Table I. Methylation of Various Compounds by Trimethylsulfonium Hydroxide (Me_3SOH)

compd	registry no.	compd/Me_3SOH[a] mol ratio	reaction temp, °C	reaction time, min	product	registry no.	yield, %[b]
$(CH_3)_2CHCO_2H$	79-31-2	1.3	120	20	$-CO_2CH_3$	547-63-7	quant.
$(CH_3)_3CCO_2H$	75-98-9	1.3	120	20	$-CO_2CH_3$	598-98-1	quant.
$HOCH_2CH_2SH$	60-24-2	1.1	100	20	$-SCH_3$	5271-38-5	quant.
C_6H_5OH	108-95-2	1.1	100	20	$-OCH_3$	100-66-3	quant.
C_6H_5SH	108-98-5	1.1	80	20	$-SCH_3$	100-68-5	quant.
$C_6H_5NH_2$	62-53-3	2.0	110	30	$-NHCH_3$	100-61-8	<5
$CH_3(CH_2)_3CH_2OH$	71-41-0	3 (1.5 + 1.5)[c]	120	25 (5 + 20)[c]	$-OCH_3$	628-80-8	trace
	105-60-2	3 (1.5 + 1.5)[c]	120	30 (10 + 20)[c]	$>NCH_3$	2556-73-2	35
indazole	271-44-3	1.1	110	30	$>NCH_3$	13436-48-1	84
imidazole	288-32-4	1.1	70	20	$>NCH_3$	616-47-7	quant.
benzotriazole (Ben)	95-14-7	1.2	110	30	m^1Ben	13351-73-0	62
					m^2Ben	16584-00-2	11
cytosine (Cyt)	71-30-7	1.1	110	5	m^1Cyt	1122-47-0	90
deoxyguanosine (dG)	961-07-9	1.1	80	30	m^1dG	5132-79-6	70

[a] Used amount of a compound: dG, 1 mmol; all others, 10 mmol. [b] quant. refers to a quantitative yield, which was judged by gas chromatography and the NMR spectrum of the reaction mixture. Yields indicated by numbers were calculated on the basis of the isolated amounts of products. [c] Repeated addition of the Me_3SOH solution and heating of the reaction mixture for the time specified. See Experimental Section also.

yguanosine was obtained as crystals by treatment of the reaction mixture at 50 °C and 10 mmHg to remove DMF and subsequent agitation of the residue with methanol; it was recrystallized from methanol. 1-Methyl- and 2-methylbenzotriazoles were isolated according to the previous paper.[7] Products were identified by comparison of their IR and NMR spectra as well as comparison of boiling point and melting point with literature values or those of authentic samples.

Registry No.—Trimethylsulfonium hydroxide, 17287-03-5; trimethylsulfonium iodide, 2181-42-2; silver oxide, 20667-12-3.

References and Notes

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(6) B. Singer in "Progress in Nucleic Acid Research and Molecular Biology", Vol. 15, W. E. Cohn Ed., Academic Press, New York, 1975, p 219. Biological Study of Me_3SOH is now under way.
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Chromic Acid Oxidation of [*n*.3.2]Propellanols

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Recently the chemistry of propellanes, particularly structure reactivity relationships, has drawn much attention.[1] We have previously reported on the synthesis and reactivity of [*n*.3.2]propellane derivatives.[2] In the course of these studies, we have noted the remarkable effect of the size of alicyclic rings (5–8) on the photochemical behavior of bicyclic enones[2d–f] and on the stereoselectivity in the hydride reduction of [*n*.3.2]propellanones[2g] and have pointed out that the ring size effect is attributable to the steric effect associated with the conformational flexibility of the ring systems. In view of the above findings, we decided to investigate the chromic acid oxidation of exo and endo [*n*.3.2]propellanols (**1–5**), involving a cyclopentanol moiety, a cyclobutane ring, and one of five- to eight-membered alicyclic rings as the third ring. Since it has been well known that the rate-determining step in the chromic acid oxidation of secondary alcohols is the decomposition of the intermediate chromate ester,[3] and the acceleration of the decomposition rate is thought to be due to the relief of unfavorable nonbonded interactions which exist in the ground state of the molecule,[4,5] remarkable distinction in steric effect of the third rings on the oxidation rate may be expected, especially in the endo alcohol system.

The alcohols were prepared as described previously;[2e,g] the bicyclo[3.2.0]heptan-2-ol moiety in these alcohols had rigid boat geometry practically independent of conformational flexibility of the third rings.[2e,g]

The rate constants of the chromic acid oxidation of propellanols are summarized in Table I.[6] The relative rate constants ($k_{\rm rel}$) for the tricyclic exo alcohol system increase slightly with increasing the size of the third ring. On the other hand, $k_{\rm rel}$ for the endo alcohols increases remarkably with increasing the size of the third ring and, especially, in the case of endo [6.3.2]propellanol **4N**, the rate is considerably enhanced compared with other endo alcohols. These facts indicate that, in the endo alcohol system, nonbonded interactions between the endo hydroxyl group and hydrogens of the third rings become greater as they become conformationally more flexible. This seems to contradict our previous findings that corformational flexibility of alicyclic rings reduces unfavorable nonbonded interactions in the transition state of reactions such as the photocycloaddition of bicyclic enones[2d–f] and the nucleophilic addition of metal hydride to [*n*.3.2]propellanones.[2g] However, the transition state of the chromic acid oxidation of secondary alcohols (elimination of the chromate ester group in the rate-determining step) may be susceptible to acceleration due to steric crowding around the endo hydroxyl group particularly from some flexible ring such as cyclooctane as is illustrated below.

