generalization is valid; these include such groups as halo, hydroxy, and methoxy substituents ("normal" substituents). For a number of substituents such as acetoxy, acetamido, nitro, and (2,4-dinitrophenyl)thio, however, there are considerable differences between the shift data in Tables I and II; in these cases the 5-exo substituent induces on the average more than a 0.12 ppm shift. These substituents are referred to as "abnormal" substituents.

The next two tables of chemical shifts for substituted nortricyclenes are organized as follows: Table III contains data for compounds with endo "normal" substituents at C-5, and Table IV for endo "abnormal" substituents at C-5. In Table III we can compare the shifts for C-3 protons (geminal to functional groups of monosubstituted nortricyclenes) to the corresponding protons for compounds with C-5 substituents that are endo and thus close to the C-3 protons. The shifts for exo,exo "abnormally substituted" compounds are compared in Table IV to those for 3,5-disubstituted compounds whose endo-3 protons are influenced by "abnormal" endo-C-5 substituents.

We now shall consider some published results which seem to be inconsistent with the generalizations above. Compounds have been isolated that have been assigned structure 10 for both the fluorochloro- and fluorobromo-



10 11 12 12a



12b

10-12: X = Cl, Br

nortricyclenes.[51] Upon comparison to the data in Tables I and III, the reported shift difference for the 3-H proton (compared to the 3-H proton for 3-fluoronortricyclene) is found to be surprisingly small (0.14 and 0.17 ppm, respectively), while the reported difference for the 5-H proton (compared to 3-chloro- and 3-bromonortricyclene) is quite large (0.55 and 0.75 ppm, respectively). The reported shifts imply that the structures of the dihalides should be 11, rather than 10. In analogous fashion, ^{1}H NMR data for 3-acetamido-5-halonortricyclenes (Table II, entries 37 and 38; Table III, entries 10 and 15; Table IV, entries 14 and 15) permit unambiguous assignments for the corresponding configurations.

NMR signal assignments reported[30] for 3-H and 5-H in compounds of general structure 12 should be altered; those in the 2.45–2.54 ppm range must be due to 4-H, whereas those in the 2.75–2.80 and in the 3.59–3.68 ppm range apply to, respectively, endo-3-H of structure 12a and endo-3-H signals of structure 12b. Entry 12 of Table III shows that an endo-C-5 bromine induces a downfield shift for a nearby endo-3-H similar in magnitude to other C-3 substituted compounds (entries 13–15, Table III).

Now let us consider the effect of C-3 epimerization upon the chemical shift of the 3-H proton. Specifically, in Table V we shall compare the chemical shift of the exo- vs. endo-3 protons while holding the C-5 substituent in the exo position. The analogous epimerization in norbornane systems converting a proton from an endo to an exo position induces a downfield shift of ca. 0.5–0.8 ppm, and this has been used as a tool for configurational assignments (see ref 7 and references cited therein). In contrast the data on Table V indicate that C-3 epimerization causes no more than a 0.21-ppm difference in chemical shift of the 3-H proton, and this difference is of the order of magnitude of the error in measurement of these chemical shifts. This is not surprising in view of our discussions of the preceding tables and of the significantly different symmetry of nortricyclene systems compared to norbornane systems.

The last two rows of Table V deserve comment. Epimerization at the carbon bearing an HgCl group leads to an *upfield* shift of ca. 0.21 ppm. An even larger upfield shift of 0.63 ppm was found for the $C_6H_5SO_2$ group. Although some sort of shielding by benzene might explain the latter, at present there is no straightforward explanation for these results.

The ^{1}H NMR spectra of endo,endo-disubstituted isomers deserve comment. In view of the irregularity of changes in chemical shifts due to configuration changes and of the small magnitude of these changes, discrimination between the exo,exo and endo,endo isomers by this method is unreliable. Lanthanide shift reagents have been employed in such cases.[70]

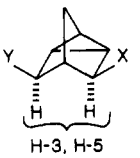
The data of Tables I–V give rise to the following equation for calculating the chemical shifts of H-3 (δ_3) of 3,5-disubstituted nortricyclenes (eq 4) where δ_0 is simply the

$$\delta_3 = \delta_0 + \Delta_s + \Delta_{de} \quad (4)$$

chemical shift for the proton at C-3 in the 3-nortricyclyl system, Δ_s is the change in shift for the C-3 proton due any substitution at C-5 (this increment is added regardless of whether the C-5 substituent is exo or endo), and Δ_{de} is the deshielding effect of an endo substituent at C-5. For the majority of substituents, Δ_s is small or zero. Numerical results (accompanied by confidence intervals for $\alpha = 90\%$, where possible) are listed in Table VI. For Δ_s to be other than zero, data from Table II must suggest Δ_s-type shifts greater than the error range for H-3 listed in Table I.

The assignment of configuration for the 3- and 5-position of nortricyclene nitro nitrates 13 and 14 (Chart I)[49,68] can be made with the aid of eq 4. Compounds 13 and 14 were formed along with dinitro compounds 6 and 7 when N_2O_4 was added to norbornadiene; compound 14 had been obtained previously during the addition of acetyl nitrate to norbornadiene.[49] Downfield signals (Chart I) for both compounds are assigned to the protons in the H–C–ONO_2

Table II. Chemical Shifts of the 3-H and 5-H Protons in 3-*exo*,5-*exo*-Disubstituted Nortricyclenes 1



