Methyltriphenoxyphosphonium Iodide (MTPI); Induced Dehydration and Dehydrohalogenation in Aprotic Solvents

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Methyltriphenoxyphosphonium iodide (MTPI) is an effective dehydration and dehydrohalogenation reagent under mild conditions when 1,3-dimethylimidazolidin-2-one is used as an aprotic solvent in place of the more normally used hexamethylphosphoric triamide (HMPT). Since previously suggested mechanisms had proposed alcohol–HMPT interaction as an important mechanistic step, this result coupled with comparative product geometric isomer distributions and the conjugated : non-conjugated triene product ratios leads to the conclusion that MTPI–alcohol interaction with displacement of phenoxide is the primary step in the reaction. In dimethyl sulphoxide (DMSO) alcohol dehydration is hindered by DMSO–MTPI interaction yielding dimethyl sulphide.
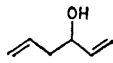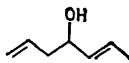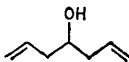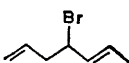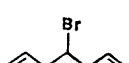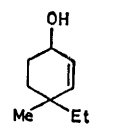
METHYLTRIPHENOXYPHOSPHONIUM iodide (MTPI) has in the past few years proven to be a versatile and useful reagent for effecting a number of different transformations. Originally, Landauer and co-workers [1,2] demonstrated that MTPI could convert primary, secondary, and tertiary alcohols to the corresponding iodides in excellent yield. Hutchins and co-workers [3] utilized MTPI in hexamethylphosphoric triamide (HMPT) to dehydrate secondary alcohols, and these studies were extended by Spangler and Hartford [4,5] to the syntheses of conjugated substituted hexa-1,3,5-trienes and cyclohexa-1,3-dienes in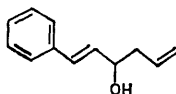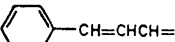 good yield and high purity under very mild conditions. More recently, Yamada et al.[6] utilized MTPI to convert substituted ethylene oxides to olefins stereospecifically. In all the above studies, the role of MTPI in the various reactions, as well as that of the solvent,[7,8] has prompted a great deal of speculation. This present study is an attempt to evaluate previous mechanistic speculations and to determine the limits of the synthetic utility of MTPI.

RESULTS AND DISCUSSION

A variety of saturated and unsaturated alcohols, and dienyl halides, were treated with MTPI in HMPT, 1,3-dimethylimidazolidin-2-one (DMI), and in a few instances, DMSO. In all cases the reaction conditions, concentrations, etc., were identical, and the products were isolated in identical fashion. The isolated products are shown in Table 1, while the geometric isomer ratios and unconjugated : conjugated triene ratios obtained for various dienols and dienyl bromides are listed in Table 2. The isolated yields are, in most cases, comparable in HMPT and DMI. It is clear from the product analysis that DMI can be used in place of HMPT in both dehydration and dehydrohalogenation reactions. This fact demonstrates that HMPT is serving as a good solvent rather than an active reactant, as proposed by both Monson [8] and Hutchins.[3] The results in Table 2 also indicate that olefin formation is not necessarily linked to the formation of intermediate iodides. For example, while the $E,Z : E,E$ ratio in the hepta-1,3,5-triene dehydration products is the same as the dehydrohalogenation product in HMPT, there is a significant difference in these product ratios in DMI. The same is true of the
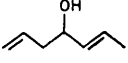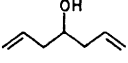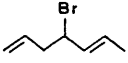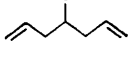
Z/E ratios of the unconjugated triene formed in DMI. These discrepancies have led us to postulate a more comprehensive MTPI reaction scheme that is not only more in keeping with the observed data, but is also consistent with the original observation of Landauer [1,2] that MTPI can react with alcohols directly without solvent participation and with the previous study in our laboratory [5] which clearly demonstrated the particip-

TABLE 1

MTPI dehydration and dehydrohalogenation products [a]

