TABLE II
PMR CHEMICAL SHIFTS (δ) OF SOME PYRIMIDINE 1-OXIDES[a]

Compd	H_2	H_4	H_5	H_6	Substituent
Pyrimidine 1-oxide	9.14	8.62	7.75	8.66	
5-Methylpyrimidine 1-oxide	8.97	8.51		8.59	2.44
5-Bromopyrimidine 1-oxide	9.08	8.70		8.96	
5-Methoxypyrimidine 1-oxide	8.78	8.38		8.44	4.73
5-Dimethylaminopyrimidine 1-oxide	8.38	8.00		8.11	3.03
4-Methylpyrimidine 1-oxide	9.03		7.64	8.55	2.63
6-Methylpyrimidine 1-oxide	9.12	8.47	7.74		2.61

[a] Dilute 0.2 *M* solutions in D_2O.

Neutralization of these strongly basic solutions regenerates the pyrimidine *N*-oxides quantitatively. That these covalent hydration processes are indeed independent of the exchange reactions was shown by converting the pyrimidine *N*-oxide to its totally covalently hydrated species (as shown by pmr) by dissolving it in 2.5 *N* NaOD. After 3 hr, the pyrimidine *N*-oxide was recovered unchanged (no H → D exchange) upon acidification.

Studies that are directed towards establishing the structures of these products and the equilibria involved in these processes are in progress.

Experimental Section

Nmr spectra were obtained with a Varian HA-100 spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6E instrument equipped with a solid sample injector. The ionizing voltage employed was 80 eV. Elemental analyses were determined by Mrs. K. Decker and Mrs. V. Gindelsperger of this department.

Preparation of the *N*-Oxides.—The pyrimidine *N*-oxide[7] and the methylpyrimidine *N*-oxides[8] were prepared by known procedures.

5-Bromopyrimidine 1-Oxide.—This compound was prepared according to the oxidation procedure described by Kobayashi, Kumadaki, and Sato.[9] The compound was obtained in 19% yield, mp 166–167°. *Anal.* Calcd for $C_4H_3N_2BrO$: C, 27.44; H, 1.73; N, 16.01. Found: C, 27.43; H, 2.03; N, 15.79.

5-Methoxypyrimidine 1-Oxide.—This compound was prepared from 5-methoxypyrimidine in 61% yield by the procedure described in ref 9, mp 161.5–162.5°. *Anal.* Calcd for $C_5H_6N_2O_2$: C, 47.61; H, 4.80; N, 22.22. Found: C, 47.70; H, 4.83; N, 22.21.

5-Dimethylaminopyrimidine 1-Oxide.—This compound was prepared by heating a solution of 5-bromopyrimidine 1-oxide (0.1 g, 0.57 mmol) in 40% aqueous dimethylamine (3 ml) in a sealed tube on a steam bath for 4 hr. The cooled solution was made basic and continuously extracted with chloroform. The chloroform extract was dried, and the solvent was removed *in vacuo*. The crude product was purified by sublimation followed by recrystallization from carbon tetrachloride to afford 0.46 g (20%) of 5-dimethylaminopyrimidine 1-oxide, mp 153–154°. *Anal.* Calcd for $C_6H_9N_3O$: C, 51.79; H, 6.52; N, 30.20. Found: C, 51.70; H, 6.55; N, 30.23.

Determination of Rate Constants.—The appropriate *N*-oxide was weighed into an nmr tube and 0.4 ml of D_2O was added. The solution was then allowed to come to 31°, and the HA-100 instrument was adjusted. An initial spectrum was then obtained, and 0.1 ml of the appropriate concentration of aqueous NaOD at 31° was then added with shaking.

(7) T. Kato, H. Yamanaka, and T. Shibata, *Yakugaku Zasshi*, **87**, 1096 (1967).

(8) M. Ogata, H. Watanabe, K. Togi, and H. Kamo, *Tetrahedron Lett.*, 19 (1964).

