a difunctional compound is first blocked by reaction onto a polymer support.[22] The unblocked function is then converted to a desired function followed by subsequent release (and regeneration) of the first group from the polymer in sequential steps. However, each step is conducted stoichiometrically and independently. Another ingeneous use of stoichiometric reactions conducted sequentially and using polymer supports is the "wolf and lamb" reaction concept of Patchornik et al.[23] In this approach, two different reagents are anchored to polymers, and a reagent acts as a soluble "messenger" between the solid phases. A reagent, such as acetophenone, can be converted to its enolate anion by polymeric tritylllithium, and this enolate may then react with a polymer-bound ester in a typical Claison condensation to generate the enolate of a β-diketone in a single pot. By cascading this product into a second pot containing polymer-bound hydrazine, for example, diazoles can be produced. However, these reactions are not catalytic. Therefore, the sequential approach described in this paper is fundamentally different.

Experimental Section

Aldol Condensation of Ketones. In a typical preparation, acetone (2.0 mL, 27.1 mmol) and Nafion-H (0.6504 g, 0.542 mmol) were charged to a nitrogen-purged Fischer-Porter aerosol compatibility tube. The tube was sealed with a head containing a pressure gauge. The tube was warmed to the desired temperature and stirred for the specified reaction time. Upon completion, the tube was cooled to room temperature. Products were analyzed on a Hewlett-Pachard Model 5712A gas chromatograph using a $^1/_8$ in. × 6 ft copper column packed with 15% Carbowax 20M on Chromosorb W support [temperature program: from 60 °C (2 min) at 8 °C/min to 100 °C]. Each product was identified by addition of an authentic sample to the reaction solution, and the mixture was analyzed with three different temperature programs. The product was assigned only when the authentic samples gave a single peak with the experimental sample peak at the three different temperature programs used. Quantitative GLC data were obtained via electronic integration with a Hewlett-Packard Model 3380A reporting integrator. Area-normalization (with response-factor correction) calibration techniques were used to determine yields and product distributions. The temperature program for crossed condensation of benzaldehyde/acetone was from 150 °C (2 min) at 8 °C/min to 200 °C. Isothermal (150 °C) conditions were employed for the 2,5-hexanedione system.

Aldol Condensation–Hydrogenation of Ketones. In a typical preparation, acetone (5.0 mL, 67.8 mmol), Nafion-H (1.6260 g, 1.355 mmol), and 10% palladium on activated carbon (0.1442 g, 0.1355 mmol) were charged to a nitrogen-purged Fischer-Porter tube. The tube was sealed with a head containing a pressure gauge and a vent inlet valve. The tube was pressurized and vented three times with hydrogen followed by raising of the pressure to that desired with hydrogen. The tube was then placed in an oil bath, preequilibrated at the proper temperature, and stirred for the desired reaction time. The reaction was conducted at constant pressure by connecting the reaction tube to a gas reservoir via stainless-steel tubing and a pressure-control valve. Thus, the pressure to the reaction tube remained constant. The tube was then cooled and the gas was vented. The reaction solution was filtered and analyzed quantitatively by GLC according to the method described above.

Acknowledgment. Partial support of this work by the National Science Foundation, (Grant No. NSF-DAR-7824875) is gratefully acknowledged. Samples of Nafion-H were supplied by C. M. Fischer of Du Pont de Nemours Co. Dr. Yasuziro Kawabata prepared the resin-bound Wilkinson's catalyst and carried out the aldol condensation–hydrogenation of acetone using this resin with Nafion-H.

Registry No. Acetone, 67-64-1; mesityl oxide, 141-79-7; 4-methyl-2-pentanone, 108-10-1; 2-propanol, 67-63-0; Nafion-H, 63937-00-8; Amberlite IR-120, 9002-23-7; $(PPh_3)RhCl$, 14694-95-2; benzaldehyde, 100-52-7; benzylacetone, 2550-26-7; toluene, 108-88-3; 2,5-hexanedione, 110-13-4; 2,5-dimethylfuran, 625-86-5.

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Novel Synthetic Reactions Using Bis(2,2,2-trifluoroethoxy)triphenylphosphorane

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Alkoxy- or (acyloxy)(2,2,2-trifluoroethoxy)triphenylphosphoranes which were prepared in situ by the ligand exchange of bis(2,2,2-trifluoroethoxy)triphenylphosphorane with alcohols or carboxylic acids were found to behave as potential alkylating or acylating reagents for the preparation of a variety of esters, amides, sulfides, and ketones.

The chemistry of phosphoranes has been developed mainly for the purpose of studying stereochemistry around the phosphorus atom.[1-4] However, with exception of phosphonium salts and phosphoranes with halogen ligands, no reports have appeared for the utilization of phosphoranes for synthetic reactions, except those for dehydration and/or alkylation leading to epoxides,[5] esters,[6] ethers,[6-9] and heterocycles.[9-14] In fact, reported synthetic routes for phosphoranes so far include only (i) the condensation of trivalent phosphorus compounds with quinones, α-diketones or carboxylic acids,[15-17] (ii) the oxidative addition

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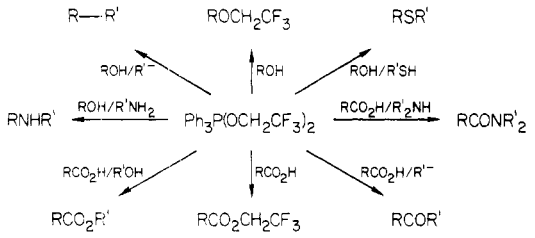
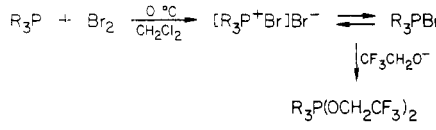
Scheme I