1

entry	subst X	subst Y	chemical shift HCX	chemical shift HCY	ref	chem shift change[a] HCX	chem shift change[a] HCY
1	F	F	4.53	4.53	50, 51	−0.10	−0.10
2	F	Cl	4.51	3.81	51	−0.12	−0.04
3	F	Br	4.54	3.87	51	−0.09	−0.04
4	Cl	Cl	3.86	3.86	27	0.01	0.01
5			3.88	3.88	52	0.03	0.03
6	Cl	CCl_3	3.83	2.75[53]	30	0.02	0.03
7			3.95	2.78	24	0.10	0.06
8	Cl	$(C{=}O)OCH_3$	3.96	3.23[23]	54	0.11	
9	Cl	SePh	3.96	3.96[23]	55	0.11	
10	Cl	OCH_3	3.89	3.40	56	0.04	0.01
11	Cl	BCl_2	3.91	2.18	57	0.06	
12	Br	CCl_3	3.92	2.80	30	0.01	−0.11
13	Br	$PhSO_2$	3.79	3.04	58	−0.12	
14	Br	4-$CH_3C_6H_4SO_2$	3.79	3.04	59	−0.12	
15	Br	OCH_3	3.91	3.39	56	0.00	0.00
16	OCH_3	OCH_3	3.35	3.35	60	−0.04	−0.04
17			3.33	3.33	56	−0.06	−0.06
18	OH	2-$CH_3C_6H_4S$	3.70	3.03	40	−0.10	−0.07
19	$OCOCH_3$	HgCl	4.55	2.59	61	−0.07	
20			4.64	2.68	62	0.02	
21	$OCOCH_3$	HgBr	4.60	2.66	35	−0.02	
22	$OCOCH_3$	$(C{=}O)OCH_3$	4.65	2.56	63	0.03	
23	SPh	SPh	3.19	3.19	37a	0.05	0.05
24			3.18	3.18	37a	0.04	0.04
25			3.18	3.18	37b	0.04	0.04
26	$O(C{=}O)CH_3$	$O(C{=}O)CH_3$	5.34	5.34	64, 23	(0.72)	(0.72)
27			4.71	4.71	37b	0.09	0.09
28			4.70	4.70	37b	0.08	0.08
29	$O(C{=}O)CH_3$	Cl	4.60	3.98	71	−0.02	0.13
30			4.52	3.84	35, 23	−0.10	−0.01
31			4.62	3.99	61	0.00	0.14
32	$OCOCH_3$	2,4-$(NO_2)_2C_6H_3S$	4.72	3.41	7	0.10	0.13
33			4.86	3.56	17	0.14	0.28
34			4.91	3.59	37c	0.29	0.31
35	Cl	2,4-$(NO_2)_2C_6H_3S$	4.16	3.52	65	0.31	0.28
36	$O(C{=}O)CH_3$	2-$NO_2C_6H_4S$	4.86	3.50	7	0.24	0.26
37	$NH(C{=}O)CH_3$	Cl	3.95	4.05	48, 66	0.13	0.20
38	$NH(C{=}O)CH_3$	Br	3.92	4.08	48, 66	0.10	0.17
39	NO_2	$O(C{=}O)CH_3$	4.40	4.68	67	−0.01	0.06
40			4.45	4.70	68	0.04	0.08
41	NO_2	NO_2	4.53	4.53	37b	0.12	0.12
42			4.53	4.53	37b	0.12	0.12
43			4.52	4.52	37b	0.11	0.11
44	$OCOC_6H_5$	$OCOC_6H_5$	5.05	5.05	52	0.15	0.15
45			4.88	4.88	70, 23	−0.02	−0.02
46			5.07	5.07	37b	0.14	0.14
47			5.03	5.03	37a	0.13	0.13

[a] Calculated by substracting the chemical shift for the proton on the carbon bearing each of X or Y of the monosubstituted compound (data from Table 1) from the shift of HCX or HCY for the disubstituted compound.

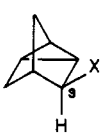
units. Since a value for the Δ_{de} term for the ONO_2 group was not available, a value of 0.6 was assumed on the basis of shifts caused by the $OCOCH_3$, $OCOC_6H_5$, and $OClO_3$ groups (Table VI); this assumes that the first atom, the oxygen, is the major influence upon the chemical shift. Comparison of calculated and observed chemical shifts (Chart I) permits assignment of structures **13** and **14** to the adducts obtained and rejection of structure **15**.

Thus it is clear that Coulson's observations (see above) are essentially correct. We have extensively expanded the data base for this approach and suggested an equation format for the use of our data.

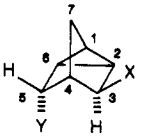
^{13}C NMR Spectra of 3,5-Disubstituted Nortricyclenes. Literature ^{13}C NMR data for nortricyclenes are sparse and are not systematic.[77] Moreover, a published account of the hazards of configuration and signal assignments has appeared.[14] Available data for epimeric pairs of compounds **1** and **2** are collected in Table VII.

(71) Neale, R. S.; Whipple, E. B. *J. Am. Chem. Soc.* **1964**, *86*, 3130.
(72) The configurations are corrected as per the discussion in this paper.
(73) Henshaw, B. C.; Rome, D. W.; Johnson, B. L. *Tetrahedron* **1971**, *27*, 2955.
(74) Solvents: (a) acetone-d_6; (b) methanol-d_4 + D_2O.
(75) Schienbaum, M. L. *J. Org. Chem.* **1970**, *35*, 2785.
(76) Gancarz, R. A.; Kice, J. L. *Tetrahedron Lett.* **1980**, *21*, 4155.
(77) For example, see: Breitmaier, E.; Voelter, V. *^{13}C NMR Spectroscopy*, 2nd ed.; VCH International: Weinheim, New York, 1978; pp 136–137.

Table III. The Deshielding Effect of "Normal" *endo*-5-Substituents in 3,5-Disubstituted Nortricyclenes 2



N[a]

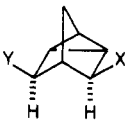


2

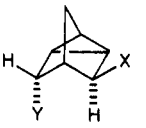
entry	subst Y	subst X	chem shift of H-3 in N[a]	chem shift of H-3 in 2	ref	effect of Y
1	F	F	4.63	5.22	51	0.59
2	F	Cl	3.85	4.42	51, 72	0.57
3	F	Br	3.91	4.55	51, 72	0.64
4	Cl	Cl	3.85	4.53	27	0.68
5	Cl	Cl	3.85	4.53	52	0.68
6	Cl	CCl_3	2.72	3.68	30	0.96
7	Cl	OCH_3	3.39	4.06	33	0.67
8	Cl	OCH_3	3.39	4.16	56	0.77
9	Cl	$O(C{=}O)CH_3$	4.62	5.30	61	0.68
10	Cl	$NHCOCH_3$	3.82	4.62	48, 66	0.80
11	Cl	$2,4\text{-}(NO_2)_2C_6H_3S$	3.28	4.10	7	0.82
12	Br	CCl_3	2.72	3.59	30	0.87
13	Br	OCH_3	3.39	4.06	33	0.67
14	Br	OCH_3	3.39	4.10	56	0.71
15	Br	$NHCOCH_3$	3.82	4.68	48, 66	0.86
16	OCH_3	OCH_3	3.39	3.95	60	0.56
17	OCH_3	OCH_3	3.39	3.97	63	0.58
18	OCH_3	$OCOCH_3$	4.62	5.13	63	0.51
19	CCl_3	Br	3.91	4.89	10	0.98
20	$COOCH_3$	$OCOCH_3$	4.62	4.93	56	0.31
21	$COOCH_3$	Cl	3.85	4.23	25	0.38
22	HgCl	$OCOCH_3$	4.62	4.81	61	0.19
23	CH_3	OH	3.80	4.05	73	0.25
24	OH	$2\text{-}CH_3C_6H_4S$	3.10	3.70	40	0.60
25	SC_6H_5	SC_6H_5	3.14	3.97	37a	0.83
26	SC_6H_5	SC_6H_5	3.14	4.03	37a	0.89
27	SC_6H_5	SC_6H_5	3.14	3.98	37a	0.84
28	SC_6H_5	SC_6H_5	3.14	4.00	37a	0.86
29	SC_6H_5	SC_6H_5	3.14	4.00	37b	0.86

[a] N = 3-substituted nortricyclyl compounds.

