91759-91-0; (S)-6, 91759-92-1; (S)-7, 91759-93-2; (S)-8, 78156-22-6; 9, 78156-24-8; 10, 91759-94-3; $(PhO)(EtO)_2CH$, 14444-77-0; HC≡CH, 74-86-2; $NH_2OH·HCl$, 5470-11-1; (+)-(S)-2-methylbutanenitrile, 25570-03-0; (+)-(S)-2-*sec*-butylallylmagnesium chloride, 91759-96-5; (π-cyclopentadienyl)(1,5-cyclooctadiene)-(+)-(S)-2-*sec*-butylallylmagnesium chloride, 12184-35-9; 2-bromopyridine, 109-04-6; 2-lithiopyridine, 17624-36-1; 2-[1-hydroxy-3-(2,2-diethoxyethyl)-4-methylhexyl]pyridine, 91759-97-6.

Organic Reactions at High Pressure. Preparation of Wittig Phosphonium Salts at Ambient Temperature[1]

William G. Dauben,* John M. Gerdes, and Richard A. Bunce[2]

Department of Chemistry, University of California, Berkeley, California 94720

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As applications of the versatile Wittig reaction[3,4] are directed toward the synthesis of more complex olefins, the requisite phosphonium salts must frequently incorporate labile functional groups and stereochemically sensitive centers.[3a,d] The presence of sensitive functionality may limit the use of standard elevated temperature conditions (80–140 °C) for salt formation[3,4] and, therefore, provide impetus for developing a new mild method for quaternization of triphenylphosphine. In an S_N2 type of displacement reaction which results in ionization, the reaction possesses a negative volume of activation, $\Delta V^{\ddagger}$, and such a reaction should be accelerated under very high pressure (15 kbar, 1.5 GPa). The most typical process of this type is the Menshutkin reaction which involves an amine and an alkyl halide, tne $\Delta V^{\ddagger}$ having been reported to lie between −20 and −50 $cm^3\ mol^{-1}$.[5]

$$R_3N + R'X \rightarrow R_3N^+R'\ X^-$$

The accelerated rates observed for this type of charge developing reaction at high pressure are understood by considering the components of the $\Delta V^{\ddagger}$ parameter,[6] which include the intrinsic term or van der Waals volumes and the solvation term related to changes in the volume of the solvating medium brought about by the solute. Reduction of the intrinsic and solvation volumes, resulting from the new bond formation between two molecules and electrostriction of the dipolar medium,[7] respectively, also occurs during the reaction of a trialkyl phosphite with an alkyl iodide, the initial process of the Arbuzov reaction. The observed rate enhancement at elevated pressure, a factor of ten-fold at 2.5 kbar pressure[8] due in part to a charge development along the reaction course, should also be found in the reaction of triphenylphosphine with primary and secondary halides. The present work shows the great utility of high pressure rate enhancement in the formation of phosphonium salts, permitting reaction to occur between 20 and 40 °C.

$$Ph_3P + RX \rightarrow PH_3P^+R\ X^-$$

A variety of alkyl bromides and chlorides have been evaluated in their reaction with triphenylphosphine in different solvents, at different temperatures, and at high (15 kbar, 1.5 GPa) and low (1 bar) pressure, and the results are summarized in Table I. All reactions at elevated pressure were carried out at either 20 °C or 40 °C for 24 or 36 h. The melting points of the resultant, analytically pure salts were compared with those previously reported. Ambient (1 bar) pressure control experiments were performed using identical ratios of reagents and solvent and were allowed to react at 20 °C and 80 °C for the indicated times.