Scheme II[a]



[a] R = Ph, Bu, NMe_2.

of peroxy compounds of phosphines,[9-11,18,19] and (iii) the reaction of trivalent phosphorus compounds with alkyl arylsulfenates.[20]

On consideration of the electronic effect of the ligand, fluoroalkyl or fluoroalkoxy groups having a strong electron-withdrawing effect are expected to stabilize the phosphoranes. Recently, Schmutzler and co-workers[21] have reported the preparation of pentakis(hexafluoroisopropoxy)phosphorane, of which, however, no reactions are mentioned.

We recently outlined in a preliminary account[22,23] a convenient method for the preparation of bis(2,2,2-trifluoroethoxy)triphenylphosphorane and some of its reactions with alcohols and carboxylic acids, affording 2,2,2-trifluoroethylated ethers and esters.

The rapid ligand exchange of one of the 2,2,2-trifluoroethoxyl groups of bis(2,2,2-trifluoroethoxy)triphenylphosphorane (1) with alcohol or carboxylic acid, giving (2,2,2-trifluoroethoxy)alkoxytriphenylphosphorane (2) or (2,2,2-trifluoroethoxy)(acyloxy)triphenylphosphorane (3), which affords a positive alkyl or acyl group, has a marked effect on the use of phosphoranes in organic synthesis. It is interesting to compare the behavior of the phosphoranes containing trigonal-bipyramidal phosphine with that of phosphonium salts.[24]

This work describes the synthetic utilization of bis(2,2,2-trifluoroethoxy)triphenylphosphorane which is a useful reagent with unusual properties for synthetic work as shown in Scheme I.

Results and Discussion

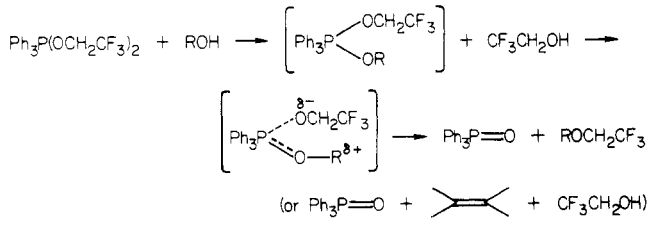
The preparation of the bis(2,2,2-trifluoroethoxy)triorganophosphoranes we used is simpler than that reported by other workers.[9-11,15-20] Thus, triphenylphosphine, tributylphosphine, or tris(dimethylamino)phosphine was brominated in methylene dichloride at 0 °C, and the resulting phosphine dibromide was allowed to react with an ethereal solution of sodium 2,2,2-trifluoroethoxide to produce the corresponding bis(2,2,2-trifluoroethoxy)triorganophosphoranes (Scheme II).

Table I. Preparation and NMR Data of $R_3P(OCH_2CF_3)_2$

R	yield,[a] %	NMR chemical shifts, ppm: ^{31}P[c]	^{19}F[b] ($J_{CH_3-CH_2}$)	^{1}H (J_{CH_2-P})
Ph	95	70.3	72.5 (9.0)	2.87 (4.2)
Bu	95	70.7	75.3 (8.6)	3.90 (4.3)
NMe_2	94	69.2	73.4 (7.8)	2.79 (4.0)

[a] Yields were determined from the signal intensities of ^{19}F NMR by using $PhCF_3$ as an internal standard. [b] From internal CCl_3F in $CDCl_3$. [c] From external H_3PO_4 (85%) in CH_2Cl_2.

Scheme III[a]



[a] R = alkyl or acyl.

The reaction proceeded smoothly at 0 °C, but the resulting phosphoranes were so unstable that they could not be isolated, though various attempts were made. These compounds were very sensitive to moisture and were readily hydrolyzed to phosphine oxide and 2,2,2-trifluoroethanol quantitatively. They are, however, stable enough in solution and can be stored for several weeks at room temperature.

The evidence of phosphorane structure was definitely established by various NMR spectra (see Table I). As a typical example, the ^{31}P NMR spectrum[25] for bis(2,2,2-trifluoroethoxy)triphenylphosphorane, $Ph_3P(OCH_2CF_3)_2$, has only one signal at 70.3 ppm split by an OCH_2 group. According to the literature, this chemical shift should be ascribed to the trigonal-bipyramidal geometry of phosphorane. Another proof was observed in the ^{1}H NMR spectrum. The signal at δ 2.87 due to the protons of the OCH_2CF_3 group is an overlapping quartet of doublets ($J_{CH_2-CF_3}$ = 9.0 Hz, J_{CH_2-P} = 4.2 Hz), and a high-field shift relative to that of CF_3CH_2OH was observed. This must be caused by the shielding effect of the ring current of the two equatorial phenyl groups.[18] These results suggest that the phosphoranes exhibit a trigonal-bipyramidal geometry, with OCH_2CF_3 groups occupying the apical positions.[1,2]

2,2,2-Trifluoroethyl Ethers and Esters from Alcohols and Carboxylic Acids. It was reported that some phosphoranes act as good dehydrating agents to lead to heterocycles.[9-14] For our bis(2,2,2-trifluoroethoxy)triphenylphosphorane, we found that it is very susceptible to the attack of O-nucleophiles such as alcohols and carboxylic acids, affording 2,2,2-trifluoroethyl ethers and esters in good yields, respectively. With cyclic alcohols such as cyclohexanol or borneol, however, dehydration giving olefins perferentially proceeded.