Substrate	Solvent	Isolated product (% yield)
OH	DMI [b]	$CH_2=CHCH=CHCH=CH_2$ (53)
	HMPT [b]	$CH_2=CHCH=CHCH=CH_2$ (56)
	DMSO [b]	$CH_2=CHCH=CHCH=CH_2$ (15) [c]
OH	DMI	$MeCH=CHCH=CHCH=CH_2$ (23)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (21)
	HMPT	$MeCH=CHCH=CHCH=CH_2$ (65)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (30)
OH	DMI	$MeCH=CHCH=CHCH=CH_2$ (3)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (30)
	HMPT	$MeCH=CHCH=CHCH=CH_2$ (tr)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (49)
Br	DMI	$MeCH=CHCH=CHCH=CH_2$ (37)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (18)
	HMPT [d]	$MeCH=CHCH=CHCH=CH_2$ (34)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (17)
Br	DMI	$MeCH=CHCH=CHCH=CH_2$ (17)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (34)
	HMPT	$MeCH=CHCH=CHCH=CH_2$ (8)
		$CH_2=CHCH_2CH=CHCH=CH_2$ (47)
OH (Me, Et ring)	DMI	(69)
	HMPT	(Me Et) (58)
(phenyl, OH)	DMI	$—CH=CHCH=CHCH=CH_2$ (47) (three isomers)
OH (Me ring)	DMSO	(41) [e]
	HMPT	(54)
	DMI	(Me) (52)

[a] All reactions carried out at 50—60 °C (H_2O bath) for 2 h. [b] DMI = 1,3-dimethylimidazolidin-2-one, HMPT = hexamethylphosphoric triamide, DMSO = dimethyl sulphoxide. [c] In DMSO, Me_2S was also formed in varying amounts relative to the percentage dehydration. [d] 4-Bromohexa-1,3-diene contains some 6-bromohexa-1,4-diene, and is a dynamic allylic mixture.

TABLE 2

MTPI dehydration and dehydrohalogenation product isomer distribution

Compound	Solvent	Conjugated triene			Unconjugated triene			Product ratio unconjugated : conjugated
		E,E	Z,E	Ratio	E	Z	Ratio	
(OH structure)	DMI	56	44	0.79	64	36	0.56	0.94 : 1
	HMPT	67	33	0.49	100	0		0.47 : 1
(OH structure)	DMI	60	40	0.67	61	39	0.64	12.1 : 1
	HMPT				100			
(Br structure)	DMI	68	32	0.47	100	0		0.37 : 1
	HMPT	67	33	0.49	100	0		0.47 : 1
(Br structure)	DMI	67	33	0.49	84	16	0.19	2.0 : 1
	HMPT	58	42	0.72	100			5.8 : 1

ation of carbocations in the overall dehydration process (Scheme).

Thus, depending on the substrate structure, carbocation, direct substitution, or elimination processes can dominate the reaction sequence from the original alcohol–MTPI intermediate. No dehydration occurs when various alcohols are treated with HMPT or DMI in the absence of MTPI. Similarly, dienyl bromides do not dehydrohalogenate readily in either DMI or HMPT at 50 °C. Clearly, the first key stage in dehydration is the interaction between MTPI and the alcohol, regardless of solvent.

In an attempt to determine if other elimination reactions could be induced by MTPI in HMPT or DMI, 3-acetoxyhexa-1,5-diene, 3-ethoxyhexa-1,5-diene, and 4-methylcyclohexylamine were treated with MTPI at 50—60 °C. No elimination products were obtained, and no discernible reactions occur between the 3-acetoxy- and 3-ethoxy-dienes and MTPI. 4-Methylcyclohexylamine reacts slowly with MTPI, presumably by displacement of the three phenoxy-groups forming the corresponding phosphoric triamide; however, no volatile elimination products were formed.

Dehydration studies were also attempted with DMSO as solvent. Both hex-1,5-dien-3-ol and 4-methylcyclohexanol yielded the expected hexa-1,3,5-triene and 4-methylcyclohexene dehydration products; however, an additional product, dimethyl sulphide, was also produced in appreciable quantities. Since an oxidation–reduction process must be competing with the dehydration reaction, DMSO cannot be recommended as a solvent for MTPI-induced processes even though it is a good dehydrohalogenating solvent for dienyl halides with AgNO₃ or DBU.[5] Indeed, if MTPI is treated with DMSO in the absence of the alcohol, dimethyl sulphide is formed in appreciable quantities. We postulate that the polar sulphoxide must compete with the alcohol for the available MTPI, thus lowering dehydration yields.