Table IV. Deshielding Effects of "Abnormal" Endo Substituents in 3,5-Disubstituted Nortricyclenes 1 and 2



1

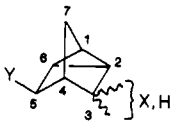


2

entry	subst Y	subst X	proton shfts (δ) HCX in 1	proton shfts (δ) HCX in 2	ref	deshielding effect of Y
1	$O(C{=}O)CH_3$	$O(C{=}O)CH_3$	5.34	4.97–5.14	23, 64	
2	$O(C{=}O)CH_3$	$O(C{=}O)CH_3$	4.71	5.20	37b	0.49
3	$O(C{=}O)CH_3$	$O(C{=}O)CH_3$	4.70	5.20	37b	0.50
4	$O(C{=}O)CH_3$	$O(C{=}O)CH_3$	4.70	5.20	37b	0.50
5	$O(C{=}O)CH_3$	Cl	3.98	4.40	71	0.42
6	$O(C{=}O)CH_3$	Cl	3.84	4.34	35	0.50
7	$O(C{=}O)CH_3$	$2,4\text{-}(NO_2)_2C_6H_3S$	3.41	3.93	7	0.52
8	$O(C{=}O)CH_3$	$2,4\text{-}(NO_2)_2C_6H_3S$	3.50	3.96	17	0.50
9	$O(C{=}O)CH_3$	$2,4\text{-}(NO_2)_2C_6H_3S$	3.59	4.02	37c	0.43
10	$O(C{=}O)CH_3$	$2\text{-}NO_2C_6H_4S$	3.50	3.95	7	0.45
11	$O(C{=}O)C_6H_5$	$O(C{=}O)C_6H_5$	5.05	5.62	69	0.57
12	$O(C{=}O)C_6H_5$	$O(C{=}O)C_6H_5$	5.07	5.60	37b	0.53
13	$NH(C{=}O)CH_3$	$NH(C{=}O)CH_3$	3.77[70,74a]	4.00[74b,75]		0.23
14	$NH(C{=}O)CH_3$	Cl	4.05	4.42	48, 66	0.37
15	$NH(C{=}O)CH_3$	Br	4.08	4.31	48, 66	0.23
16	NO_2	NO_2	4.53	4.93	37b	0.40
17	NO_2	NO_2	4.53	4.92	37a	0.39
18	NO_2	$O(C{=}O)CH_3$	4.68	4.91	68	0.23
19	$C_6H_5SO_2$	Br	3.79	4.92	58	1.13
20	$OClO_3$	NO_2	4.58	5.15	18	0.57

Data listed in this table were subjected to one of the following cross-checks: (i) The structures and configurations of the compounds were unambiguously established by either X-ray analysis (entries 1–5) or by symmetry (entries

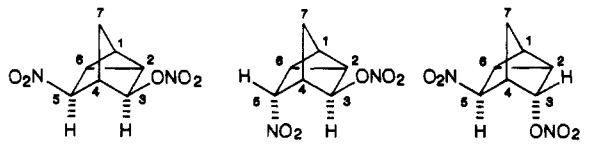
Table V. Effect of C-3 Epimerization upon the ^1H NMR Shift of 3,*exo*-5-Disbustituted Nortricyclenes



entry	subst X	subst Y	H_{endo}[a]	H_{exo}[b]	ref	$\Delta\delta$[c]	$\Delta\delta_{av}$[d]
1	F	F	4.53	4.74	51	0.21	F
2		Cl	4.51	4.72	51	0.21	0.21
3		Br	4.54	4.75	51	0.21	
4	Cl	Cl	3.86	3.95	27	0.09	
5			3.88	3.98	52	0.10	Cl
6		$O(C{=}O)CH_3$	3.99	3.95	61	−0.04	0.08
7		OCH_3	3.89	3.98	56	0.09	
8		CCl_3	3.83	4.08	30	0.21	
9		$NH(C{=}O)CH_3$	4.05	4.05	48, 66	0.00	
10	Br	OCH_3	3.91	3.96	56	0.05	
11		SO_2Ph	3.79	3.92	58	0.13	Br
12		CCl_3	3.92	3.99	30	0.07	0.07
13		$NH(C{=}O)CH_3$	4.08	4.10	48, 66	0.02	
14	OCH_3	OCH_3	3.35	3.51	60	0.16	OCH_3
15			3.33	3.52	63	0.19	0.18
16	$O(C{=}O)CH_3$	Cl	4.60	4.75	71	0.15	
17			4.52	4.67	35	0.15	
18		$2,4\text{-}(NO_2)_2C_6H_3S$	4.72	4.92	7	0.20	$O(C{=}O)CH_3$
19		$2\text{-}NO_2C_6H_4S$	4.86	4.86	7	0.00	0.105
20		$O(C{=}O)CH_3$	4.71	4.77	37b	0.06	
21			4.70	4.77	37b	0.07	
22	$O(C{=}O)C_6H_5$	$O(C{=}O)C_6H_5$	5.05	5.08	69	0.03	$O(C{=}O)C_6H_5$
23			5.07	5.10	37b	0.03	0.03
24	OH	$2\text{-}CH_3C_6H_4S$	3.70	3.80	40	0.10	
25	$OClO_3$	NO_2	5.02	5.15	18	0.13	
26	SePh	$4\text{-}CH_3C_6H_4SO_2$	3.34	3.19	42	−0.15	
27	NO_2	NO_2	4.53	4.68	37b	0.15	
28			4.52	4.64	37a	0.12	
29	$COOCH_3$	$O(C{=}O)CH_3$	2.56	2.51	56	−0.05	
30	SPh	PhS	3.19	3.34	37a	0.15	C_6H_5S
31			3.18	3.37	37a	0.19	0.18
32			3.18	3.37	37b	0.19	
33	HgCl	$O(C{=}O)CH_3$	2.59	2.38	61	−0.21	
34	SO_2Ph	Br	3.65	3.02	58	−0.63	

[a] Chemical shift (δ, ppm) for endo-3-H of compound 1. [b] Chemical shift (δ, ppm) for exo-3-H of compound 2. [c] $\Delta\delta = \delta_{Hexo} - \delta_{Hendo}$. [d] Average $\Delta\delta$ for cited functional group.

