Brief Communications

Quaternary ammonium salts as alkylating agents in the synthesis of tertiary phosphine oxides

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A procedure was developed for the synthesis of tertiary phosphine oxides by alkylation of secondary phosphine oxides with quaternary ammonium salts.

Key words: alkylation, diethylphosphine oxide, diphenylphosphine oxide, ammonium salts, trimethyl(phenyl)ammonium iodide, trimethyl(3-methylbut-2-enyl)ammonium chloride, dimethylbis(3-chlorobut-2-enyl)ammonium chloride, triethyl(prop-2-ynyl)ammonium bromide.

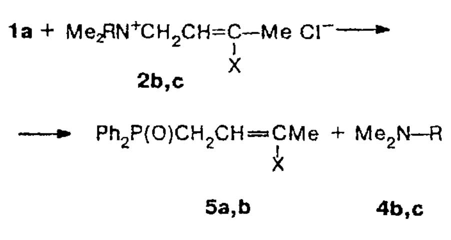
Alkylation of hydrophosphoryl compounds with alkyl halides is widely covered in the literature. In some cases, tertiary amines were used for generating P-anions.[1,2] Many works have been devoted to the conducting of the Michaelis—Becker reaction under conditions of phase transfer catalysis and in a superbasic medium in the case of phosphine oxides.[3—6]

In this work, we report a new convenient procedure for the synthesis of tertiary phosphine oxides. It is known that quaternary ammonium salts are widely used for alkylation of CH-, OH-, and NH-acids. We found that these salts can also be used for alkylation of PH-acids, in particular, of secondary phosphine oxides. Thus, heating of diphenylphosphine oxide (**1a**) with trimethyl(phenyl)ammonium iodide (**2a**) at 120 °C afforded methyldiphenylphosphine oxide (**3a**) in 83.3% yield. Correspondingly, when an alkali was added, dimethylaniline (**4a**) was isolated from the reaction mixture in 74.4% yield. An analogous result was obtained in the case of diethylphosphine oxide (**1b**). The yields of diethylmethylphosphine oxide (**3a**) and dimethylaniline were 66.6 and 74.4%, respectively.

$$\underset{\mathbf{1a,b}}{R_2P(O)H} + \underset{\mathbf{2a}}{Me_3PhN^+I^-} \rightarrow \underset{\mathbf{3a,b}}{R_2P(O)Me} + \underset{\mathbf{4a}}{Me_2NPh}$$

R = Ph (**a**), Et (**b**)

The reactions proceeded smoothly also with trimethyl(3-methylbut-2-enyl)- (**2b**) and dimethylbis(3-chlorobut-2-enyl)ammonium chlorides (**2c**). Their reactions with **1a** afforded diphenyl(3-methylbut-2-enyl)- (**5a**) and diphenyl(3-chlorobut-2-enyl)phosphine oxides (**5b**) in 60 and 59% yields, respectively. Simultaneously, the corresponding tertiary amines were isolated from the reaction products:



$$\mathbf{1a} + \underset{\mathbf{2b,c}}{Me_2RN^+CH_2CH{=}\underset{X}{C}{-}Me\ Cl^-} \longrightarrow \underset{\mathbf{5a,b}}{Ph_2P(O)CH_2CH{=}\underset{X}{C}Me} + \underset{\mathbf{4b,c}}{Me_2N{-}R}$$

2b, **4b**, **5a:** R = X = Me
2c, **4c**, **5b:** R = $CH_2CH{=}CClMe$, X = Cl

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Table 1. Yields and physicochemical constants of the compounds obtained

Compound	Yield (%)	M.p./°C (b.p.; *p*/Torr)	IR, ν/cm^{-1}	^{1}H NMR ($CDCl_3$), δ, *J*/Hz	Reference
3a	83.3	111—112*	—	—	3
3b	66.6	(84; 3)*	—	—	8
4a	74.4	(77; 13) 163—164**	—	—	—
4b	56.0	216**	—	—	7
4c	86.0	(135—137; 680) 119—120**	—	—	7
5a	60.0	155—156	1655 (C=C), 1595 (C=C, Ph), 1190 (P=O)	1.5—1.7 (m, 6 H, $=CMe_2$); 3.05 (dd, 2 H, PCH_2, $J = 14$); 5.85 (br.q, =CH, $^3J = 7.0$); 7.2—7.85 (m, 10 H, Ph);	4
5b	59.1	102—103	1660 (C=C), 1590 (C=C, Ph), 1190 (P=O), 810 (C—Cl)	1.84—2.03 (br.d, 3 H, =CMe, $^5J = 4.0$); 3.23 (dd, 2 H, CH_2, $^2J_{P,H} = 14.0$, $^3J_{H,H} = 7.3$); 5.58 (qd, 1 H, =CH, $^3J_{P,H} = {}^3J_{H,H} = 7.3$); 7.74—7.9 (m, 10 H, Ph)	4
6 + 7	50.0	—	2130 (α-C≡C), 1970 (C=C=C), 1590 (C=C, Ph)	2.00 (d, Me, $J = 4.0$); 5.05 (m, $=CH_2$, $J_{P,H} = 10.0$); 5.62 (m, =CH, $J_{H,H} = 6.7$, $J_{P,H} = 2.7$); 7.2—7.9 (m, 10 H, Ph)	—
7	80.0	96—98	2190 (C≡C), 1585 (C=C, Ph)	2.00 (d, Me, $J = 4.0$); 7.2—7.9 (m, 10 H, Ph)	4