Although phosphoranes such as $(n\text{-Bu})_3P(OCH_2CF_3)_2$ and $(Me_2N)_3P(OCH_2CF_3)_2$ are effective in some reactions, the phosphorane $Ph_3P(OCH_2CF_3)_2$ is more efficient than other phosphoranes, $(n\text{-Bu})_3P(OCH_2CF_3)_2$ and $(Me_2N)_3P(OCH_2CF_3)_2$, with respect to stability, reactivity, and the overall yields.

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Table II. Preparation of CF_3CH_2 Ethers and Esters

ROH or RCO_2H	product	yield, %	bp, °C (mmHg) [mp, °C]	^{19}F NMR, ppm ($J_{CF_3-CH_2}$, Hz)
n-$C_5H_{11}OH$	n-$C_5H_{11}OCH_2CF_3$ [a]	68	135.5-136.5	72.8 (8.1)
n-$C_8H_{17}OH$	n-$C_8H_{17}OCH_2CF_3$ [d]	77	164.5-165.5	73.5 (9.0)
$PhCH_2OH$	$PhCH_2OCH_2CF_3$ [d]	84	74-76 (11)	72.4 (9.0)
$PhCH_2CH_2OH$	$PhCH_2CH_2OCH_2CF_3$ [d]	70	193-194	72.5 (8.1)
	CH_2=CHPh	11	144.5-145.5	
$C_6H_{13}CH(Me)OH$	$C_6H_{13}CH(Me)OCH_2CF_3$ [d]	72	178-179	72.8 (8.5)
$PhCH(Me)OH$	$PhCH(Me)OCH_2CF_3$ [d]	59	171-172	74.8 (9.6)
cyclohexanol	cyclohexene	71	82-83	
borneol	camphene	61	[51-52]	
$PhCO_2H$	$PhCO_2CH_2CF_3$ [b]	82	77 (13)	72.8 (8.4)
n-$C_3H_7CO_2H$	n-$C_3H_7CO_2CH_2CF_3$ [c]	85	111-112	73.8 (8.9)
n-$C_4H_9CO_2H$	n-$C_4H_9CO_2CH_2CF_3$ [c]	80	138.5-140	73.9 (8.7)

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Table III. Preparation and Physical Properties of $RCH(OCH_2CF_3)_2$

R	product	yield, %	bp, °C (mmHg) [lit.][a]	^{19}F NMR, ppm ($J_{CF_3-CH_2}$, Hz)
i-Pr	i-$PrCH(OCH_2CF_3)_2$	87	87-89 (65) [85-87 (63)]	72.7 (8.6)
n-C_5H_{11}	n-$C_5H_{11}CH(OCH_2CF_3)_2$	72	65-67 (80) [65-67 (81)]	72.5 (8.5)
n-C_6H_{13}	n-$C_6H_{13}CH(OCH_2CF_3)_2$	89	82-83 (60) [82-85 (57)]	73.7 (8.5)

[a] Kitazume, T.; Ishikawa, N. *Yuki Gosei Kagaku Kyokaishi* 1979, *37*, 81.

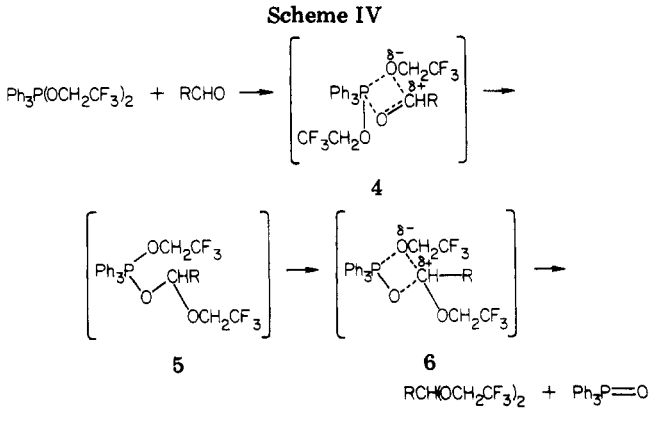
The reaction mechanism is speculated as shown in Scheme III. Thus, ligand exchange at one of the trifluoroethoxyl groups occurs as the first step. Pseudorotation around the phosphorus atom would take place, and the following nucleophilic attack of trifluoroethoxide ion on the positive carbon atom of the alkyl or acyl group leads to the trifluoroethyl ether or ester and phosphine oxide (Table II).

2,2,2-Trifluoroethyl Acetals from Aldehydes. On consideration of the affinity of bis(2,2,2-trifluoroethoxy)-triphenylphosphorane for an oxygen atom, aliphatic aldehydes were expected to react with the phosphorane. In this case, it was impossible to replace the trifluoroethoxy ligand with an aldehyde group carrying no protonic hydrogen. Nevertheless, the oxygen atom of the aldehyde was able to coordinate to the phosphorus atom probably through the formation of **5** by a four-centered process, and bis(2,2,2-trifluoroethyl) acetal **7** was obtained together with phosphine oxide (Scheme IV, Table III).