EXPERIMENTAL

Gas-liquid chromatography (g.l.c.) was performed with a Hewlett–Packard 5480A dual-column instrument equipped with ¾-in × 20-ft 15% Carbowax 20M on Chromosorb W SS columns. U.v. spectra were recorded with a Perkin-Elmer Model 202 spectrophotometer and i.r. spectra with a Pye–Unicam Model 3-200 spectrometer. N.m.r. spectra were

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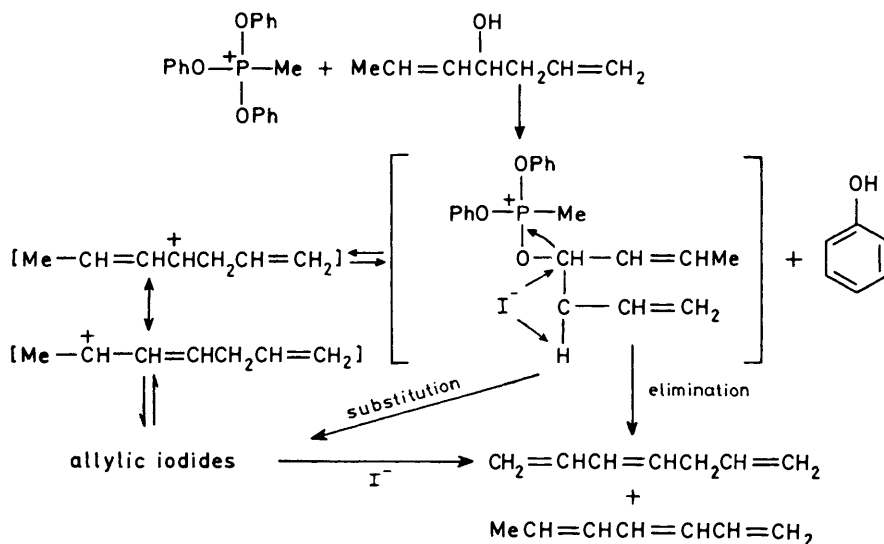
determined as solutions in $CDCl_3$ ($SiMe_4$ as internal reference) using a Varian A-60A spectrometer. All trienic spectra were recorded for mixtures of geometric isomers.

Dehydration of Alcohols; General Procedure for Volatile Products.—Hexa-1,5-dien-3-ol (4.9 g, 0.050 mol) was added to a mixture of methyltriphenoxyphosphonium iodide [9] (35 g) in 100 ml of 1,3-dimethylimidazolidin-2-one (or HMPT or DMSO). The resulting dark reddish-brown reaction mixture was heated at 50—60 °C for 2 h, and then distilled directly at reduced pressure (*ca.* 15 mmHg). The volatile product(s) were trapped in a receiver cooled by a solid CO_2–acetone bath, warmed to room temperature, and analysed by g.l.c. In DMI and HMPT, the only product was hexa-1,3,5-triene (2.1 g, 53% in DMI and 2.2 g, 56% in HMPT). In DMSO two products were obtained: hexa-1,3,5-triene (0.6 g, 15%) and dimethyl sulphoxide (2.4 g). Z/E-Isomer ratios were obtained from g.l.c. by comparison with an authentic sample.

Dehydration of Alcohols; General Procedure for Nonvolatile Products.—1-Phenylhexa-1,5-dien-3-ol (8.7 g, 0.050 mol) in DMI (25 ml) was added to a mixture of MTPI (35 g) in DMI (75 ml), and the resulting mixture was heated as described above for volatile product mixtures. After heating, the reaction product was poured into ice–water and an excess of sodium carbonate was added to the resulting mixture. After stirring for 1 h or longer, the colour gradually changed from reddish-brown to pale yellow. The product was extracted in pentane, dried with anhydrous magnesium sulphate and isolated by solvent removal under vacuum (3.7 g, 47%). G.l.c. analysis showed the presence of three geometric isomers which were not completely separable, but identifiable as 1-phenylhexa-1,3,5-triene.

