# Preparation and Synthetic Use of Trimethylsilyl Polyphosphate. A New Stereoselective Aldol-Type Reaction in the Presence of Trimethylsilyl Polyphosphate

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A study has been made of the preparation of a new polyphosphate reagent, trimethylsilyl polyphosphate (PPSE), and its use in organic synthesis. The reaction of phosphorus pentoxide with hexamethyldisiloxane in solvent (dichloromethane or benzene), in the strict absence of acid catalyst, affords a clear solution of PPSE which is composed mainly of cyclic and linear tetramers of phosphoric acid trimethylsilyl ester. PPSE is essentially aprotic and soluble in organic solvents and is capable of activating oxygen functionalities to induce synthetically useful reactions. In the present paper, the reaction of aryl methyl ketones with 3 equiv of aromatic aldehydes in the presence of PPSE was found to afford *meso*-5-acyl-2,4,6-trisubstituted-1,3-dioxanes stereoselectively. The reaction mechanism of this condensation is also briefly discussed.

Polyphosphoric acid ethyl ester (PPE), prepared by the reaction of phosphorus pentoxide with ether, has long attracted attention among chemists because of its characteristic structure and reactivities.[1-5] PPE is composed of cyclic and linear tetraphosphoric acid esters and it differs from well-known polyphosphoric acid (PPA)[6] in that it is essentially aprotic[7] and soluble in organic solvents. This reagent also displays strong dehydration power and is frequently used as a reagent for dehydrative condensations,[8,9] including use in biochemically interesting reactions.[2,10,11]

Our aim was to develop a new and synthetically useful polyphosphoric acid ester. And, it was found that phosphorus pentoxide reacted rapidly, in the strict absence of acid catalyst, with hexamethyldisiloxane in a solvent such as dichloromethane, benzene, or chloroform at reflux.[12,13] The resulting colorless or slightly yellowish clear solution afforded on concentration a viscous oil, which was designated by us as trimethylsilyl polyphosphate (*poly*phosphoric acid trimethylsilyl *e*ster: PPSE).[12]

The composition of PPSE was recently disclosed by Yamamoto and Watanabe on the basis of $^{31}P$ NMR measurement.[14] Quite interestingly, the mixture consists mainly of three tetraphosphoric acid trimethylsilyl esters, namely, isocyclotetraphosphate (**1**), cyclotetraphosphate (**2**), and linear tetraphosphate (**3**), as major components together with a small amount of tetrakis(trimethylsilyl) pyrophosphate (**4**) (Scheme I). For example, PPSE prepared in dichloromethane is composed of **1** (52%), **2** (29%), **3** (15%), and **4** (4%). It should be noted that tris(trimethylsilyl) phosphate is not detected at all in the mixture. These results are in sharp contrast to those obtained in the reaction of phosphorus pentoxide with hexamethyldisiloxane in the presence of acid catalyst.[13,14]

We have investigated the synthetic utilization of PPSE and have found that various ketoximes are rearranged to the corresponding amides and that carboxamides are rapidly dehydrated by PPSE into nitriles.[15] Furthermore, alcohols are cleanly converted into the alkyl iodides by the action of sodium iodide in the presence of PPSE.[16] It was also found that the PPSE–NaI reagent system was effective for the reduction of various sulfoxides, α-halo ketones, and benzoins to sulfides, parent ketones, and deoxybenzoins, respectively.[17] In addition, Yamamoto and