The advantages in using high pressure are very apparent in the preparation of phosphonium salts from alkyl bromides. As shown in entry 1, *n*-butyl bromide in acetonitrile under high pressure at 20 °C for 24 h was converted to the phosphonium salt in 72% yield. At 1 atm pressure at the same temperature in the same solvent but for 36 h reaction time, no reaction occurred; at 80 °C, however, a 55% yield of salt was obtained. Of special interest are the increased 15 kbar salt formation yields of 89% and 82% which result from using the more effective 7:3 mole ratio of benzene: toluene solvent system (low dielectric constant)[7] and the mole to mole ratio of reactants, respectively. The other primary bromides (entries 2 and 3) also quaternized triphenylphosphine best at elevated pressure. The required heating for the ambient pressure reaction of the bromo ketal (entry 3), brought about deketalization, thus making the carbonyl protected salt only preparable by use of the high pressure procedure. The same is true for the primary chloride (entry 4) which at 80 °C and atmospheric pressure gave only a 13% yield of salt, whereas with high pressure at 40 °C the yield was raised to 33% (not optimized).

Turning attention to secondary bromides, which are known to react sluggishly in the S_N2 displacement reaction, the few known examples of phosphonium salt preparations[10,11] (entries 5 and 6) all required extreme heating (120–140 °C). These substrates were ideally suited for this high pressure procedure. The atmospheric pressure control experiment of *sec*-butyl bromide (entry 5) showed no reaaction at 20 °C but when heated neat at 120 °C (sealed tube) yielded the salt in 95% yield. Under the standard high pressure conditions at 40 °C using either a 2:1 or 1:1 molar ratio of reactants, yields of 58% and 55% were obtained. With cyclopentyl bromide (entry 6), a temperature of 200 °C was needed for the 1 atm pressure control and the yield was only 43%. Under high pressure at 20 °C, a 52% yield was obtained and this could be raised to 79% by using a large excess of the bromide.[14] An

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(2) National Institutes of Health Postdoctoral Fellow, 1981–1983. Present address: Department of Chemistry, Oklahoma State University, Stillwater, OK 74078.

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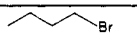
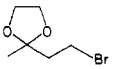
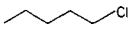
Table I. Alkylation of Triphenylphosphine with Primary and Secondary Halides at 15 kbar Pressure[a]

		reaction conditions				1 bar controls				
entry	RX	solvent	T, °C	t, h	$RP^+Ph_3X^-$ yield,[c] %	solvent[b]	T, °C	t, h	yield,[c] %	ref
1		A	20	24	89	B	20	36	0	9
		A	20	24	82[d]	C	80	4	55	
		B	20	24	72					
2	n-$C_{10}H_{21}CH_2Br$	A	20	36	59	A	20	36	0	
		B	20	36	26	A	80	36	41	
3		A	20	36	92	A	20	36	0	
						A	80	36	*e*	
4		A	40	36	0					
		B	20	36	8	B	20	36	0	
		B	40	36	33	B	80	36	13	
5		B	40	36	58	B	20	36	0	10
		B	40	36	55[d]	D	120	18	95	
6		A	20	24	11					11
		B	20	36	52	B	20	36	0	
		B	20	36	79[f]	D	200	12	43	
7		A	40	36	0					12
		B	20	36	5	B	20	36	0	
		B	40	36	46	B	80	36	11	
8		A	20	36	84	A	20	36	28	
9		A	20	36	94	A	20	36	61	13
						C	70	2		

[a] Except where noted, all reactions were carried out by using a 0.25 mmol:0.5 mmol:0.8 mL ratio of triphenylphosphine/halide/solvent. [b] Solvents were A, 7:3 mole ratio of PhH/$PhCH_3$; B, CH_3CN; C, PhH; D, no solvent. [c] Yields are isolated and unoptimized. [d] Reaction was run using a 0.50 mmol:0.50 mmol:0.8 mL ratio of PPh_3/RX/solvent. [e] Deketalized with heating. [f] Reaction was run using a 0.25 mmol:10.0 mmol:0.2 mL ratio of PPh_3/RX/solvent.