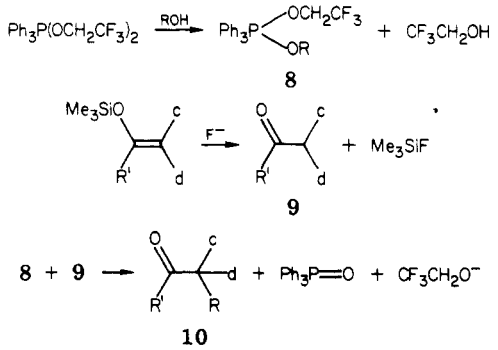
Carbon–Carbon Bond Formation. The next step is the carbon–carbon chain extension by the direct cross coupling reaction of alcohols or carboxylic acids with C-nucleophiles.[26-31]

Since we postulated the presence of (2,2,2-trifluoroethoxy)alkoxy- or -(acyloxy)triphenylphosphorane with a positive alkyl group in our reaction, we have attempted to design the carbon–carbon bond formation by one-pot cross coupling of alcohols or carboxylic acids with carbanions. The reaction between **8** and Grignard reagents was carried out first. However, 2,2,2-trifluoroethyl alcohol released in this system reacts readily with Grignard reagents, and the yields of the expected products were not so good. For this purpose, an enolate anion generated from the silyl enol ether and fluoride ion was most efficient, and

Scheme IV



Scheme V



it readily attacked a positive carbon atom in alkoxy- or (acyloxy)phosphorane to form a carbon–carbon bond (Scheme V).

The experimental results that no cross coupling reaction occurred without an alcohol and that trifluoro ethers were produced from alcohols and the phosphorane in the presence of potassium fluoride supported the mechanism that the ligand exchange of one of the 2,2,2-trifluoroethoxyl groups for an alkoxy group took place first, and the resulting **8** would include a positive alkyl group. A carbanion

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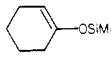
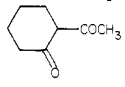
Table IV. Formation of Carbon-Carbon Bonds

ROH or RCO_2H	reagent	product[a]	bp, °C (mmHg) [mp, °C]	yield, %
$PhCH_2OH$	MeMgBr	$PhCH_2CH_3$	135-136, 26 (10)[b]	44
PhCH(Me)OH	MeMgBr	$PhCH(CH_3)_2$	151-152, 38 (10)[b]	52
trans-CH_3CH=$CHCH_2OH$	PhMgBr	*trans*-CH_3CH=$CHCH_2Ph$	108-110 (15)	41
trans-CH_3CH=$CHCH_2OH$	$PhC(OSiMe_3)$=CH_2	*trans*-CH_3CH=$CHCH_2CH_2COPh$	100-103 (6)	72
cis-CH_3CH=$CHCH_2OH$	$PhC(OSiMe_3)$=CH_2	*cis*-CH_3CH=$CHCH_2CH_2COPh$	101-102 (6)	66
trans-PhCH=$CHCH_2OH$	PhMgBr	*trans*-PhCH=$CHCH_2Ph$	123-125 (1)	48
trans-PhCH=$CHCH_2OH$	$PhC(OSiMe_3)$=CH_2	*trans*-PhCH=$CHCH_2CH_2COPh$	131-133 (1)	72
CH_2=CHCH(Me)OH	PhMgBr	CH_2=CHCH(Me)Ph	133-135	51
trans-CH_3CH=$CHCO_2H$	PhMgBr	*trans*-CH_3CH=CHCOPh	90-92 (8)	54
$PhCO_2H$	MeMgBr	PhCOMe	80 (11), 79 (10)[b]	52
$PhCO_2H$	$PhC(OSiMe_3)$=CH_2	$PhCOCH_2COPh$	[80-81], [81][b]	82
CH_3CO_2H			109-110 (15)	87

[a] The structures were also confirmed by spectral data. [b] Value given in the literature: Ritchey, W. M. "Spectral Data and Physical Constants for Organic Compounds", CRC Press: Cleveland, OH; 1975. [c] New compound. The microanalysis was in satisfactory agreement with the calculated values.

Table V. Preparation of Unsymmetrical Sulfides

ROH	R'SH	product[a]	bp, °C (mmHg) [mp, °C]	yield, %
EtOH	PhSH	EtSPh	47-48 (1.5), 206[b]	95
n-PrOH	$PhCH_2SH$	*n*-$PrSCH_2Ph$	83-84 (6), 112 (14)[b]	63
$PhCH_2OH$	PhSH	$PhCH_2SPh$	[42-44], [44][c]	95
$PhCH_2CH_2OH$	PhSH	$PhCH_2CH_2SPh$	123-125 (1), 185 (13)[d]	95
$PhCH_2OH$	BuSH	$PhCH_2SBu$	102-104 (2), 96 (1)[e]	57
$PhCH_2CH_2OH$	$PhCH_2SH$	$PhCH_2CH_2SCH_2Ph$	156-157 (1), 133 (0.5)[e]	76
cis-CH_3CH=$CHCH_2OH$	PhSH	*cis*-CH_3CH=$CHCH_2SPh$	105-107 (2)	95
trans-CH_3CH=$CHCH_2OH$	PhSH	*trans*-CH_3CH=$CHCH_2SPh$	106-107 (12), 70 (1.3)[f]	95
trans-CH_3CH=$CHCH_2OH$	$PhCH_2SH$	*trans*-CH_3CH=$CHCH_2SCH_2Ph$	99-100 (5), 86 (0.5)[g]	71
trans-CH_3CH=$CHCH_2OH$	BuSH	*trans*-CH_3CH=$CHCH_2SBu$	70-71 (8), 187[b]	40
CH_2=CHCH(Me)OH	PhSH	CH_2=CHCH(Me)SPh	97-99 (11)	89
CH_2=CHCH(Me)OH	EtSH	CH_2=CHCH(Me)SEt	87-89 (35)	78
trans-PhCH=$CHCH_2OH$	PhSH	*trans*-PhCH=$CHCH_2SPh$	131-133 (1)	87