Scheme I

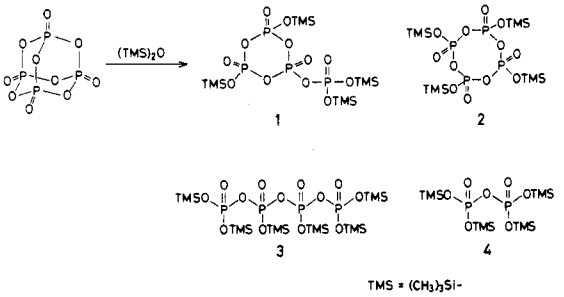


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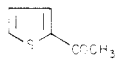
Table I. PPSE-Promoted Aldol-Type Condensation of Aryl Methyl Ketones with 3 Equiv of Aromatic Aldehydes

| ketone | aldehyde | time, h[a] | product | yield, %[b] | mp, °C |
|---|---|---|---|---|---|
| $C_6H_5COCH_3$ | $C_6H_5CHO$ | 1.5 | 5a | 73 | 199-200 |
| $C_6H_5COCH_3$ | $p$-$ClC_6H_4CHO$ | 2 | 5b | 50 | 228-229 |
| $C_6H_5COCH_3$ | $o$-$ClC_6H_4CHO$ | 12 | 5c | 81 | 191-192 |
| $p$-$ClC_6H_4COCH_3$ | $C_6H_5CHO$ | 1.5 | 5d | 63 | 220-221 |
| $p$-$ClC_6H_4COCH_3$ | $p$-$ClC_6H_4CHO$ | 12 | 5e | 31 | 208-210 |
| $p$-$ClC_6H_4COCH_3$ | $o$-$ClC_6H_4CHO$ | 12 | 5f | 70 | 161-163 |
| $C_{10}H_7COCH_3$ ($\beta$) | $C_6H_5CHO$ | 14 | 5g | 39 | 243-244 |
| $p$-$CH_3OC_6H_4COCH_3$ | $C_6H_5CHO$ | 48 | 5h | 74 | 212-213 |
| $p$-$CH_3OC_6H_4COCH_3$ | $o$-$ClC_6H_4CHO$ | 40 | 5i | 63 | 190-192 |
| $p$-$IC_6H_4COCH_3$ | $C_6H_5CHO$ | 16.5 | 5j | 56 | 244-246 |
|  | $C_6H_5CHO$ | 3 | 5k | 23 | 185-186 |

[a] All reactions were carried out at room temperature. [b] Yield after chromatography.

Watanabe recently demonstrated that PPSE is an effective reagent for the synthesis of benzimidazoles, indoles, and isoquinoline derivatives.[14]

These results exhibit the inherent reactivities of PPSE, that is, the ability of PPSE to effectively activate an oxygen functionality by interaction with a phosphorus atom or trimethylsilyl moiety. The ultraphosphate component in cyclic tetramer 1 is considered to be most significant for the activation of hydroxy groups. Moreover, the high solubility of PPSE in organic solvents, its aprotic nature, and its strong dehydration power render PPSE synthetically useful.

On the basis of these facts, we postulated the use of PPSE for the promotion of the cross-aldol reaction, since this reaction has been well recognized as one of the most important methods for the regio- and stereoselective construction of acyclic systems,[18] particularly useful intermediates for the total synthesis of biologically active natural products.[19] Our work was undertaken with the assumption that PPSE might effectively generate an enol or an enol equivalent (trimethylsilyl enol ether or enol phosphate species) from a ketone component and at the same time activate aldehyde by interaction with the trimethylsilyl or phosphate moiety of PPSE; that is, an aldol reactioin of a ketone with an aldehyde was proposed to occur in the presence of PPSE.

## Results and Discussion

As an initial trial the reaction of acetophenone with benzaldehyde in the presence of PPSE was conducted.