Table II. Formation of Alkyltriphenylphosphonium Sulfonate Salts at 15 kbar Pressure[a]

		reaction conditions				1 bar controls				
entry	RX	solvent[b]	T, °C	t, h	$RP^+Ph_3X^-$ yield,[c] %	solvent[b]	T, °C	t, h	yield,[c] %	ref
1		B	20	36	90	B	20	36	5	4b
						B	80	36	70	
						C	170	6	86	
2		B	20	36	71	B	20	36	0	
						B	80	36	56	
3	n-$C_9H_{19}CH_2OTs$	A	20	36	82	A	20	36	0	
						A	80	48	54	
4		A	20	36	63	A	20	36	0	
						A	80	36	65	

[a] All reactions were carried out with a 0.25 mmol:0.5 mmol:0.8 mL ratio of triphenylphosphine/sulfonate/solvent. [b] Solvents were A, 7:3 mole ratio of PhH/$PhCH_3$; B, CH_3CN; C, PhH. [c] Yields are isolated and unoptimized.

equally striking result was that obtained with cyclohexyl chloride (entry 7) which under high pressure at 40 °C gave the salt in 46% yield, whereas at 80 °C and 1 bar pressure only an 11% yield was obtained. With the more reactive secondary bromides (entries 8 and 9) reasonable reaction yield could be obtained in 36 h under ambient pressure and temperature control conditions. In this same period of time, the yields of product could be doubled or tripled at high pressure.

Although halides are most used in the preparation of phosphonium salts, the halide preparation from an alcohol with sensitive groupings often causes problems. This problem is usually bypassed by preparing the halide from the corresponding sulfonate ester. It is known that these latter esters can be directly converted to phosphonium salts which, in turn, can be used to generate ylides; it is surprising that this process is rarely used.[4] A limited study of the preparation of sulfonate phosphonium salts is reported in Table II. It is seen (entries 1–4) that both primary and secondary mesylates and tosylates are prepared in high yield at room temperature and high pressure. At 1 bar pressure, practically no reaction occurs at room temperature but good yields can be obtained at 80 °C. Thus, again the use of the high pressure techniques permits the reaction to be run at room temperature.

A survey of all the present results shows that reactants with aromatic substituents and the primary bromides react better in benzene–toluene solution while most of the secondary bromides and sulfonates react better in acetonitrile. The high pressure technique allows formation of phosphonium salts on a preparative scale. This salt formation at ambient temperature coupled with the low temperature preparation of mesylates from alcohols[15] provides an attractive mild (≤20 °C) sequence for the overall transformation of an alcohol to its olefin homologue. This sequence should find application in the preparation of olefins

(14) The effects of altering the relative ratio of reactants and solvent have been noted before, see ref 3c.

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with labile functional groups and sensitive stereochemical centers.

Experimental Section

General Methods. Benzene, toluene, and acetonitrile were distilled under nitrogen atmosphere from CaH_2; diethyl ether was distilled from sodium benzophenone ketyl. The construction and use of the high pressure apparatus employed in this study has been described previously.[16] IR spectra were recorded on a Perkin-Elmer Model 281 spectrometer either as a thin film (NaCl plates) or pellet (KBr). Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkely. Mass spectra were recorded on a Kratos MS-50 high resolution mass spectrometer.

General Procedure for High Pressure and Ambient Pressure Reactions. A solution of triphenylphosphine (0.25 mmol), alkyl halide or sulfonate (0.50 mmol), and solvent (0.8 mL, acetonitrile or benzene:toluene, 7:3 mole ratio) in a Teflon tube clamped at both ends was pressurized at 15 kbar (1.5 GPa) hydrostatic pressure for 24–36 h at 20–40 °C (see Tables I and II for solvent and exact conditions). The reactions were cooled (if necessary), depressurized, and concentrated under reduced pressure to afford the crude phosphonium salts which were washed with anhydrous ethyl ether. The precipitated phosphonium salts were collected, washed repeatedly with ether, and dried under vacuum. The salts showed characteristic bands at 1450–1425 cm^{-1} (s), 1120–1100 cm^{-1} (s), 1010–990 cm^{-1} (m-s), and 730–720 cm^{-1} (s).[4b,17] The control runs were performed at 1 bar pressure, 36–48 h, and 20–80 °C, with an identical ratio of reagents in each case with those described for their respective high pressure runs. The following new compounds were prepared.