* MS, *m/z* [M$^+$]: **3a**, 216; **3b**, 120. ** M.p. of picrate.

The reaction of compound **1a** with triethyl(prop-2-ynyl)ammonium bromide (**2d**) afforded a mixture of alkylation products containing the allenic (**6**) and prop-1-ynyl (**7**) groups. Apparently, the latter were formed as a result of one- and two-stage prototropic isomerization of the initial reaction product, *viz.*, diphenyl(prop-2-ynyl)phosphine oxide. Also one cannot rule out that the reaction proceeded with the transfer of the reaction center to the terminal carbon atom. The resulting mixture of isomers was transformed into pure isomer **7** under the action of ethanolic EtONa.

$$\mathbf{1a} + \underset{\mathbf{2d}}{Et_3N^+CH_2C{\equiv}CH\ Br^-} \rightarrow [Ph_2P(O)CH_2C{\equiv}CH] \rightarrow$$

$$\rightarrow \underset{\mathbf{6}}{Ph_2P(O)CH{=}C{=}CH_2} + \underset{\mathbf{7}}{Ph_2P(O)C{\equiv}C{-}Me}$$

$$(\mathbf{6} + \mathbf{7}) \xrightarrow{EtONa} \mathbf{7}$$

Experimental

The NMR spectra were recorded on a Perkin—Elmer 1213 spectrometer operating at 60 MHz with Me_4Si as the internal standard. The IR spectra were obtained on a Specord-75 spectrophotometer (thin film). The mass spectra were measured on an MKh-1320 instrument with direct inlet of the specimen into the ionization zone.

Alkylation of diphenyl- (1a) and diethylphosphine oxides (1b) with quaternary ammonium salts (general procedure). A mixture of phosphine oxide (0.01 mol) and ammonium salt (0.01 mol) was heated at 120—125 °C for 10 h. Then benzene (chloroform in the case of alkylation with salt **2d**) and water were added to the reaction mixture. The organic layer was separated and dried with $MgSO_4$ and the solvent was distilled off *in vacuo*. Compound **3b** was purified by distillation. The remaining tertiary phosphine oxides were purified by recrystallization from EtOH. The aqueous layer was alkalized, amines were extracted with ether, and the extract was dried with $MgSO_4$. Tertiary amines were isolated by distillation. The resulting compounds were identified as picrates whose melting points did not show depression on mixing with the authentic samples. The amount of compound **4b** was determined by titration of the ethereal layer. Compounds **2b**, **2c**, and **4c**-HCl were prepared according to known procedures.[9,10]

The yields and physicochemical constants of the compounds obtained are given in Table 1.

Isomerization of compounds 6 and 7. Several drops of a solution of EtONa in EtOH was added to a mixture of compounds **6** and **7** (1 g) and the reaction mixture was kept overnight. Then EtOH was distilled off, and the residue was extracted with ether. Distillation of the ethereal extract gave diphenyl(prop-1-ynyl)phosphine oxide in a yield of 0.8 g.

References

1. A. J. Kirby and S. G. Warren, *The Organic Chemistry of Phosphorus (Reactions in Organic Chemistry)*, Elsevier, New York, 1967.
2. *Reaktsii i metody issledovaniya organicheskikh soedinenii* [*Reactions and Methods of Investigation of Organic Compounds*], Khimiya, Moscow, 1966, **15**, 41 (in Russian).
3. E. N. Tsvetkov, I. G. Malakhova, and M. I. Kabachnik, *Zh. Obshch. Khim.*, 1985, **55**, 11 [*J. Gen. Chem. USSR*, 1985, **55** (Engl. Transl.)].
4. R. A. Khachatryan, R. K. Lulukyan, S. A. Ovsepyan, and M. G. Indzhikyan, *Arm. Khim. Zh.* [*Arm. J. Chem.*], 1985, **38**, 377 (in Russian).
5. R. A. Khachatryan, S. V. Sayadyan, N. Yu. Grigoryan, and M. G. Indzhikyan, *Zh. Obshch. Khim.*, 1988, **58**, 2473 [*J. Gen. Chem. USSR*, 1988, **58** (Engl. Transl.)].
6. N. Yu. Grigoryan, R. A. Khachatryan, and M. G.