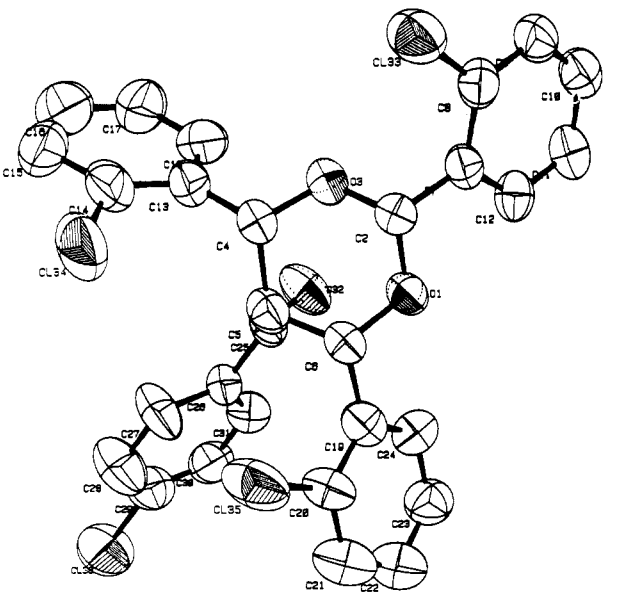
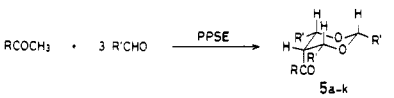


**Figure 1.** ORTEP plot of the final crystallographic model for **5f** excluding hydrogen ($R$ = 0.091). Numbering system is arbitrary and corresponds to that in the supplementary material.

The isolated product was not the expected aldol adduct, 1,3-diphenyl-3-hydroxypropan-1-one, but 5-benzoyl-2,4,6-triphenyl-1,3-dioxane (**5a**).[20,21] The structure of **5a** was



assigned on the basis of spectral data ($^1$H NMR, $^{13}$C NMR, MS, and IR) together with elemental analysis. In a similar manner, various aryl methyl ketones were allowed to react with aromatic aldehydes in the presence of PPSE. All products isolated displayed satisfactory spectral data supporting 1,3-dioxane derivatives. In order to further confirm the above structural assignment, one of the products, 5-($p$-chlorobenzoyl)-*cis*-2,*cis*-4,*cis*-6-tris($o$-chlorophenyl)-1,3-dioxane (**5f**) was subjected to single-crystal X-ray analysis, and its structure and relative stereochemistry were unequivocally determined. A computer-generated ORTEP drawing of the crystallographic model is shown in Figure 1.

(13) Several research groups have reported that when a mixture of phosphorus pentoxide and hexamethyldisiloxane was subjected to prolonged heating or was refluxed in the presence of acid catalyst, tris(trimethylsilyl) phosphate was produced as the major product. (a) Sauer, R. O. *J. Am. Chem. Soc.* **1944**, *66*, 1707. (b) Voronkov, M. G. *Zhur. Obshch. Khim.* **1955**, *25*, 437. (c) Mileshkevich, V. P.; Karlin, A. V. *Ibid.* **1970**, *40*, 2573.

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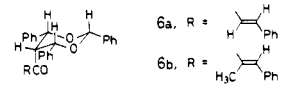
(19) For recent notable examples, see: (a) Masamune, S.; Choy, W.; Kerdesky, F. J. A.; Imperiali, B. *J. Am. Chem. Soc.* **1981**, *103*, 1566. (b) Masamune, S.; Hirama, M.; Mori, S.; Ali, Sk. A.; Garvey, D. S. *Ibid.* **1981**, *103*, 1568. (c) Masamune, S.; Kaiho, T.; Garvey, D. S. *Ibid.* **1982**, *104*, 5521. (d) Masamune, S.; Lu, L. D.-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *Ibid.* **1982**, *104*, 5523. (e) Masamune, S.; Ellingboe, J. W.; Choy, W. *Ibid.* **1982**, *104*, 5526. (f) Masamune, S.; Imperiali, B.; Garvey, D. S. *Ibid.* **1982**, *104*, 5528.

(20) A preliminary account of a portion of this work has appeared: Imamoto, T.; Yokoyama, H.; Yokoyama, M. *Tetrahedron Lett.* **1982**, *23*, 1467.

(21) An example of aldol-type addition forming a 1,3-dioxane derivative was reported by Lumma and Ma; 2-butanone was condensed in trifluoroacetic acid with 3 mol of formaldehyde to produce 5-acetyl-1,3-dioxane. Lumma, W. C.; Ma, O. H. *J. Org. Chem.* **1970**, *35*, 2391.