Chart I. Proton Chemical Shifts for Nortricyclene Nitro Nitronates



	13		14		15	
	δ_5	δ_3	δ_5	δ_3	δ_5	δ_3
obsd	4.50	4.93	4.55, 4.56	5.24, 5.25[49,68]		
calcd[a]		4.89	~4.5	5.29	~5	4.8-4.9

[a] Calculated using eq 4.

6–8). (ii) All questionable signal assignments were confirmed by double resonance experiments of the $^{13}C(^1H)$ heteronuclear variety. These data show that the only regular change in chemical shift occurs for C-5; transformation of the 5-Y substituent from exo to endo causes a downfield shift of ca. 1–4 ppm. The limited number of data in Table VII prevents great confidence in this empirical generalization. Changes in the C-3 chemical shift can vary in sign and are often very small. Also C-7 shifts move downfield upon conversion of the C-5 substituent from exo to an endo position, but in many cases these are small shifts.

The underlying reasons for these chemical shift changes are not known. Neither γ-gauche nor other steric compression arguments [e.g., β-effects[78]] seem to apply evenly. Interestingly, γ-gauche effects have been used for configurational assignments for a number of nortricyclene derivatives.[2,13,55,79–82] An attempt to examine the validity of this approach on 3,5-dibromonortricyclenes led one author[84] to make "the rather surprising observation" that an exo,exo isomer had a C-7 signal 3.1 ppm downfield of the endo,exo isomer, a shift opposite to that expected for a γ-gauche effect. Later that author revised[16a] his previous[2,14,84] configurational assignments.

Conclusions

In summary the following statements can be made. First a "nearest-neighbor" deshielding effect on ^1H NMR signals seems to be a reliable basis for assignment of configurations of the substituted positions of 3,5-disubstituted nortri-

(78) Bierbeck, H.; Saunders, J. K. *Can. J. Chem.* **1976**, *54*, 2985.
(79) Garratt, D. G.; Beaulieu, P. L.; Morisett, V. M. *Can. J. Chem.* **1980**, *58*, 1021.
(80) Garratt, D. G.; Kabo, A. *Can. J. Chem.* **1980**, *58*, 1030.
(81) Lippmaa, E.; Pehk, T.; Paasivirta, J. *Org. Magn. Reson.* **1973**, *5*, 277; cf. ref. 83.
(82) McCulloch, A. W.; McInnes, A. G.; Smith, D. G.; Walter, J. A. *Can. J. Chem.* **1976**, *54*, 2013.
(83) The assignments of signals in the ^{13}C NMR spectrum of nortricyclanol carried out in an earlier publication[81] were not supported in a later publication.[62]
(84) Garratt, D. G. *Can. J. Chem.* **1980**, *58*, 1327.

Table VI. Parameters for Equation 4. Calculation of ^1H Chemical Shifts in 3,5-Disubstituted Nortricyclenes

entry	subst	δ_0[a]	Δ_s[b]	Δ_{de}[c]
1	F	4.63 ± 0.32	0.0	0.59 ± 0.09
2	Cl	3.85 ± 0.03	0.0	0.76 ± 0.07
3	Br	3.91 ± 0.12	0.0	0.78 ± 0.12
4	I	3.79 ± 0.06		
5	OH	3.80	0.0	0.60
6	OCH_3	3.39 ± 0.03	0.0	0.55 ± 0.05
7	$O(C{=}O)CH_3$	4.62 ± 0.05	0.13 ± 0.05	0.48 ± 0.05
8	$O(C{=}O)C_6H_5$	4.90	0.15 ± 0.03	0.56 ± 0.04
9	$NH(C{=}O)CH_3$	3.82 ± 0.09	0.19 ± 0.09	0.28 ± 0.14
10	NO_2	4.41 ± 0.01	0.12 ± 0.02	0.40 ± 0.03
11	CCl_3	2.72	0.0	0.98
12	COOH		0.0	0.35 ± 0.20
13	SCH_2Ph	1.74		
14	$S(O)CH_2Ph$	2.66		
15	SPh	3.14	0.0	0.86 ± 0.02
16	$2,4\text{-}(NO_2)_2C_6H_3S$	3.28 ± 0.16	0.21 ± 0.12	
17	$2\text{-}NO_2C_6H_4S$	3.24	0.24	
18	$2\text{-}CH_3C_6H_4S$	3.10	0.0	
19	$2,4,6\text{-}(CH_3)_3C_6H_2S$	2.80		
20	$4\text{-}ClC_6H_4S$–			
21	SO_2Ph			1.13
22	HgCl		0.0	0.19
23	CH_3			0.25
24	$OClO_3$		0.17	0.79
25	ONO_2	4.77	0.0	

[a] Chemical shift[d] for H-3 of 3-substituted nortricyclenes (13). [b] Chemical shift change[d] for endo H-3 due to exo-5 substitution (1). Data from Table II. [c] Chemical shift change[d] for endo H-3 due to endo-5 substitution (2). Data from Tables III and IV. [d] ± confidence intervals for α = 90%.

cyclenes. A measure of this effect has been proposed in the form of an empirically based equation which accurately predicts the chemical shifts for protons at C-3 and C-5 of 3,5-disubstituted nortricyclenes of well-established configuration. Specifically, choices among exo,exo isomer **1** and the two exo,endo isomers **2** and **3** can usually be made. Second, variations in the ^{13}C NMR chemical shifts for the same compounds cannot always be explained in terms of steric-compression effects (γ-gauche or β effects) induced by configuration changes at C-5 and it seems likely that more data are needed to establish the nature of these spectra–structure correlations.