[a] The structures were also confirmed by spectral data. [b] Anderson, H. H. *J. Chem. Eng. Data* 1964, *9*, 272. [c] Lapkin, I. I., et al. *Zh. Obshch. Khim.* 1962, *32*, 745. [d] Rabilloud, G. *Bull. Soc. Chim. Fr.* 1967, 384. [e] Yamazaki, K. *Nippon Kagaku Kaishi* 1959, *80*, 1361. [f] Cope, C. *J. Am. Chem. Soc.* 1950, *72*, 59. [g] Bryan, J. J.; et al. *Can. J. Chem.* 1971, *49*, 325.

from the silyl enol ether–potassium fluoride system[31-35] will attack the positive carbon atom of the alkyl group to afford the product.

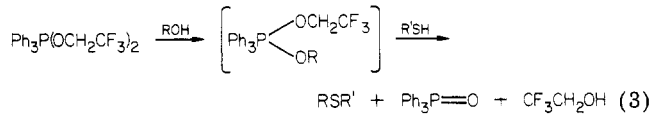
This reaction appears to be particularly efficient for regioselective carbon–carbon bond cross coupling together with retention of configuration. No allylic rearrangement was observed in the reaction with allylic alcohols (Table IV).

$$\textit{cis}\text{- or }\textit{trans}\text{-}CH_3CH{=}CHCH_2OH \xrightarrow{1/PhCOCH_2^-} \textit{cis}\text{- or }\textit{trans}\text{-}CH_3CH{=}CHCH_2CH_2COPh \quad (1)$$

$$CH_2{=}CHCH(Me)OH \xrightarrow{1/Ph^-} CH_2{=}CHCH(Me)Ph \quad (2)$$

Synthesis of Unsymmetrical Sulfides. An importance of the chemistry of sulfides in organic synthesis has been recognized in recent years.[36] However, very few convenient methods for the preparation of unsymmetrical sulfides have been known so far. Regarding the condensation of alcohols and thiols, those of alkoxides and thiols with a phosphonium salt system[37] and of alcohols and thiols with an onium salt system[38] were reported.

In our studies on the phosphorane, one-pot, regioselective synthesis of unsymmetrical alkyl aryl and aryl aryl sulfides utilizing the high dehydrating potentiality of bis(2,2,2-trifluoroethoxy)triphenylphosphorane occurred as indicated in eq 3.



$$RSR' + Ph_3P{=}O + CF_3CH_2OH \quad (3)$$

Alkanethiols such as butane- or propanethiol sometimes reacted with bis(2,2,2-trifluoroethoxy)triphenylphosphorane to give the corresponding disulfides in a reaction sequence involving an oxidation–reduction process. Further, the fact that *cis*- and *trans*-crotonyl and *trans*-cinnamyl alcohols gave the corresponding *cis*- and *trans*-crotonyl and *trans*-cinnamyl sulfides with the retention of configuration suggests that the reaction does not proceed through a S_N1-like mechanism. It is also noted that no allylic rearrangements were observed in these procedures. (Table V).

Preparation of Secondary Amines and N-Substituted Amides. The next synthetic application of the phosphorane is the preparation of secondary amines and N-substituted amides, which is the first example based on the trigonal-bipyramidal phosphorus compound, with ex-

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(36) See, for example: Tagaki, W. "Sulfides in Organic Chemistry of Sulfur"; Oae, S., Ed.; Plenum: New York and London, 1977; pp 231–295 and references cited therein.
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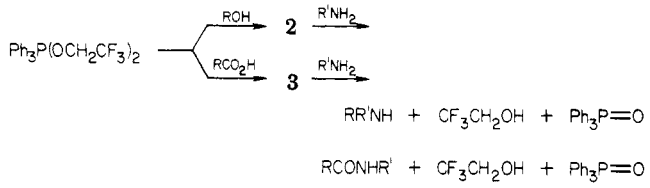
Table VI. Preparation of Secondary Amines and Amides

ROH or RCO_2H	RNH_2	product[a]	bp, °C (mmHg)	yield, %
n-$C_8H_{17}OH$	n-$BuNH_2$	n-$C_8H_{17}NHBu$	159-160 (25)	73
$PhCH(Me)OH$	n-$PrNH_2$	$PhCH(Me)NHPr$	176-177 (15)	73
$PhCH_2OH$	$PhNH_2$	$PhCH_2NHPh$	130-132 (2), 171.5 (10)[b]	71
trans-$CH_2CH=CHCH_2OH$	$PhNH_2$	*trans*-$CH_3CH=CHCH_2NHPh$	136-138 (21)	64
$CH_2=CHCH(Me)OH$	$PhNH_2$	$CH_2=CHCH(Me)NHPh$	125-127 (19)	66
CH_3CO_2H	n-$BuNH_2$	$CH_3CONHBu$	135-137 (5), 229[b]	80
CH_3CO_2H	$PhNH_2$	$CH_3CONHPh$	114-116 (1), 304[b]	81
$PhCO_2H$	n-$PrNH_2$	$PhCONHPr$	120-121 (21)	85
$PhCO_2H$	$PhNH_2$	$PhCONHPh$	159-160 (51), 117-119 (10)[b]	79
trans-$CH_3CH=CHCO_2H$	n-$BuNH_2$	*trans*-$CH_3CH=CHCONHBu$	127-129 (2)	75

[a] The structures were confirmed by spectral data. [b] Value is that in the literature: "Handbook of Chemistry and Physics", 55th ed.; CRC Press: Cleveland, OH; 1974.