1-Undecyltriphenylphosphonium bromide: failed to crystallize; IR (thin film) 1440, 1103, 995, 720 cm^{-1}. Anal. Calcd for $C_{29}H_{38}PBr$: C, 70.01; H, 7.70; Br, 16.06. Found: C, 69.53; H, 7.30; Br, 15.42.

[3-(1,3-Dioxolan-2-yl)butyl]triphenylphosphonium bromide: amorphous foam; IR (pellet) 1450, 1120, 1005, 730 cm^{-1}. Anal. Calcd for $C_{24}H_{26}O_2PBr$: C, 63.03; H, 5.73. Found: C, 62.77; H, 5.76.

(1-Phenylethyl)triphenylphosphonium bromide: mp 224–225 °C; IR (pellet) 1440, 1100, 1000, 728 cm^{-1}. Anal. Calcd for $C_{26}H_{24}PBr$: C, 69.81; H, 5.46; Br, 18.03. Found: C, 69.67; H, 5.48; Br, 18.20.

1-Pentyltriphenylphosphonium chloride: mp 171–173 °C; IR (pellet) 1448, 1115, 1005, 730 cm^{-1}. Anal. Calcd for $C_{23}H_{26}PCl$: C, 74.89; H, 7.10. Found: C, 75.00; H, 6.99.

Cyclohexyltriphenylphosphonium chloride: amorphous foam; IR (pellet) 1448, 1120, 1000, 728 cm^{-1}; mass spectrum, exact mass calcd for $C_{24}H_{26}PCl$ minus HCl m/e 344.1726, found m/e 344.1699.

2-Butyltriphenylphosphonium methanesulfonate: mp 183–185 °C; IR (pellet) 1438, 1100, 995, 720 cm^{-1}. Anal. Calcd for $C_{23}H_{25}O_3SP$: C, 66.97; H, 6.11; S, 7.77. Found: C, 66.26; H, 6.64; S, 7.74.

1-Decyltriphenylphosphonium *p*-toluenesulfonate: mp 94–96 °C; IR (pellet) 1452, 1125, 1005, 730 cm^{-1}. Anal. Calcd for $C_{35}H_{43}O_3SP$: C, 73.14; H, 7.54; S, 5.58. Found: C, 72.89; H, 7.54; S, 5.79.

2-Butyltriphenylphosphonium *p*-toluenesulfonate: mp 197–199 °C; IR (pellet) 1445, 1115, 1015, 728 cm^{-1}. Anal. Calcd for $C_{39}H_{31}O_3SP$: C, 70.99; H, 6.37. Found: C, 70.77; H, 6.32.

Concentration-Dependent High Pressure Reactions. *n*-Butyltriphenylphosphonium Bromide. A solution of triphenylphosphine (1.5 mmol), *n*-butyl bromide (0.5 mmol), and 7:3 benzene:toluene (0.8 mL) was pressurized at 15 kbar, 20 °C, for 24 h. The sample was depressurized and the crude phosphonium salt processed as described above to afford 165 mg (82%) of *n*-butyltriphenylphosphonium bromide; mp 240–241 °C (lit.[9] mp 242–243 °C).

Preparative scale reaction of triphenylphosphine (11.4 mmol) and *n*-butyl bromide (11.4 mmol) in 7:3 benzene:toluene (5 mL) at 15 kbar pressure, 20 °C for 36 h, afforded, after usual ethyl ether processing, 4.15 g (91%) of *n*-butyltriphenylphosphonium bromide.