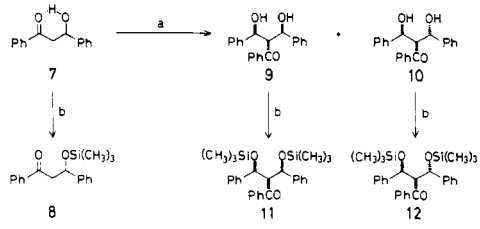
One of the features of this new condensation is that the major products are *meso*-5-acyl-1,3-dioxane derivatives with equatorially oriented triaryl groups in the 2-, 4-, and 6-positions and with acyl group in an axial position. These products were stereoselectively formed in a one-pot reaction, even though the sequential process involves two carbon–carbon and two carbon–oxygen bond formations. It is also noteworthy that the use of PPSE as the reagent is critical for this condensation. Thus, no reaction proceeded in the presence of tris(trimethylsilyl)phosphate under the same conditions. The use of PPE in place of PPSE resulted in the formation of $\alpha,\beta$-unsaturated carbonyl compounds, probably due to the strong dehydration power of PPE.

As is shown in Table I, this PPSE-promoted condensation is applicable to various combinations of aromatic methyl ketones and aryl aldehydes but has some limitations in aliphatic systems. For instance, the reaction of acetone with benzaldehyde afforded 5-cinnamoyl-2,4,6-triphenyl-1,3-dioxane (**6a**) in 24% yield. The same com-




pound was obtained from *trans*-4-phenyl-3-buten-2-one and 3 equiv of benzaldehyde in 43% yield. The reaction of 2-butanone with benzaldehyde under similar conditions produced **6b** in 39% yield. Further attempts have been made to extend this condensation reaction to other aliphatic ketones such as 4-methyl-3-penten-2-one, 3-methyl-2-butanone, and cyclopropyl methyl ketone. However, in these cases complicated side reactions were noted and the corresponding 1,3-dioxane derivatives could not be isolated.

Our attention has next turned to the elucidation of the reaction pathway leading to *meso*-1,3-dioxane derivatives. Thus, as a model system, we investigated the reaction of acetophenone with benzaldehyde. At first, we prepared all possible intermediates by a different route starting from 1,3-diphenyl-3-hydroxypropan-1-one (**7**). The tri-

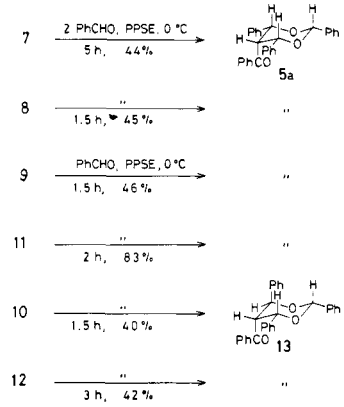



a, 2 LDA, $ZnCl_2$; $C_6H_5CHO$; b, $(CH_3)_3SiCl$, $(C_2H_5)_3N$, DAMP.

methylsilyl derivative **8** was prepared by the standard procedure. *meso*-Keto diol **9** and *d,l*-keto diol **10** were synthesized by successive treatments of **7** with 2 equiv of lithium diisopropylamide (LDA) and benzaldehyde in the presence of zinc chloride. Each isomer was then converted into the respective trimethylsilyl derivatives **11** and **12**.

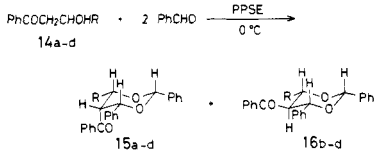
The compounds thus prepared were allowed to react with benzaldehyde in the presence of PPSE. As is summarized in Scheme II, aldol **7** and *meso*-keto diol **9** were converted into *meso*-1,3-dioxane derivative **5a**, while the *d,l*-keto diol **10** led to *d,l*-1,3-dioxane derivative **13**. These results indicate that no apparent equilibrium between **7**, **9**, and **10** is established under the conditions. The silyl derivatives **8**, **11**, and **12** were also stereospecifically converted into **5a** and **13**, respectively. In these cases the reactions presumably proceed as follows: the silyl derivatives are subjected to desilylation in the presence of PPSE to generate **7** and **10**, respectively, which subsequently

Scheme II




react with benzaldehyde to give 1,3-dioxane derivatives.