Scheme VI



ception of phosphonium salts,[25,39] and phosphoryl compounds.[40-42]

In these reactions, secondary amines and amides were formed by the attack of primary amines on the positive carbon atom of the (trifluoroethoxy)alkoxy- or (trifluoroethoxy)(acyloxy)triphenylphosphorane at −60 °C without pseudorotation. Radwell and co-workers have revealed that 2,2,2-trifluoroethyl esters are activated esters which give amides by the reaction with amines.[43] However, our experimental results revealed that the reaction including pseudorotation giving 2,2,2-trifluoroethyl esters was retarded at −60 °C, and this supported the direct interaction between **2** or **3** (Scheme VI) with amines and not that between trifluoroethyl esters or trifluoroethyl acylates and amines (Table VI).

With respect to these results, we believe that the presently reported procedures provide an available and selective synthetic method, including the preparation of sulfides, amines, and amides and the carbon–carbon bond formation leading to ketones by one-pot cross coupling condensation, and that the phosphorane $Ph_3P(OCH_2CF_3)_2$ is more advantageous than other phosphorus reagents[30,33-38] under several different types of reaction conditions.

Experimental Section

General Procedures. All reactions were carried out under a nitrogen atmosphere. All commercial reagents were used without purification. Solvents, e.g., Et_2O and THF, were purified by distillation from $LiAlH_4$. CH_2Cl_2 was washed with water and then purified by distillation from $CaCl_2$. Infrared spectra were obtained by using a JASCO A-102 spectrometer and KBr pellets. The ^1H (internal Me_4Si) and ^{19}F (external CF_3CO_2H) NMR spectra were recorded by using a Varian EM-390 spectrometer. Mass spectra were obtained by using a Hitachi M-52 spectrometer at 20 eV. Yields were those of the products actually isolated.

Bis(2,2,2-trifluoroethoxy)triphenylphosphorane. A mixture of sodium 2,2,2-trifluoroethoxide (20 mmol) prepared from sodium hydrate (20 mmol) and 2,2,2-trifluoroethanol (20 mmol) in freshly dried diethyl ether (20 mL) in situ and triphenylphosphine (10 mmol) in methylene chloride (20 mL) was stirred at 0 °C for 5 min. Into the mixture was added bromine (10 mmol) slowly at 0 °C. After the mixture was stirred for 1 h at that temperature, the precipitates were removed by filtration, and the solvent was evaporated under dynamic vacuum, yielding a crude solid. As bis(2,2,2-trifluoroethoxy)triphenylphosphorane is extremely hygroscopic, it could not be isolated in pure form, while its solution in methylene chloride was stable enough. The yield determined by ^{19}F NMR with benzylidyne trifluoride as an internal standard was 95%. In the mass spectrum, the molecular ion (M^+, m/e 460) appeared.

Bis(2,2,2-trifluoroethoxy)tri-*n*-butylphosphorane. Tri-*n*-butylphosphine (10 mmol) was used as in the reaction above and worked up similarly. Bis(2,2,2-trifluoroethoxy)tri-*n*-butylphosphorane decomposes to give bis(2,2,2-trifluoroethyl) ether in 20% yield, after 24 h at room temperature. In the mass spectrum, the molecular ion (M^+, m/e 400) appeared.

Bis(2,2,2-trifluoroethoxy)tris(dimethylamino)phosphorane. Tris(dimethylamino)phosphine (10 mmol) was reacted in the above reaction and worked up similarly. The molecular ion (M^+, m/e 361) and other appropriate fragment peaks appeared in the mass spectrum.

2,2,2-Trifluoroethyl Benzyl Ether. Into a solution of bis(2,2,2-trifluoroethoxy)triphenylphosphorane, obtained from triphenylphosphine (10 mmol), sodium 2,2,2-trifluoroethoxide (20 mmol), and bromine (10 mmol) in methylene chloride (20 mL)–diethyl ether (20 mL), was added benzyl alcohol (10 mmol) at room temperature. After the mixture was stirred 1 h, the solvent was removed. The residual oily material was distilled under vacuum to yield 2,2,2-trifluoroethyl benzyl ether in an 84% yield.

A lower yield of 2,2,2-trifluoroethyl benzyl ether (30%) was obtained when bis(2,2,2-trifluoroethoxy)tri-*n*-butylphosphorane was used in the above reaction. Bis(2,2,2-trifluoroethoxy)tris(dimethylamino)phosphorane also gave 2,2,2-trifluoroethyl benzyl ether in a 70% yield.

2,2,2-Trifluoroethyl Benzoate. Benzoic acid (10 mmol) was used as in the above reaction, and the reaction mixture was worked up similarly. Distillation in vacuo gave 2,2,2-trifluoroethyl benzoate in an 82% yield.

1,1-Bis(2,2,2-trifluoroethoxy)hexane. Hexanal (10 mmol) and bis(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol) in a methylene chloride (20 mL)–diethyl ether (20 mL) mixture were reacted for 1 h at room temperature, and the reaction mixture was worked up in a manner similar to that mentioned above. Distillation in vacuo gave 1,1-bis(2,2,2-trifluoroethoxy)hexane in an 87% yield.