2-Butyltriphenylphosphonium Bromide. Acetonitrile (0.8 mL) was charged with triphenylphosphine (0.5 mmol) and 2-butylbromide (0.5 mmol) and then subjected to 15 kbar pressure, 40 °C for 36 h. Depressurization, followed by workup described above, yielded 110 mg (55%) of 2-butyltriphenylphosphonium bromide; mp 234–238 °C (lit.[10] mp 235–238 °C).

Cyclopentylphosphonium Bromide. Treatment of triphenylphosphine (0.25 mmol) with excess cyclopentyl bromide (10.0 mmol) in acetonitrile (0.2 mL) at 15 kbar pressure, 20 °C for 36 h, afforded, after ether processing, 81 mg (79%) of cyclopentyltriphenylphosphonium bromide; mp 260–261 °C (lit.[11] mp 262–263 °C).

Registry No. Ph_3P, 603-35-0; *n*-$C_{10}H_{21}CH_2Br$, 693-67-4; *n*-$C_9H_{19}CH_2OTs$, 5509-08-0; *n*-butyltriphenylphosphonium bromide, 1779-51-7; 1-undecyltriphenylphosphonium bromide, 60669-22-9; 1-butyl-3-(1,3-dioxolanyl)triphenylphosphonium bromide, 71864-02-3; 1-pentyltriphenylphosphonium chloride, 35171-60-9; 2-butyltriphenylphosphonium bromide, 3968-92-1; cyclopentyltriphenylphosphonium bromide, 7333-52-0; cyclohexyltriphenylphosphonium chloride, 91949-56-3; (1-phenylethyl)triphenylphosphonium bromide, 30537-09-8; (1-(ethoxycarbonyl)-ethyl)triphenylphosphonium bromide, 30018-16-7; 1-butyltriphenylphosphonium methanesulfonate, 91949-57-4; 2-butyltriphenylphosphonium methanesulfonate, 91949-58-5; 1-decyltriphenylphosphonium *p*-toluenesulfonate, 91949-59-6; 2-butyltriphenylphosphonium *p*-toluenesulfonate, 91949-60-9; *n*-butyl bromide, 109-65-9; 2-(2-bromoethyl)-2-methyl-1,3-dioxolane, 37865-96-6; 1-pentyl chloride, 543-59-9; *sec*-butyl bromide, 78-76-2; cyclopentyl bromide, 137-43-9; cyclohexyl chloride, 542-18-7; 1-phenylethyl bromide, 585-71-7; ethyl 2-bromopropanoate, 535-11-5; *n*-butyl methanesulfonate, 1912-32-9; *sec*-butyl methanesulfonate, 16156-54-0; *sec*-butyl *p*-toluenesulfonate, 715-11-7.

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Further Evidence for Nitrenium Ion Intermediacy in *N*-Phenylhydroxylamine Rearrangement to Aminophenol

L. A. Sternson* and R. Chandrasakar

Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, Kansas 66045

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N-Arylhydroxylamines (AH) are highly reactive products formed by metabolic oxidation of primary arylamines.[1,2] In aqueous solution, at neutral pH,[3] they are readily oxidized to nitrosobenzenes, nitrobenzenes, *p*-nitrosophenols, and azo- and azoxybenzenes.

In the absence of O_2, the stability of *N*-phenylhydroxylamine (PHA) and substituted *N*-phenylhydroxylamines is greatly enhanced,[3] except in the strongly acidic region where AH's undergo O_2-independent rearrangement to the corresponding aminophenol.[4] The mechanism of this rearrangement in aqueous solution has not been clearly elucidated. Both bimolecular[5] and unimolecular[6] pathways have been suggested. Attempts to resolve this controversy through ^{18}O-labeling studies have been inconclusive. Rearrangement of ^{18}O-labeled *N*-

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