Dehydrohalogenation of Halides; General Procedure.—4-Bromohepta-1,6-diene (11.3 g, 0.065 mol) was treated with MTPI in DMI or HMPT (100 ml). After heating for 2 h at 50—60 °C, the product was isolated in the same manner as described above for volatile products from dehydration. In both DMI (3.3 g, 55%) and HMPT (3.1 g, 51%), two products were obtained, hepta-1,3,5-triene and hepta-1,3,6-triene (Table 1).

Identification of Products.—Hepta-1,3,5-triene,[10] hexa-1,3,5-triene,[11] and 1-phenylhexa-1,3,5-triene [12] were prepared separately and compared with the products generated by the reactions described in this work. The geometric identity of the various isomers have been established previously. Hepta-1,3,6-triene and 4-methylcyclohexene are commercially available, and 5-methyl-5-ethylcyclohexa-1,3-diene has been prepared previously.[4] 1-Phenylhexa-1,3,5-triene was compared to an authentic sample [12] by u.v., n.m.r., and i.r. spectroscopy for the mixture of three geometric isomers obtained. HMPT, DMI, and DMSO were all reagent grade and available commercially.

3-Acetoxyhexa-1,5-diene.—Hexa-1,5-dien-3-ol (39.2 g, 0.40 mol) was added to acetic anhydride (81.6 g, 0.80 mol) and triethylamine (60.6 g, 0.60 mol), and then 4-dimethylaminopyridine (1 g) was added as catalyst. The reaction mixture

warmed rapidly, but never achieved reflux. The mixture was stirred overnight, then poured into 3N HCl (1 l). The organic product was extracted with ether (3 × 200 ml), washed with aqueous sodium carbonate solution and then water, dried with anhydrous magnesium sulphate, and distilled, b.p. 55—56 °C (15 mmHg) (45.6 g, 81%), n_D^{23} 1.4275; τ 8.0 (s, 3 H, acetate Me), 7.5—7.8 (t, 2 H, methylene), 4.9—5.2 (m, 6 vinyl H and 1 tertiary C–H) (Found: C, 68.74; H, 8.72. Calc. for $C_8H_{12}O_2$: C, 68.54; H, 8.63%).

3-Ethoxyhexa-1,5-diene.—Hexa-1,5-dien-3-ol (49 g, 0.50 mol) was added to a suspension of sodium chips (12 g) in THF (200 ml). The resulting mixture was refluxed for 24 h, after which time the sodium had been consumed. The mixture was cooled (ice-bath) and ethyl bromide (60 g) was added, along with further THF (50 ml). The resulting mixture was stirred overnight at 25 °C, then heated at 60 °C for 6 h, poured into ice–water, and the organic product extracted with ether. The ether solution was washed with brine, dried with anhydrous magnesium sulphate, and distilled at reduced pressure, b.p. 25—35 °C (15 mmHg). G.l.c. analysis indicated the presence of *ca.* 25% hexa-1,5-dien-3-ol, along with the desired product. Fractional distillation through a 10-in Vigreux column produced pure 3-ethoxyhexa-1,5-diene (35 g, 56%), b.p. 26—28 °C (15 mmHg), n_D^{23} 1.4120; τ 8.7—9.0 (t, J 7 Hz, 3 H, Me), 7.5—7.8 (m, 2 H, CH_2), 6.0—6.6 (m, 3 H, tertiary CH and CH_2–O), and 3.8—5.1 (m, 6 vinyl H) (Found: C, 75.95; H, 11.27. Calc. for $C_8H_{14}O$: C, 76.13; H, 11.18%).

Reaction of DMSO with MTPI.—MTPI (35 g) was dissolved in DMSO (100 ml) and the mixture heated for 2 h at 50—60 °C. The volatile product was isolated as described above (2.5 g) and g.l.c. analysis showed it to be composed solely of dimethyl sulphide, τ 7.92.

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