Indzhikyan, *Zh. Obshch. Khim.*, 1989, **59**, 814 [*J. Gen. Chem. USSR*, 1989, **59** (Engl. Transl.)].
7. A. T. Babayan and A. G. Terzyan, *Dokl. Akad. Nauk Arm. SSR* [*Dokl. Acad. Sci. Arm. SSR*], 1948, **9**, 105 (in Russian).
8. J. Meisenheimer, J. Gasper, and M. Horing, *Ann.*, 1926, 449, 213.
9. A. T. Babayan and G. T. Martirosyan, *Dokl. Akad. Nauk Arm. SSR* [*Dokl. Acad. Sci. Arm. SSR*], 1960, **30**, 271 (in Russian).
10. A. T. Babayan and N. P. Gambaryan, *Izv. Akad. Nauk Arm. SSR, Ser. Fiz.-Mat. Tekhn. Nauk* [*Bull. Acad. Sci. Arm. SSR, Div. Phys.-Math. Sci.*], 1950, **3**, 563 (in Russian).

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Flavonoid glycosides from *Thalictrum squarrosum* St. ex Willd. and *Thalictrum minus* L.

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Two flavonoid allose diglycosides were found in the terrestrial part of *Thalictrum squarrosum* St. ex Willd. and *T. minus* L. (Ranunculaceae). 7,4′-Di-*O*-β-allopyranosylapigenin was isolated from *T. minus*. In *T. squarrosum*, its monoacetate was also found and characterized as 7-*O*-(6-*O*-acetyl-β-allopyranosyl)-4′-*O*-(β-allopyranosyl)apigenin. The sites of attachment of the carbohydrate residues were determined by HMBC; the location of the acetate group was identified by ROESY. Both substances were isolated from these plants for the first time.

Key words: *Thalictrum*, flavonoids, glycosides; ^{1}H and ^{13}C NMR spectroscopy, FAB MS.

The majority of plant species of the *Thalictrum* genus are widely used in folk and oriental medicine. As a continuation of the study of the chemical composition of *T. squarrosum* St. ex Willd.[1] and *T. minus* L.,[2] which grow in Siberia, we isolated two flavonoid glycosides. Previously, the flavonoids of *Th. squarrosum* St. ex Willd. have not been studied.

Results and Discussion

Both glycosides (**1** and **2**) were isolated from the butanol fractions of water-methanol extracts defatted preliminarily with chloroform.

Based on the chromatographic behavior, molecular mass (595.1625 $[M + H]^+$ for **1** and 637.1724 $[M + H]^+$ for **2**), and the data of IR and UV spectra, compounds **1** and **2** were identified as flavonoid diglycosides. Along with the carbonyl group of the γ-pyrone ring (1668 cm^{-1}), compound **2** contains an ester carbonyl group (1719 cm^{-1}).

Analysis of the ^{1}H and ^{13}C NMR and UV spectra (Table 1) of compounds **1** and **2** permitted the conclusion that 5,7,4′-trihydroxyflavone (apigenin) substituted at positions 7 and 4′ is the aglycone of both compounds.[3,4]

The data of FAB mass spectra (peaks of the ions $[M + Na - 162]^+$ with *m/z* 455, $[M + H - 162]^+$ with *m/z* 433, and $[M + H - 324]^+$ with *m/z* 271 for **1** and $[M + H - 42]^+$ with *m/z* 595, $[M + H - 162 - 42]^+$ with *m/z* 433, and $[M + H - 324 - 42]^+$ with *m/z* 271 for **2**) indicate that compounds **1** and **2** contain two hexose residues and, in addition, they confirm the presence of an acetate group in compound **2**.

The proton and carbon signals for the carbohydrate parts of both compounds were assigned using the COSY and HETCOR 2D procedures (see Table 1). The data obtained make it possible to conclude that in both compound **1** and compound **2**, apigenin is glycosylated by two identical hexose molecules, which are attached directly to the aglycone. The chemical shifts for the

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