Experimental Section

The ^1H NMR spectra were recorded with Tesla BS-467 (60 MHz) or Bruker WM-250 (250 MHz) spectrometers. ^{13}C NMR spectra were run with Bruker WP-60 (15.08 MHz) or Bruker WM-250 (62.89 MHz) spectrometers. Concentrations are in moles per liter (M). The chemical shifts in both the ^1H and ^{13}C NMR spectra are presented in δ values (TMS = 0.00, internal standard). The assignment of ^{13}C NMR signals was carried out with the assistance of off-resonance decoupling and heteronuclear double $^{13}C(^1H)$ resonance techniques. The IR spectra were recorded with UR-20 and IR-75 spectrometers (Karl Zeiss) and peaks are reported in wavenumbers (cm^{-1}). Electron impact mass spectra were measured at 70 eV (Varian MAT CH-6). Chemical ionization mass spectra were obtained with methane as the reagent gas (Kratos MS-30). Melting points are uncorrected.

***exo,exo*-Tricyclo[2.2.1.0^{2,6}]heptane-3,5-diol.** This was prepared as has been described:[85] ^1H NMR [$(CD_3)_2CO$, 0.29 M, 250 MHz] 1.16–1.31 (m, 3 H, H-1, H-2, H-6), 1.76 (s, 2 H, H-7a, H-7b), 3.06 (s, 3 H; H4 and 2 OH), 3.70 (s, 2 H; H-3, H-5).

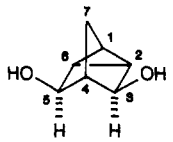


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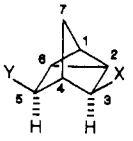
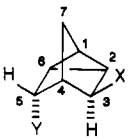
Table VII. ^{13}C Chemical Shifts in Some Stereoisomeric 3,5-Disubstituted Nortricyclenes (1 and 2)



1



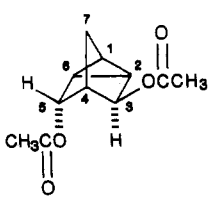
2

entry	subst	carbon no.	δ[a] 1	δ[a] 2	$\Delta\delta$[b]
1	$X = 2,4\text{-}(NO_2)_2C_6H_3S$	3	47.71	48.49	+0.78
	$Y = O(C{=}O)CH_3$	5	77.54	79.82	+2.28
		7	28.01	28.33	+0.32
2	$X = 2,4\text{-}(NO_2)_2C_6H_3S$	3	48.63	48.48	−0.15
	Y = Cl	5	62.19	64.51	+2.32
		7	27.99	29.62[c]	+1.63
3	$X = 2\text{-}(NO_2)C_6H_4S$	3	50.0	50.3	+0.3
	$Y = O(C{=}O)CH_3$	5	77.8	79.9	+2.1
		7	27.5[d,g,h]	28.0[e,g]	+0.5
4	$X = 2\text{-}(NO_2)C_6H_4S$	3	49.6	50.5	+0.9
	Y = OH	5	76.8	79.3	+2.5
		7	26.9[g]	27.8[g]	+0.9
5	$X = 2\text{-}(NO_2)C_6H_4S$	3	47.8	47.7	−0.1
	$Y = OCH_3$	5	84.5	86.5	+2.0
		7	27.2[f,g]	28.3[g]	+1.1
6	X = Y = SPh	3	52.9	50.2[i]	−2.7
		5	52.9	54.0[i]	+1.1
		7	27.6	30.6	+3.0
7	$X = Y = O(C{=}O)CH_3$	3	75.08	77.79[i]	+2.71
		5	75.08	79.02[i]	+3.94
		7	27.65	27.94	+0.29
8	X = Y =	3	75.64	78.46[i]	+2.82
	$O(C{=}O)C_6H_5$	5	75.64	79.52[i]	+3.88
		7	28.20	28.23	+0.03

[a] Chemical shift (δ, ppm) for numbered carbon in compound 1 or 2. [b] $\Delta\delta = \delta_2 - \delta_1$. [c–f] X-ray analyses of these have been published: [c] 2, ref 2; [d] 1, ref 3; [e] 2, ref 3; [f] 1, ref 5. [g] From the literature.[16a] [h] Our data: C-3, 47.72; C-5, 77.89; C-7, 27.81. [i] Selective heteronuclear double-resonance $^{13}C(^1H)$ was used to assist in signal assignments.

***exo,exo*-Tricyclo[2.2.1.0^{2,6}]heptane-3,5-diol Diacetate.** This was prepared by acetylation of the diol above and identified by IR (cf. ref 64): n^{18}_D 1.4760; ^1H NMR ($CDCl_3$, 1 M, 250 MHz) 1.58 (m, 3 H, H-1, H-2, H-6), 1.83 (t, J = 1.3 Hz, 2 H, H-7a, H-7b), 2.03 (s, 6 H, $2CO_2CH_3$), 2.3 (m, 1 H, H-4), 4.70 (d, J = 2.0 Hz, 2 H, H-3, H-5); ^{13}C NMR ($CDCl_3$, 1 M, 62.89 MHz) 12.85 (C-1), 18.00 (C-2, C-6), 21.00 (CH_3), 27.65 (C-7), 37.92 (C-4), 75.08 (C-3, C-5), 170.42 (C=O).

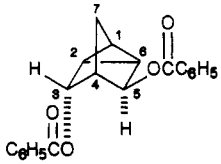
***exo,endo*-Tricyclo[2.2.1.0^{2,6}]heptane-3,5-diol Diacetate.** This was prepared by the same type of route as described above and identified by IR (cf. ref 64): n^{18}_D 1.4787; ^1H NMR ($CDCl_3$, 0.5 M, 250 MHz) 1.6–1.75 (m, 4 H, H-1, H-2, H-6, H-7a), 1.89 (d, J = 10.5 Hz, 1 H, H-7b), 2.08 (s, 6 H, $2CO_2CH_3$), 2.26 (s, 1 H, H-4), 4.77 (t, J = 2 Hz, 1 H, H-5), 5.20 (t, J = 2 Hz, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 0.3 M, 62.89 MHz) 14.36, 15.48, 16.80 (C-1, C-2, C-6) 21.12 (CH_3), 27.94 (C-7), 37.25 (C-4), 77.79 (C-3), 79.02 (C-5), 170.76 (C=O).