(9) Y. Kobayashi, I. Kumadaki, and H. Sato, *Chem. Pharm. Bull.*, **17**, 1045 (1969).

Registry No.—**1**, 36529-69-8; **2**, 36529-70-1; **3**, 36529-71-2; **4**, 17758-50-8; **5**, 17043-94-6; 4-methylpyrimidine 1-oxide, 17758-54-2; 6-methylpyrimidine 1-oxide, 33342-83-5.

Selective Dehydration of Secondary Alcohols with Methyltriphenoxyphosphonium Iodide in Hexamethylphosphoramide

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The perennial problem of effecting mild dehydrations of alcohols without rearrangement and the recent interest in elimination reactions induced by nucleophiles in polar aprotic solvents[2] prompt this report of the use of methyltriphenoxyphosphonium iodide (MTPI) in hexamethylphosphoramide (HMPA) as a mild reagent system for the selective dehydration of secondary alcohols.

An attempt to convert *trans*-4-*tert*-butylcyclohexanol into the corresponding cis iodide with MTPI[3] in HMPA resulted instead in an excellent yield (88%) of 4-*tert*-butylcyclohexene in only 15 min at room temperature. In view of the ease and effectiveness of the procedure and its potential utility as a mild dehydration method, the generality of the reaction was investigated.

A variety of alcohol types was subjected to MTPI and the results presented in Table I. In each case the alcohol was treated with a twofold excess of MTPI in HMPA (5 ml per mmol of alcohol) at the temperature listed. The reactions were conveniently monitored by glpc using internal standards and, upon completion, worked up by dilution with water or aqueous potassium hydroxide and extraction with cyclohexane. The results indicate that secondary alcohols are effectively dehydrated with no indication of rearrangements detected. Furthermore, in most cases a high predominance of the more stable Saytzeff alkene is formed (entries 5, 7, 8, 12, 13), often with substantial stereoselectivity for the *E* geometric isomer (entries 12, 14, 15). Primary alcohols are converted into the corresponding iodide in excellent yield (entry 16), but subsequent dehydrohalogenation is evidently slow under

(1) Undergraduate National Science Foundation Fellow, 1971.

(2) (a) G. Biale, D. Cook, D. J. Lloyd, A. J. Parker, I. Stevens, J. Takahashi, and S. Winstein, *J. Amer. Chem. Soc.*, **93**, 4735 (1971); (b) G. Biale, A. J. Parker, S. G. Smith, I. Stevens, and S. Winstein, *ibid.*, **92**, 115 (1970); (c) D. J. Lloyd, D. M. Muir, and A. J. Parker, *Tetrahedron Lett.*, 3015 (1971); (d) D. J. Lloyd and A. J. Parker, *ibid.*, 637 (1971); (e) J. Avraamides and A. J. Parker, *ibid.*, 4043 (1971).

(3) Methyltriphenoxyphosphonium iodide is an efficient reagent for conversion of alcohols into the corresponding iodides; see S. R. Landaner and H. N. Rydon, *J. Chem. Soc.*, 2224 (1953); J. Verheyden and J. Moffat, *J. Org. Chem.*, **35**, 2319 (1970). A review of the use of various phosphorus derivatives for the preparation of iodides is provided by H. R. Hudson, *J. Chem. Soc. B*, 664 (1968).