Next, we tried the stereoselective cross coupling of three different carbonyl compounds. This was achieved by the reaction of the preformed aldol with an aldehyde in the presence of PPSE. Thus, treatment of 3-(*p*-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one (**14a**) with ben-




a, R = *p*-$ClC_6H_4$-
b, R = $C_2H_5$-
c, R = *n*-$C_3H_7$-
d, R = $C_6H_5(CH_2)_2$-

zaldehyde in the presence of PPSE at 0 °C for 1.5 h afforded 5-benzoyl-4-(*p*-chlorophenyl)-2,4-diphenyl-1,3-dioxane (**15a**) in 63% yield: in this case other isomeric 1,3-dioxanes could not be detected. On the other hand, the aldols prepared from aliphatic aldehydes and acetophenone produced two kinds of stereoisomers (**15b–d** and **16b–d**) with almost a 1:1 ratio in 37~80% combined yields.

Finally, we examined the acetalization of benzaldehyde with several kinds of alcohols using PPSE as the condensation reagent, and it was found that the PPSE-promoted acetalization was well suited to sterically congested secondary alcohols. For example, the reaction of 1,3-diphenyl-1,3-propanediol with benzaldehyde, which corresponds to the model system for the final step of PPSE-promoted aldol reaction, afforded the corresponding acetal in almost quantitative yield. This method, however, was ineffective with primary alcohols such as methanol, benzyl alcohol, 1,2-ethanediol, and 1,3-propanediol, presumably because these alcohols preferably attack PPSE to result in the formation of alkyl phosphate species.

On the basis of these results, we considered the reaction pathway of the PPSE-promoted stereoselective aldol reaction to be as is illustrated in Scheme III. Thus, in the

Scheme III

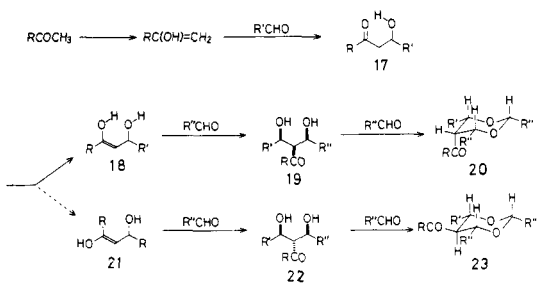


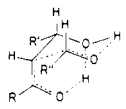
Table II. Spectral and Analytical Data of 1,3-Dioxanes (5a-k)[a]