***exo,exo*-Tricyclo[2.2.1.0^{2,6}]heptane-3,5-diol Dibenzoate.** This was prepared by benzoylation of the corresponding diol (above) and identified by IR (cf. ref 69): ^1H NMR ($CDCl_3$, 0.2 M, 250 MHz) 1.68 (br s, $w_{1/2}$ = 12 Hz, 1 H; H-1), 1.79 (br s, $w_{1/2}$ = 9 Hz, 2 H; H-2, H-6), 2.07 (br s, $w_{1/2}$ = 6 Hz, 2 H; H-7a,7b), 2.59 (br s, $w_{1/2}$ = 6 Hz, 2 H, H-1, H-4), 5.07 (br s, $w_{1/2}$ = 6 Hz, 2 H, H-3, H-5), 7.45 (t, J = 7 Hz, 4 H, 2 H-3′, 2 H-5′), 7.57 (t, J

= 7 Hz, 2 H, 2 H-4'), 8.05 (d, J = 3.5 Hz, 4 H; 2 H-2', 2 H-6'); ^{13}C NMR ($CDCl_3$, 0.24 M, 62.89 MHz) 13.09 (C-1), 18.41 (C-2, C-6), 28.20 (C-7), 38.29 (C-4), 75.64 (C-3, C-5), 128.40, 129.67, 130.55, 132.99 (aromatic ring), 166.13 (C=O).

***exo,endo*-Tricyclo[2.2.1.0^{2,6}]heptane-3,5-diol Dibenzoate.** This diester was prepared by the same route as the preceding compound and was identified by IR (cf. ref 60): ^{1}H NMR ($CDCl_3$, 0.23 M, 250 MHz) 0.83–1.03 (m, 1 H), 1.23–1.51 (m, 1 H), 1.81 (d, J = 5 Hz), 1.72 (d, J = 9 Hz, 1 H, H-7a), 2.10 (d, J = 9 Hz, 1 H, H-7b), 2.47 (s, $w_{1/2}$ = 6 Hz, 1 H, H-4), 5.10 (br s, $w_{1/2}$ = 5 Hz, 1 H, H-5), 5.60 (s, $w_{1/2}$ = 6 Hz, 1 H, H-3), 7.40–7.75 (m, 6 H), 7.95–8.25 (m, 4 H); ^{13}C NMR ($CDCl_3$, 0.24 M, 62.89 MHz) 14.69, 15.80, 17.21 (C-1, C-2, C-6), 28.23 (C-7), 37.74 (C-4), 78.76 (C-3), 79.52 (C-5), 128.28, 129.43, 129.57, 132.83, 132.92 (aromatic ring), 166.29 (C=O).



3-(Benzoyloxy)tricyclo[2.2.1.0^{2,6}]heptan-3-ol. This benzoate was prepared by benzoylation of the nortricyclanol: n^{18}D 1.5557; ^{1}H NMR ($CDCl_3$, 0.84 M, 60 MHz) 1.32, 1.65, 1.84, 2.02 (m, 5 H), 2.15 (br s, $w_{1/2}$ = 5 Hz, 1 H, H-4), 4.90 (br s, $w_{1/2}$ = 4 Hz, 1 H, H-3), 7.2–7.7, 7.95–8.3 (m, 5 H); ^{13}C NMR ($CDCl_3$, 1.6 M, 15.08 MHz) 11.35, 13.11, 13.90 (C-1, C-2, C-6), 30.48 (C-5, C-7), 33.57 (C-4), 80.44 (C-3), 128.34, 130.59, 132.78, 134.60 (aromatic ring), 166.59 (C=O).

Tricyclo[2.2.1.0^{2,6}]heptanone. Nortricyclanol (0.145 g, 1.3 mmol) was dissolved in 2 mL of anhydrous dichloromethane and PCC (CrO_3·C_5H_5N·HCl; 0.45 g, excess) was added under dry argon. When the reaction was over (TLC monitor), the mixture was filtered through silica gel and the solvent was removed; the resulting residue (81 mg) was a mixture of the desired ketone (80% by ^{1}H NMR), and pyridine and was used for oxime preparation without purification.

Tricyclo[2.2.1.0^{2,6}]heptanone Oxime. Hydroxylamine hydrochloride (2.7 g) was added to the solution of 2.8 g of nortricyclanone in 3.9 mL of pyridine and 10 mL of methanol. The mixture was refluxed for 1–3 h, the solvent was removed, and the residue was dissolved in chloroform and filtered. After the evaporation of solvent, traces of pyridine were azeotropically removed with toluene. The yield of the crude product was near to quantitative. A colorless oil was obtained by distillation: MS EI, m/z (relative intensity) 123 (29) M^+, 122 (18), 107 (13) $M - O^+$, 106 (33) $M - OH^+$, 105 (17) $M - H_2O^+$, 93 (12), 91 (14), 80 (32), 79 (100), 78 (40), 77 (50); IR (CCl_4) 3603 (ν_{OH}); IR (neat) 1700 ($\nu_{C=N}$), 803 (nortricyclene fragment).

3-Bromo-3-nitrotricyclo[2.2.1.0^{2,6}]heptane. Nortricyclanone oxime (1.31 g, 10.7 mmol) and $NaHCO_3$ (2.65 g) were dissolved in a mixture of 50 mL of water and 10 mL of dioxane. The solution was added to a suspension of NBS in water under vigorous stirring and cooling in an ice bath. After 1 h the mixture was permitted to warm to room temperature and extracted with hexane (5 × 20 mL), and the organic layer was concentrated to 3–5 mL. The resulting blue solution of 3-bromo-3-nitrosonortricyclene was mixed with 50 mL of 65% nitric acid and 10 mL of 30% hydrogen peroxide and stirred for several hours until decolorization occurred. The organic layer was separated, washed with aqueous $KHCO_3$, and dried with $MgSO_4$. The solvent was removed and the residue crystallized spontaneously: yield 0.33 g (14%); IR (KBr) 657 (ν_{C-Br}), 806 (nortricyclene fragment), 1343 ($\nu_s(NO_2)$), 1550 ($\nu_a(NO_2)$); MS EI, m/z (relative intensity) 173 (6.5), 171 (6.5) $M^+ - NO_2$, 91 (100) $M^+ - NO_2$ – HBr.