The steric environment is quite different for the exo OH group which is located at the opposite side of the third ring and at the outside of the envelope of the cyclopentane ring owing to the rigid boat conformation of the bicyclo[3.2.0]heptan-2-ol moiety.[2g] Consequently, only slight enhancement of the rate constants with increasing in the size of the third rings is expected and may be ascribed to a little increase of nonbonded interactions between the endo hydrogen (α to the OH) and the hydrogens of the third rings.

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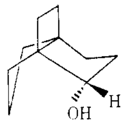
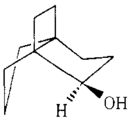
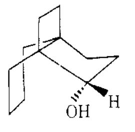
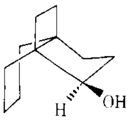
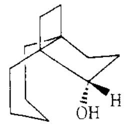
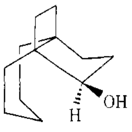
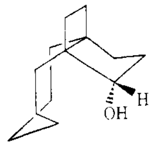
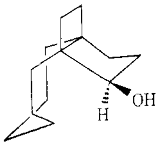
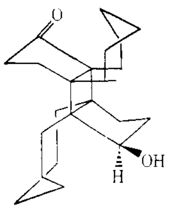
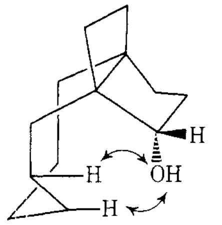
Table I. Rate Constants for the Chromic Acid Oxidation of [*n*.3.2]Propellanols at 30 ± 0.05 °C in 95% Acetic Acid

endo alcohol	registry no.	k_2, $M^{-1}\,s^{-1}$	k_{rel}	exo alcohol	registry no.	k_2, $M^{-1}\,s^{-1}$	k_{rel}	k_{endo}/k_{exo}
 1N	68457-30-7	3.33 ± 0.05	1.00	 1X	68457-32-9	4.40 ± 0.17	1.32	0.757
 2N	68509-83-1	6.08 ± 0.13	1.83	 2X	68509-85-3	5.95 ± 0.05	1.77	1.02
 3N	68457-31-8	8.08 ± 0.20	2.43	 3X	68457-33-0	6.86 ± 0.04	2.06	1.18
 4N	68509-84-2	(1.44 ± 0.08) × 10	4.32	 4 X	68509-86-4	8.05 ± 0.23	2.42	1.78
				 5X	66922-00-7	(4.02 ± 0.16) × 10^2	121	



On the other hand, in the case of the highly congested pentacyclic exo propellanol **5X**,[2e] a very large rate enhancement was observed. This is probably due to unusually great nonbonded interactions between the exo hydroxyl group and hydrogens of the cis-fused cyclooctane ring facing across the cyclobutane ring.

In conclusion, the third rings of [*n*.3.2]propellanols brought about striking differences in steric acceleration of their chromic acid oxidation. The differences are attributable to the distinction in the degree of steric crowding around the hydroxyl group which can be associated with conformational flexibility of the third rings.

A solvolytic study of various derivatives of the above propellanols is in progress and will be reported separately.

Experimental Section

The alcohols were prepared by lithium aluminum hydride reduction or by Meerwein-Ponndorf reduction of the corresponding ketones as described previously.[2e,g] Oxidation rates were measured spectrophotometrically[5c,i] in a thermostated cell holder of a Hitachi 356 spectrometer at 350 nm at 30 ± 0.05 °C in 95% acetic acid. The concentration of the alcohols was in the 4–6 × 10^{-3} M range and that of chromic acid (CrO_3) was about 2 × 10^{-4} M. In the case of **5X**, both concentrations were about one-fiftieth of those in other cases. Good straightline plots for the log *A* vs. time relationship were obtained from which first-order rate constants (k_1) were determined. Second-order rate constants (k_2) were obtained from k_1 and the initial alcohol concentration. The values given in Table I are averages from at least three measurements. Products of the oxidation, checked by GLC, were only the corresponding ketones.

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(6) Wiberg has shown that the Cr^V species is also responsible for oxidation of secondary alcohols and that it oxidizes in a similar manner to Cr^{VI} via an ester intermediate.[7] Since our rate measurements were carried out spectrophotometrically recording the decrease of abospriton of Cr^{VI} at 350 nm, the observed oxidation rates were governed by the disappearance of only Cr^{VI} species.

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