| compd | IR (KBr) C=O, $cm^{-1}$ | $^1H$ NMR; $^{13}C$ NMR (in $CDCl_3$) |
|---|---|---|
| 5a | 1670 | 4.25 (t, 1 H, $J$ = 3.5 Hz), 5.45 (d, 2 H, $J$ = 3.5 Hz), 6.05 (s, 1 H), 7.0-7.7 (m, 18 H), 7.9-8.1 (m, 2 H); 51.2, 80.0, 102.3, 125.8, 126.9, 127.1, 127.6, 128.1, 128.2, 129.0, 131.3, 138.4, 138.6, 140.0,197.7 |
| 5b | 1670 | 4.2 (t, 1 H, $J$ = 3.2 Hz), 5.4 (d, 2 H, $J$ = 3.2 Hz), 5.95 (s, 1 H), 7.0-8.0 (m, 17 H) |
| 5c | 1685 | 5.05 (t, 1 H, $J$ = 3.2 Hz), 5.8 (d, 2 H, $J$ = 3.2 Hz), 6.6 (s, 1 H), 6.9-7.7 (m, 16 H), 8.4-8.6 (m, 1 H) |
| 5d | 1670 | 4.2 (t, 1 H, $J$ = 3.0 Hz), 5.45 (d, 2 H, $J$ = 3.0 Hz), 6.05 (s, 1 H), 7.0-7.7 (m, 17 H), 7.8-8.1 (m, 1 H) |
| 5e | 1670 | 4.1 (t, 1 H, $J$ = 3.4 Hz), 5.35 (d, 2 H, $J$ = 3.4 Hz), 5.95 (s, 1 H), 6.95-8.10 (m, 16 H) |
| 5f | 1680 | 4.93 (t, 1 H, $J$ = 3.2 Hz), 5.75 (d, 2 H, $J$ = 3.2 Hz), 6.5 (s, 1 H), 6.95-7.65 (m, 15 H), 8.4-8.6 (m, 1 H) |
| 5g | 1670 | 4.4 (t, 1 H, $J$ = 3.0 Hz), 5.55 (d, 2 H, $J$ = 3.0 Hz), 6.1 (s, 1 H), 7 0-8.15 (m, 22 H) |
| 5h | 1670 | 3.65 (s, 3 H), 4.17 (t, 1 H, $J$ = 3.0 Hz), 5.42 (d, 2 H, $J$ = 3.0 Hz), 6.0 (s, 1 H), 6.4-6.65 (m, 2 H), 7.0-7.6 (m, 15 H), 7.75-8.05 (m, 2 H) |
| 5i | 1660 | 3.7 (s, 3 H), 4.95 (t, 1 H, $J$ = 3.0 Hz), 5.8 (d, 2 H, $J$ = 3.0 Hz), 6.55 (s, 1 H), 6.45-6.7 (m, 2 H), 6.9-7.7 (m, 13 H), 8.4-8.65 (m, 1 H) |
| 5j | 1680 | 4.1 (t, 1 H, $J$ = 4.4 Hz), 5.39 (d, 2 H, $J$ = 4.4 Hz), 5.97 (s, 1 H), 6.65-7.6 (m, 17 H), 7.7-7.95 (m, 2 H) |
| 5k | 1640 | 4.0 (t, 1 H, $J$ = 4.0 Hz), 5.45 (d, 2 H, $J$ = 4.0 Hz), 6.03 (s, 1 H), 6.6-7.65 (m, 16 H), 7.75-8.1 (m, 2 H) |

[a] Satisfactory analytical data (±0.4% C, H) for all compounds were submitted for review.

presence of PPSE, methyl ketone is enolized and reacts with aldehyde to form aldol adduct **17**. This aldol is further subjected to enolization to form *Z* enol **18** and/or *E* enol **21**. When R′ is an aromatic group, *Z* enol is generated predominantly, and when R′ is an ethyl, *n*-propyl, or 2-phenylethyl group, both *Z* enol and *E* enol are generated comparatively. The *Z* enol **18** reacts with another aldehyde component to produce **19**, which is subsequently converted into **20**. On the other hand, *E* enol **21** reacts with aldehyde to give stereoisomeric keto diol **22**, which is acetalized to give **23**.

The stereocontrol of the reaction may be interpreted by assuming a hydrogen-linked six-membered transition state. Two transition states depicted as **24** and **25** would lead



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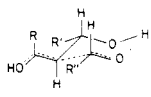

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from a *Z* enol **18** to **19** and an *E* enol **21** to **22**, respectively. In both cases, there exist minimum 1,3-diaxial interactions between substituents, and as a consequence keto diols **19** and **22** are formed stereoselectively.

## Experimental Section

Infrared spectra were recorded on a Hitachi 215 spectrometer. The $^1H$ NMR spectra were determined with Japan Electron Optics Lab. (JEOL), JNM-FX 270, FX-100, and C-60 HL. The $^{13}C$ NMR spectra were recorded with a JEOL JNM-FX 270 or FX-100. The chemical shifts are given in ppm with $Me_4Si$ as an internal standard. Mass spectra were measured on a Hitachi M-60 spectrometer at an ionizing energy of 70 eV. Microanalyses were performed with a Perkin-Elmer 240 elemental analyzer at the Analytical Center of Chiba University.