3-Nitrotricyclo[2.2.1.0^{2,6}]heptane (5). 3-Bromo-3-nitronortricyclene (0.33 g) in 5 mL of methanol was added dropwise to a suspension of 0.4 g of $NaBH_4$ in 5 mL of aqueous (1:4) methanol with stirring. After 1 h the solution was filtered, the precipitate was washed with hexane, and the combined filtrates were evaporated to dryness. Hydroxylamine hydrochloride was added until the reaction mixture became neutral. The solution was extracted with hexane (3 × 10 mL), the extract was dried ($MgSO_4$), and the solvent was removed. Chromatographic purification on silica gel lead to 83 mg (40%) of colorless oil: n^{18}D 1.4930; ^{1}H NMR ($CDCl_3$, 0.5 M, 250 MHz) 1.4–1.7 (m, 7 H), 2.56 (br s, $w_{1/2}$ = 6 Hz, 1 H, H-4), 4.41 (t, J = 1.5 Hz, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 0.5 M, 62.89 MHz) 11.6, 13.1, 13.5 (C-1, C-2, C-6), 30.3, 32.5 (C-5, C-7), 35.3 (C-4), 89.8 (C-3); IR (neat) 1380 ($\nu_s(NO_2)$), 1538 ($\nu_a(NO_2)$); MS, CI, m/z (relative intensity) 140 (0.76) M + H^+, 109 (6.7) M^+ + H – HNO, 93 (100) M^+ + H – HNO_2.

***exo,exo*-3,5-Dinitrotricyclo[2.2.1.0^{2,6}]heptane (6) and *exo*-3,*endo*-5-Dinitrotricyclo[2.2.1.0^{2,6}]heptane (7).** A solution of 2 mL (1.7 g, 18.6 mmol) of norbornadiene in 20 mL of ether was added dropwise during 0.5 h to 1.2 mL (18.6 mmol) of liquid dinitrogen tetraoxide in 10 mL of ether. The mixture was allowed to stand for 2 h at 0–5 °C and was washed with aqueous Na_2CO_3, then aqueous $KMnO_4$, and again with Na_2CO_3. Ether was removed, and the resulting slurry (ca. 0.5 g) was chromatographed on a silica gel column. Elution with benzene afforded the nitro nitrate fraction (R_f 0.48, benzene, Silufol) and the mixture of the dinitro adducts (0.17 g, R_f 0.3) from which exo,exo isomer **6** was separated by crystallization (chloroform–ether, 0 °C), yielding 0.14 g of pure product, mp 119.5–121.5 °C: ^{1}H NMR ($CDCl_3$, saturated soln, 250 MHz) 1.82 (t, J = 0.5 Hz, 2 H, H-2, H-6), 2.03 (t, J = 2.3 Hz, 1 H, H-1), 2.15 (td, J_t = 2.3 Hz, J_d = 0.5 Hz, 2 H, H-7a, H-7b), 3.28 (br s, $w_{1/2}$ = 2 Hz, 1 H, H-4), 4.53 (d, J = 2 Hz, 2 H, H-3, H-5); ^{13}C NMR [$(CD_3)_2CO$, 0.09 M, 62.89 MHz] 13.77 (C-1), 17.21 (C-2, C-6), 28.33 (C-7), 40.21 (C-4), 85.91 (C-3, C-5); IR (KBr) 790, 830 (nortricyclene fragment), 1379 ($\nu_s(NO_2)$), 1553 ($\nu_a(NO_2)$); MS CI, m/z (relative intensity) 185 (0.32) M + H^+, 138 (5.6) M + H^+ – HNO_2, 108 (100) M + H^+ – HNO_2 – NO. Anal. Calcd for $C_7H_8N_2O_4$: C, 45.66; H, 4.38; N, 15.21. Found: C, 45.65; H, 4.45; N, 15.61. An attempt to obtain pure exo,endo isomer was unsuccessful. The ^{1}H NMR spectrum ($CDCl_3$, 250 MHz) of the enriched fraction exhibited signals of equal intensity at 4.67 (t, J = 1.7 Hz, H-5), 4.93 (t, J = 1.8 Hz, H-3), ascribed to the noted protons of exo,endo isomer. The content of **7** in the mixture was less than 12% (yield of **7**: ca. 0.6% by ^{1}H NMR).

The nitro nitrate fraction (ca. 0.2 g) obtained above was separated by column chromatography on silica gel. Elution with hexane/ether (1:1) gave three fractions with R_f 0.43 (42.5 mg), 0.36 (52 mg), and 0.31 (12 mg) (R_f in heptane–ether 1:1 on Silufol plates). The first fraction was, according to IR and ^{1}H NMR, a mixture of unsaturated nitro nitrates. The other two fractions were single compounds with nitro nitrate nortricyclene structures **13** and **14**, respectively.

***exo*-3-Nitroxy-*exo*-5-nitrotricyclo[2.2.1.0^{2,6}]heptane (13):** ^{1}H NMR (0.6 M in $CDCl_3$, 60 MHz) 2.94 (br s, 1 H, H-4), 4.50 (t, J = 2 Hz, 1 H, H-5), 4.93 (s, 1 H, H-3); IR (neat) 833 (nortricyclene bond), 1380 ($\nu_s(NO_2)$), 1545 ($\nu_a(NO_2)$), 1361 ($\nu_a(NO_2)$).

***exo*-3-Nitroxy-*endo*-5-nitrotricyclo[2.2.1.0^{2,6}]heptane (14):** ^{1}H NMR ($CHCl_3$, 60 MHz) 4.55 (s, 1 H, H-5) and 5.25 (s, 1 H, H-3). The IR spectrum is virtually identical with that which has been published.[49]

***exo,exo*-3,5-Bis(phenylthio)tricyclo[2.2.1.0^{2,6}]heptane (8) and *exo*-3,*endo*-5-Bis(phenylthio)tricyclo[2.2.1.0^{2,6}]heptane (9).** A solution of 0.5 mL (0.425 g, 4.6 mmol) of norbornadiene and 1.00 g (4.6 mmol) of diphenyl disulfide in 50 mL of pentane was irradiated under argon by a medium-pressure mercury lamp for 5 h. A quartz flask equipped with a reflux condenser and an IR filter was used as the reaction vessel. When the reaction was over (TLC monitor), the solution was filtered and the filtrate was evaporated, affording a residue (1.25 g). The part of this residue (0.56 g) that was separated by chromatography (gradient elution using petroleum ether to petroleum ether/chloroform = 1:1) gave 0.253 g (40%) of a mixture of **8** and **9** in a 2:1 ratio (by ^{1}H NMR). This mixture of **8** and **9** was rechromatographed on Silpearl (Kavalier). Elution using petroleum ether–carbon tetrachloride (1:1) yielded 0.063 g of **8**, 0.064 g of **9**, and 0.118 g of a mixed fraction.