TABLE I

DEHYDRATION OF SECONDARY ALCOHOLS WITH METHYLTRIPHENOXYPHOSPHONIUM IODIDE IN HEXAMETHYLPHOSPHORAMIDE

Entry	Alcohol[a]	Temp, °C	Time, hr	Alkene yield, %[b] (isolated) Saytzeff	Hofmann
1	*trans*-4-*tert*-Butylcyclohexanol	25	0.25	88	
2	*cis*-4-*tert*-Butylcyclohexanol	25	2.5	84	
3	3-β-Cholestanol	75	6.0	(84)[c]	
4	Cholesterol	75	5.0	84 (76)	
5	*cis*-2-Methylcyclohexanol	75	1.0	82	5
		25	3.0	83	3
		25[d]	107.0	82	6
6	*trans*-2-Methylcyclohexanol	75	2.0	47	47
		25	1.0	46	7
			4.0	54	26
7	*cis*-2-Phenylcyclohexanol	75	4.0	87	5[e]
8	*trans*-2-Phenylcyclohexanol	25	24.0	71	16[e]
		75	24.0	84	14[e]
9	1-Menthol	75	1.0	54	27
10	Cyclododecanol	25	2.0	94[f]	
11	5-Nonanol	75	2.0	88	
12	2-Decanol	75	7.0	72	5
			25.0	80[g]	4
13	2-Methyl-3-octanol	75	1.0	82	10
			2.0	90	10
14	1-Phenylbutanol	75	1.0	96[h]	
15	1,2-Diphenylethanol	75	1.0	100[i] (86)	
16	1-Dodecanol	75	0.25	0[j]	
			6.5	tr[j]	
			29.0	tr[j]	
17	4-Propyl-4-heptanol	75	6.0	tr[k]	
			27.0	12[k]	
18	1-*n*-Butylcyclohexanol	25	24.0	tr[k]	

[a] Solutions 0.2 *M* alcohol–0.4 *M* methyltriphenoxyphosphonium iodide. [b] Yields determined by glpc analysis using internal standards and detector response factors, unless otherwise noted. [c] Mixture of 2- and 3-cholestene. [d] Demonstrates lack of equilibration under reaction conditions. [e] Glpc response factor assumed to be equal to that of 1-phenylcyclohexene. [f] *Ca.* 2:1 ratio of *E* and *Z* isomers, respectively. [g] 63% *E*, 17% *Z*. [h] *Ca.* 99% E, tr. *Z*. [i] 99% (*E*)-stilbene, *ca.* 1% (*Z*)-stilbene. [j] Product was 1-dodecyl iodide. [k] The remainder was starting alcohol.

the reaction conditions.[4] Tertiary alcohols are practically inert toward the reagent system (entries 17, 18) thus permitting secondary cases to be selectively dehydrated in their presence.[5]

The mechanism of the dehydration apparently involves initial conversion into the corresponding inverted iodide followed by dehydrohalogenation induced by iodide[2] and HMPA.[4,6] Evidence for this is provided by the faster rate of *trans*-4-*tert*-butylcyclohexanol over the cis isomer (Figure 1); in the former the initial axial iodo group is more favorably disposed for anticoplanar elimination. Treatment of 2-iodoctane with HMPA gave elimination, but the reaction was much faster in the presence of MTPI (Figure 2) indicating iodide anion is primarily responsible for dehydrohalogenation. The mechanism is also consistent with the unreactivity of tertiary alcohols.

The selectivity exhibited for the more stable (Saytzeff) alkenes with *E* stereochemistry has been noted for eliminations employing strong carbon bases in polar aprotic solvents (E2C eliminations)[2] and attributed to very productlike transition states.

The dehydrations of *cis*- and *trans*-2-methylcyclohexanol (entries 5 and 6) and of the corresponding 2-phenyl derivatives (entries 7 and 8) are unusual in that the Saytzeff alkene is the major product irrespective of the alcohol stereochemistry (except for entry 6). This is expected for the trans isomers in that conversion of the equatorial alcohol into the axial iodide enables anti-elimination to occur to the more stable alkene. However, the cis isomers should give the corresponding equatorial iodides which can eliminate in an anti-mechanism by ring inversion, but only with the 3-axial hydrogen to give the less substituted Hofmann product. The reluctance of forming the less stable products apparently results from competing SN2 displacement by iodide to generate the axial iodo derivative which readily eliminates to the observed Saytzeff alkenes.