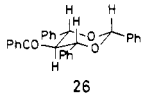
Special grade phosphorus pentoxide was purchased from Wako Pure Chemical Industries, Ltd. Hexamethyldisiloxane (Aldrich) was distilled before use. Ketones and aldehydes were also purified by distillation before use. Benzene and dichloromethane were purified by standard procedures, and tetrahydrofuran (THF) was distilled from benzophenone ketyl.

**Preparation of Trimethylsilyl Polyphosphate (PPSE).** A 300-mL two-necked round bottom flask, equipped with a reflux condenser and a Teflon-coated magnetic bar, was dried in vacuo and then flushed with argon. To this flask were added sequentially phosphorus pentoxide (20 g, 70 mmol), solvent (dichloromethane or benzene, 100 mL), and hexamethyldisiloxane (50 mL, 240 mmol). The mixture was heated at reflux for 1 h under argon until the solution was clear. Most of the solvent was removed by using a rotary evaporator and the resultant colorless or slightly yellowish liquid was diluted with 10~20 mL of dry dichloromethane. This volatile solution was used for the following condensation.[22]

**General Procedure for the Preparation of 1,3-Dioxane Derivatives (5a-k).** To a mixture of a methyl ketone (1 mmol) and aromatic aldehyde (3.5 mmol) was added 3 g[23] of a solution of PPSE in dichloromethane prepared as above. The mixture was stirred at room temperature under argon until the starting ketone was consumed.[24] The reaction mixture was diluted with dichloromethane (ca. 10 mL) and treated with saturated sodium bicarbonate solution (ca. 30 mL), and the product was extracted into dichloromethane. The combined extracts were dried over $Na_2SO_4$ and concentrated on a rotary evaporator. After removal of unreacted aldehyde in vacuo (0.01~0.1 Torr) at ca. 60 °C, the residue was purified by preparative thin-layer chromatography on silica gel using benzene or benzene–hexane (1:9) as eluent. The product was recrystallized from ethanol–chloroform.

Yields and melting points of the products are summarized in Table I. The IR and NMR data of these products are given in Table II.

It is noted that the stereoisomer of **5a**, 5-benzoyl-*trans*-2,-*trans*-4,*trans*-6-triphenyl-1,3-dioxane (**26**), was isolated on



26

treatment of **5a** with sodium borohydride in ethanol at room temperature for 15 h, although in very poor yield.[25] The product was recrystallized from methanol: mp 155.0–155.5 °C; IR (KBr) 1600 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.05 (t, 1 H, $J$ = 9.5 Hz), 5.35 (d, 2 H, $J$ = 9.5 Hz), 6.08 (s, 1 H), 7.00~7.68 (m, 20 H); $^{13}C$ NMR ($CDCl_3$) δ 58.0, 82.4, 101.6, 126.4, 126.7, 127.2, 127.6, 127.9, 128.2, 128.4, 129.0, 132.6, 137.8, 138.1, 138.9. Anal. Calcd for $C_{29}H_{24}O_3$: C, 82.83; H, 5.75. Found: C, 82.71; H, 5.81.

**5-Cinnamoyl-*cis*-2,*cis*-4,*cis*-6-triphenyl-1,3-dioxane (6a).** A mixture of benzaldehyde (428 mg, 4.03 mmol), acetone (52 mg, 0.90 mmol), and 3 g of a solution of PPSE in dichloromethane was stirred at room temperature for 2 h. The reaction mixture

(22) Removal of a trace of solvent in vacuo affords a very viscous liquid or stiff gel-like a glass. This material dissolves at room temperature in dichloromethane, chloroform, or benzene to give a volatile solution which can be used for reactions.

(23) This solution (3 g) of PPSE contained ca. 2 g of PPSE.

(24) The reaction may be monitored by thin-layer chromatography.