8: n^{18}D 1.6382; ^{1}H NMR ($CDCl_3$, 0.15 M, 250 MHz) 1.4 (m, 3 H, H-1, H-2, H-6), 1.90 (t, J = 1.4 Hz, 2 H, H-7a,b), 2.08 (d, J = 1 Hz, 1 H, H-4), 3.18 (d, J = 1.5 Hz, 2 H, H-3, H-5), 7.08–7.38 (aromatic protons); ^{13}C NMR ($CDCl_3$, 0.1 M, 62.89 MHz) 11.7 (C-1), 18.2 (C-2, C-6), 27.6 (C-7), 40.5 (C-4), 52.9 (C-3, C-5), 120.5, 128.4, 130.7, 136.3; MS EI, m/z (relative intensity) 312 (4), 311 (9), 310 (40) M^+, 244 (3), 202 (12), 201 (83.5) M^+ – PhS, 200 (5.5) M^+ – PhSH, 168 (5.5), 167 (4), 147 (3), 135 (12), 123 (20), 109 (9)

PhS$^+$, 92 (20), 91 (100). **9**: n^{18}_D 1.6390; ^{1}H NMR ($CDCl_3$, 0.1 M, 250 MHz) 1.41 (d, J = 11 Hz, 1 H, H-7a), 1.47 (m, 3 H, H-1, H-2, H-6), 2.07 (d, J = 11 Hz, 1 H, H-7b), 2.09 (s, 1 H, H-4), 3.37 (s, 1 H, H-5), 4.00 (s, 1 H, H-3), 7.09–7.47 (aromatic protons); ^{13}C NMR ($CDCl_3$, 0.14 M, 62.89 MHz) 13.44, 16.17, 17.85 (C-1, C-2, C-6), 30.64 (C-7), 39.68 (C-4), 50.19 (C-3), 53.98 (C-5), 125.89, 126.64, 128.85, 128.93, 129.60, 131.02, 136.78; MS EI, m/z (relative intensity) 312 (3), 311 (7), 310 (28) M$^+$, 244 (7.5), 202 (8), 201 (47) M$^+$ – PhS, 200 (9) M$^+$ – PhSH$^+$, 168 (6), 167 (4), 147 (5), 135 (12.5), 134 (9), 123 (22), $C_7H_7S^+$, 109 (10) PhS$^+$, 92 (17), 91 (100).

Acknowledgment. We thank Drs. V. S. Bogdanov, A. S. Shashkova, M. I. Struchkova, V. I. Kadentsev, Mr. A. I. Lutsenko, Mrs. T. Ivanova, E. Daeva, and E. Lubuzh of N. D. Zelinsky Institute of Organic Chemistry, Moscow, for spectral measurements and Prof. O. S. Chizhov and Dr. E. P. Serebrayakov for helpful discussions.

Structures of Pyrimidine Derivatives Produced by Condensation of Ethyl Cyanoacetate with Methylguanidine. Evidence for the Presence of an Imino Tautomer

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Received February 3, 1987

The reaction of ethyl cyanoacetate with methylguanidine produced two unexpected side products, in addition to previously described products, 2,6-diamino-1-methyl-4(1*H*)-pyrimidinone and 6-amino-2-(methylamino)-4-(3*H*)-pyrimidinone. The presence of an isomer of the 1-methylpyrimidine derivative was presumed on the basis of the appearance of the NMR spectra differing from that of the 1-methylpyrimidine derivative in an aprotic neutral solvent. The unexpected major product was identified as 2,6-diamino-4(3*H*)-pyrimidinone, while the minor one was in two tautomeric forms, 6-amino-1-methyl-2-(methylamino)-4(1*H*)-pyrimidinone and 6-amino-1-methyl-2-(methylimino)-1,2-dihydro-4(3*H*)-pyrimidinone. Such amino–imino tautomerization depended on a polarity of solvent and its temperature. The formation of the above two unexpected products was most probably due to the reaction of ethyl cyanoacetate with guanidine and dimethylguanidine that were formed as side products in the preparation of methylguanidine. However, a Watanabe-type N_1–C_2–N_3 replacement on the 1-methylpyrimidine derivative could not be neglected as an alternative mechanism for the formation of the diaminopyrimidine derivative. The Dimroth-type rearrangement of the 1-methylpyrimidine derivative to its 2-(methylamino) isomer occurred by catalytic action of either methylamine or guanidine under similar conditions.

In connection with the structural determination of pigments isolated from the skin of *Rhacophorus arboreus*,[1] we needed to prepare pyrimidine derivatives by condensation of ethyl cyanoacetate with methylguanidine. This condensation has been described to produce two monomethylpyrimidine derivatives, **1** and **3**.[2,3] Structure **2a** was assigned to the same product (**1**) in another reference.[4] The present paper is concerned with a reinvestigation of a literature method for the synthesis of methylguanidine and its subsequent condensation with ethyl cyanoacetate. We have now established the following four points: (i) The structures of the products reported in the literature[2-4] were structure **2a** and structure **3**, respectively. In addition, on the basis of appearance of the NMR spectra differing from that of **2a** in an aprotic solvent, the presence of an isomer (**2b**) of **2a** was presumed. (ii) The structure of the unexpected major product was structure **4** and the minor one was in two tautomeric forms **5a** and **5b**. Structure **5b** is a normally disfavored imino tautomeric form. (iii) The tautomerization of the five pyrimidine derivatives in solution depended on solvent polarity and temperature. In addition, a methyl substituent on nitrogen atoms in the pyrimidine nuclei was an important factor for stabilization of an imino tautomeric structure. (iv) The formation of the two unexpected products (**4** and **5**) was most probably caused by reaction of ethyl cyanoacetate with guanidine and dimethylguanidine, respectively, which were concomitantly formed in the preparation of methylguanidine. However, a Watanabe-type N_1–C_2–N_3 replacement[5] on **2a** with guanidine could not be neglected as an alternative mechanism for the formation of **4**. In addition, the formation of the expected product (**3**) was caused by a Dimroth-type rearrangement[6,7] on **2a** with both methylamine and guanidine.

Results and Discussion

Structures of Pyrimidines. Following the method reported for the preparation of monomethylpyrimidines,[2] ethyl cyanoacetate was condensed with methylguanidine obtained by fusion of dicyanodiamide with a large excess of methylamine. An expected major product (**2a**) (33% yield) was obtained as a precipitate and easily separated from the other products by filtration. Silica gel column chromatography of the filtrate afforded another expected product (**3**). However, its yield was very low (4%) in

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