Experimental Section

Gas chromatographic analysis were performed on a Hewlett-Packard Model 5250B chromatograph using either a 6 ft × 1/8 in. or 10 ft × 1/8 in. column packed with 10% OV-1 on 80–100 mesh Chromosorb W (DMCS). Analyses were performed using internal standards and predetermined detector response factors using authentic samples of the products. Hexamethylphosphoramide was distilled from calcium hydride and stored over 13A molecular sieves. Methyltriphenoxyphosphonium iodide was

(4) Dehydrohalogenation of primary alkyl halides occurs in HMPA, but more severe conditions are required (180–210°); see R. S. Monson, *Chem. Commun.*, 113 (1971).

(5) This was demonstrated by a competitive dehydration experiment between 1-*n*-butylcyclohexanol and *cis*-2-methylcyclohexanol; after 3 hr, 65% of 1-methylcyclohexene and 4% of 3-methylcyclohexene were produced while 80% of the 1-*n*-butylcyclohexanol was recovered.

(6) R. Hanna, *Tetrahedron Lett.*, 2105 (1968).

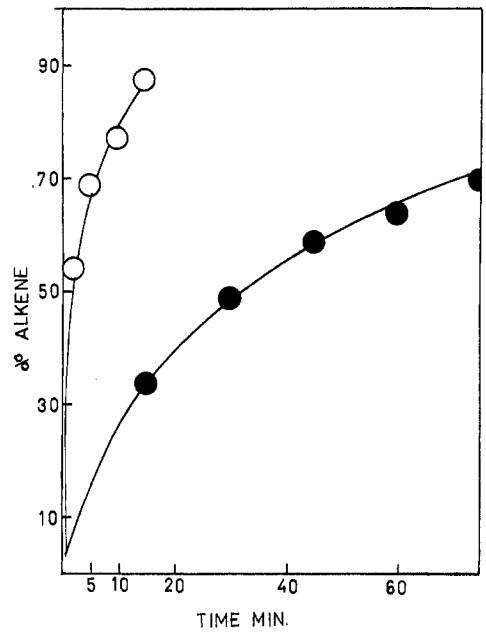

Figure 1.—Reaction of *cis*- and *trans*-4-*tert*-butylcyclohexanols with methyltriphenoxyphosphonium iodide in hexamethylphosphoramide at 75°. Reactions were 0.2 *M* in the alcohol, 0.4 *M* in the iodide. The percentages of alkenes were determined by glpc analysis using internal standards: ●, *cis*-4-*tert*-butylcyclohexanol; ○, *trans*-4-*tert*-butylcyclohexanol.

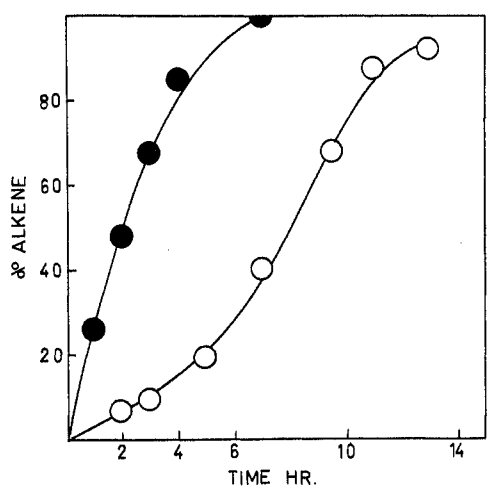

Figure 2.—Dehydrohalogenation of 2-iodooctane in hexamethylphosphoramide at 75°. Reactions were 0.2 *M* in 2-iodooctane. The percentages of alkenes were determined by glpc using internal standards: ●, no methyltriphenoxyphosphonium iodide; ○, solution 0.4 *M* in methyltriphenoxyphosphonium iodide.

prepared as described[3] and stored under dry ether. The alcohols used were commercial products except for *cis*- and *trans*-4-*tert*-butyl and *cis*- and *trans*-2-phenylcyclohexanols which were prepared by stereoselective reductions of the ketones ($IrCl_4$ complex for the cis,[7] $LiAlH_4$–$AlCl_3$ for the trans[8]).