Carbon–Carbon Bond Formation. A mixture of bis(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol), freshly dried tetrahydrofuran (20 mL), and *trans*-crotonyl alcohol (10 mmol) was stirred for 30 min at −60 °C. Into the mixture were added calcine-dried potassium fluoride (15 mmol) and styren-1-yl trimethylsilyl ether (10 mmol) at that temperature. The reaction mixture was allowed to warm to room temperature for 3 h, the whole mixture was poured into water, and the resulting oily material was extracted with diethyl ether (100 mL). On removal of the solvent, the residue was subjected to distillation under vacuum, giving the product in a 72% yield.

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(42) Shioiri, T. *Yuki Gosei Kagaku Kyokaishi* **1979**, *37*, 856 and references cited therein.
(43) Radwell, J.; Connolly, W. *J. Chem. Eng. Data* **1961**, *6*, 282.

Acetophenone. A mixture of bis(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol), benzoic acid (10 mmol), and freshly dried diethyl ether (10 mL) was stirred for 10 min at −60 °C. Into the reaction mixture was added methylmagnesium bromide (31 mmol) in diethyl ether (20 mL), and then the reaction mixture was stirred at −60 °C for 2 h. The whole mixture was poured into water, and then the oily material was extracted with diethyl ether (100 mL). After removal of the solvent, distillation gave acetophenone in a 52% yield.

***trans*-Crotonyl Phenyl Sulfide.** *trans*-Crotonyl alcohol (10 mmol) and benzenethiol (10 mmol) were added to a solution of bis(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol) in methylene chloride (20 mL)–diethyl ethher (20 mL). After being stirred for 20 h, the reaction mixture was poured into water, and the oily layer was extracted with diethyl ether (150 mL). The ethereal extract was washed with 5% aqueous sodium hydroxide solution and dried over magnesium sulfate. The solvent was removed, and the formed precipitates ($Ph_3P{=}O$) were removed by filtration. The residual oily material was distilled under vaccum, yielding *trans*-crotonyl phenyl sulfide in an 82% yield.

***N*-Benzylaniline.** A mixture of aniline (10 mmol) and bis-(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol) in methylene chloride (20 mL)–diethyl ether (20 mL), which was prepared from triphenylphosphine dibromide (13 mmol) and sodium 2,2,2-trifluoroethoxide (26 mmol) in situ, was cooled at −60 °C. Into the solution was slowly added benzyl alcohol (10 mmol) in freshly dried diethyl ether (10 mL). After being stirred for 1.5 h at that temperature, the solution was allowed to warm to room temperature. The reaction mixture was poured into water, and the ethereal layer was separated and dried over magnesium sulfate. The solvent was then removed, and the residue was distilled in vacuo, giving *N*-benzylaniline in a 71% yield.

***N*-Phenylacetamide.** Acetic acid (10 mmol) was added to a solution of bis(2,2,2-trifluoroethoxy)triphenylphosphorane (12 mmol) at −60 °C, and then aniline (10 mmol) in freshly dried diethyl ether (10 mL) was added to the mixture. After being stirred for 1 h at that temperature, the reaction mixture was worked up as above, giving *N*-phenylacetamide in an 81% yield.

Registry No. $Ph_3P(OCH_2CF_3)_2$, 67696-25-7; $Bu_3P(OCH_2CF_3)_2$, 75399-87-0; $(NMe_2)_3P(OCH_2CF_3)_2$, 75399-88-1; *i*-PrCHO, 78-84-2; *n*-$C_5H_{11}CHO$, 66-25-1; *n*-$C_6H_{13}CHO$, 111-71-7; *i*-$PrCH(OCH_2CF_3)_2$, 75399-89-2; *n*-$C_5H_{11}CH(OCH_2CF_3)_2$, 75399-90-5; *n*-$C_6H_{13}CH(OCH_2CF_3)_2$, 75399-91-6; *n*-$C_5H_{11}OH$, 75-41-0; *n*-$C_8H_{17}OH$, 29063-28-3; $PhCH_2OH$, 100-51-6; $PhCH_2CH_2OH$, 60-12-8; $C_6H_{13}CH(Me)OH$, 25339-16-6; PhCH(Me)OH, 98-85-1; cyclohexanol, 108-93-0; borneol, 507-70-0; $PhCO_2H$, 65-85-0; *n*-$C_3H_7CO_2H$, 107-92-6; *n*-$C_4H_9CO_2H$, 109-52-4; *n*-$C_5H_{11}OCH_2CF_3$, 41029-58-7; *n*-$C_8H_{17}OCH_2CF_3$, 67696-27-9; $PhCH_2OCH_2CF_3$, 67696-28-0; $PhCH_2CH_2OCH_2CF_3$, 67696-29-1; $CH_2{=}CHPh$, 100-42-5; $C_6H_{13}CH(Me)OCH_2CF_3$, 67696-31-5; $PhCH(Me)OCH_2CF_3$, 67696-30-4; cyclohexene, 110-83-8; camphene, 79-92-5; $PhCO_2CH_2CF_3$, 1579-72-2; *n*-$C_3H_7CO_2CH_2CF_3$, 371-27-7; *n*-$C_4H_9CO_2CH_2CF_3$, 1651-34-9; $PhCH_2OH$, 100-51-6; *trans*-$CH_3CH{=}CHCH_2OH$, 504-61-0; *cis*-$CH_3CH{=}CHCH_2OH$, 4088-60-2; *trans*-$PhCH{=}CHCH_2OH$, 4407-36-7; $CH_2{=}CHCH(Me)OH$, 598-32-3; *trans*-$CH_3CH{=}CHCO_2H$, 107-93-7; CH_3CO_2H, 64-19-7; MeBr, 74-83-9; PhBr, 108-86-1; $PhC(OSiMe_3){=}CH_2$, 13735-81-4; 1-trimethylsiloxycyclohex-1-ene, 6651-36-1; $PhCH_2CH_3$, 100-41-4; $PhCH(CH_3)_2$, 98-82-8; *trans*-$CH_3CH{=}CHCH_2Ph$, 935-00-2; *trans*-$CH_3CH{=}CHCH_2CH_2COPh$, 57542-05-9; *cis*-$CH_3CH{=}CHCH_2CH_2COPh$, 38376-73-7; *trans*-$PhCH{=}CHCH_2Ph$, 3412-44-0; *trans*-$PhCH{=}CHCH_2CH_2COPh$, 28069-36-5; $CH_2{=}CHCH(Me)Ph$, 934-10-1; *trans*-$CH_3CH{=}CHCOPh$, 35845-66-0; PhCOMe, 122-78-1; $PhCOCH_2COPh$, 120-46-7; 2-acetylcyclohexanone, 847-23-7; EtOH, 64-17-5; *n*-PrOH, 71-23-8; PhSH, 108-98-5; $PhCH_2SH$, 100-53-8; BuSH, 109-79-5; EtSPh, 622-38-8; *n*-$PrSCH_2Ph$, 22336-59-0; $PhCH_2SPh$, 831-91-4; $PhCH_2CH_2SPh$, 13865-49-1; $PhCH_2SBu$, 5184-47-4; $PhCH_2CH_2SCH_2Ph$, 34372-24-2; *cis*-$CH_3CH{=}CHCH_2SPh$, 36195-55-8; *trans*-$CH_3CH{=}CHCH_2SPh$, 36195-56-9; *trans*-$CH_3CH{=}CHCH_2SCH_2Ph$, 71638-76-1; *trans*-$CH_3CH{=}CHCH_2SBu$, 3001-22-7; $CH_2{=}CHCH(Me)SPh$, 701-75-7; $CH_2{=}CHCH(Me)SEt$, 71638-77-2; *trans*-$PhCH{=}CHCH_2SPh$, 5848-60-2; *n*-$BuNH_2$, 109-73-9; *n*-$PrNH_2$, 107-10-8; $PhNH_2$, 62-53-3; *n*-$C_8H_{17}NHBu$, 4088-42-0; PhCH(Me)NHPr, 66896-60-4; $PhCH_2NHPh$, 103-32-2; *trans*-$CH_3CH{=}CHCH_2NHPh$, 35755-80-7; $CH_2{=}CHCH(Me)NHPh$, 15645-60-0; $CH_3CONHBu$, 1119-49-9; $CH_3CONHPh$, 103-84-4; PhCONHPr, 10546-70-0; PhCONHPh, 93-98-1; *trans*-$CH_3CH{=}CHCONHBu$, 75399-92-7; sodium 2,2,2-trifluoroethoxide, 420-87-1; 2,2,2-trifluoroethanol, 75-89-8; triphenylphosphine, 603-35-0; tri-*n*-butylphosphine, 998-40-3; tris(dimethylamino)phosphine, 1608-26-0.

Synthesis of Substituted Quinones. 2,5-Disubstituted 1,4-Benzoquinones

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Synthetic methodology is presented which allows the facile synthesis of 2,5-disubstituted 1,4-benzoquinones. This involves the initial 1,2-addition of an alkynyllithium reagent to one of the carbonyl groups of 2,5-diethoxy- or 2,5-dichloro-3,6-dimethoxy-1,4-benzoquinone. This is followed by an analogous addition of an alkyl-, aryl-, or alkynyllithium to the remaining carbonyl to give a cyclohexa-2,5-diene-1,4-diol derivative. Acid hydrolysis of these adducts results in the 2,5-dialkylated 1,4-benzoquinones. This methodology was employed to prepare 7-chloro-6-methyl-1,2,5,8-tetrahydro-3*H*-pyrrolo[1,2-*a*]indole-5,8-dione (14), a compound having the basic ring system of the mitomycin antineoplastic antibiotics.

In a preliminary paper, we described new methodology which allowed the facile synthesis of 2,5-disubstituted quinones where one of the substituents is an alkynyl group and the other can be an alkynyl, alkenyl, alkyl, or aryl substituent.[1] In the present paper, we give the full details of this methodology and illustrate its utility in the synthesis of 7-chloro-6-methyl-1,2,5,8-tetrahydro-3*H*-pyrrolo[1,2-*a*]indole-5,8-dione (14), a compound having the basic ring system of the mitomycin antineoplastic antibiotics.

The rationale for developing a synthetic route to 2,5-disubstituted 1,4-benzoquinones stems from the fact that a wide variety of naturally occurring quinones exist[2] in which the nucleus is functionalized in this manner. However, no general methodology currently allows the facile construction of such structural features. Described here is a method which provides a simple solution to this problem. Specifically, we have observed that organolithium reagents undergo 1,2-addition to the carbonyl groups of 2,5-diethoxy-1,4-benzoquinone (1). Acid hy-

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