Dehydration of Alcohols. General Procedure.—The method is presented in the text. The relative amount of solvent may be reduced for preparative applications. The isolation procedure is illustrated for the preparation of (*E*)-stilbene.

(*E*)-Stilbene.—A solution of 1,2-diphenylethanol (1.19 g, 6.0 mmol) and MTPI (5.4 g, 12 mmol) in 20 ml of HMPA was stirred at 75° for 1.0 hr, poured into 100 ml of aqueous KOH, and extracted three times with 25 ml of cyclohexane. The cyclohexane solution was washed three times with water and dried ($MgSO_4$). Removal of the solvent at reduced pressure and recrystallization of the resulting solid from ethanol afforded 928 mg (86%) of product as colorless plates, identical in all respects with authentic (*E*)-stilbene.

(7) E. L. Eliel, T. W. Doyle, R. O. Hutchins, and E. C. Gilbert, *Org. Syn.*, **50**, 13 (1970).

(8) E. L. Eliel, R. J. L. Martin, and D. Nasipuri, *ibid.*, **47**, 16 (1967).

Registry No.—**1**, 937-06-4; **2**, 937-05-3; **3**, 80-97-7; **4**, 57-88-5; **5**, 7443-70-1; **6**, 7443-52-9; **7**, 16201-63-1; **8**, 2362-61-0; **9**, 1490-04-6; **10**, 1724-39-6; **11**, 623-93-8; **12**, 1120-06-5; **13**, 2653-34-6; **14**, 614-14-2; **15**, 614-29-9; **16**, 112-53-8; **17**, 2198-72-3; **18**, 5445-30-7; MTPI, 17579-99-6; HMPA, 680-31-9.

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Oxidation Products of Ethyl α-Safranate

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Carotenoids with six-membered alicyclic end groups are widespread in nature.[1] Many organisms are capable of introducing carbonyl and/or alcohol functions at C-3 and C-4 into the α- or β-ionone rings of such carotenoids, while a few bacteria and the Japanese sea sponge have the ability to dehydrogenate the terminal cyclohexene rings to their aromatic counterparts. Relatively few methods have been developed for the total synthesis of such end groups[2] and it became of interest to inquire whether ethyl α-safranate (**1**), for which we recently described a simple and efficient synthesis,[3] could be transformed to versatile monocyclic intermediates and then to carotenoids.

Addition of ethyl α-safranate (**1**) to a solution of potassium *tert*-butoxide in glyme produced an orange solution undoubtedly containing the anion **2**. This color was discharged quickly when oxygen was bubbled through the solution and after work-up the hydroperoxide **3** (34%), the keto ester **4** (43%), and ethyl 2,6-dimethylbenzoate (**6**) (3%) could be isolated by chromatography. The structures of **3** and **4** rest on their spectral properties exclusively (see Experimental Section) while the aromatic ester **6** was compared with an authentic sample. The relative proportions of hydroperoxide **3** and ketone **4** depend on the method of isolation, and not unexpectedly the hydroperoxide **3** turned out to be a very labile compound and readily lost the elements of water, giving the ketone **4**. Injection into a gas chromatograph caused its decomposition to a mixture of **4**, **5**, and **6** in a ratio of 8:1:1. Mechanistic studies on the formation and decomposition of the hydroperoxide **3** were not undertaken but it seems to be the initial product derived from addition of oxygen

(1) B. C. L. Weedon in "Carotenoids," O. Isler, Ed., Birkhäuser Verlag, Basel, 1971, p 29.

(2) H. Mayer and O. Isler in "Carotenoids," O. Isler, Ed., Birkhäuser Verlag, Basel, 1971, p 325.

(3) G. Büchi and H. Wüest, *Helv. Chim. Acta*, **54**, 1767 (1971).