(25) The reduction of **5a** with $NaBH_4$ did not proceed under these conditions, probably owing to steric hindrance.

Table III. Crossed-Condensation Products[a]

| product | yield, % | mp, °C | IR (KBr) C=O, $cm^{-1}$ | $^1H$ NMR; $^{13}C$ NMR (in $CDCl_3$) |
|---|---|---|---|---|
| 15a | 63 | 177-178 | 1680 | 4.2 (t, 1 H, $J$ = 3.0 Hz), 5.35-5.53 (m, 2 H), 5.98 (s, 1 H), 7.0-7.6 (m, 17 H), 7.75-8.00 (m, 2 H) |
| 15b | 18 | 136 | 1680 | 0.9 (t, 3 H, $J$ = 7.0 Hz), 1.17-1.95 (m, 2 H), 3.87-4.35 (m, 2 H), 5.25 (d, 1 H, $J$ = 3.5 Hz), 7.05-8.00 (m, 15 H) |
| 16b | 19 | 144-145 | 1670 | 0.74-1.4 (m, 5 H), 3.86-4.52 (m, 2 H), 5.55 (d, 1 H, $J$ = 10 Hz), 5.93 (s, 1 H), 7.1-8.0 (m, 15 H) |
| 15c | 36 | 143-145 | 1680 | 0.6-1.9 (m, 7 H), 3.90 (t, 1 H, $J$ = 3.2 Hz), 4.1-4.5 (m, 1 H), 5.25 (d, 1 H, $J$ = 3.2 Hz), 5.80 (s, 1 H), 7.00-7.95 (m, 15 H); 13.7, 18.9, 35.6, 49.0, 78.8, 80.1, 102.1, 125.9, 126.9, 127.5, 128.1, 128.2, 128.9, 132.0, 138.6, 138.8, 139.9, 198.3 |
| 16c | 44 | 127-128 | 1665 | 0.8-1.8 (m, 7 H), 4.40-4.75 (m, 2 H), 5.62 (d, 1 H, $J$ = 10 Hz), 6.01 (s, 1 H), 7.2-7.7 (m, 13 H), 7.8-8.0 (m, 2 H); 13.7, 18.8, 29.1, 52.7, 73.9, 76.4, 93.8, 126.2, 127.8, 128.0, 128.2, 128.9, 133.6, 136.3, 138.3, 139.9, 198.2 |
| 15d | 21 | 159 | 1680 | 1.1-2.28 (m, 2 H), 2.73 (t, 2 H, $J$ = 7.0 Hz), 3.77 (t, 1 H, $J$ = 3.3 Hz), 3.9-4.3 (m, 1 H), 5.1 (d, 1 H, $J$ = 3.3 Hz), 5.7 (s, 1 H), 6.97-8.0 (m, 20 H) |
| 16d | 19 | 144.0-144.5 | 1670 | 1.06-3.1 (m, 4 H), 3.87-4.8 (m, 2 H), 5.62 (d, 1 H, $J$ = 10 Hz), 6.08 (s, 1 H), 6.87-8.0 (m, 20 H) |

[a] Satisfactory analytical data (±0.3% for C, H) for all compounds were submitted for review.

was worked up in a similar manner described above and the product was isolated by preparative TLC using benzene–hexane (1:1) as eluent (97 mg, 24%). This product was recrystallized from ethanol–chloroform to give light yellow needles: mp 180–181 °C; IR (KBr) 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.43 (t, 1 H, $J$ = 3.0 Hz), 5.45 (d, 2 H, $J$ = 3.0 Hz), 6.1 (s, 1 H), 7.0~8.1 (m, 22 H); $^{13}C$ NMR ($CDCl_3$) δ 58.3, 79.4, 101.9, 125.3, 126.5, 126.8, 127.8, 127.9, 128.3, 128.4, 128.7, 129.2, 130.0, 135.1, 138.2, 140.6, 196.8. Anal. Calcd for $C_{31}H_{26}O_3$: C, 83.38; H, 5.87. Found: C, 83.07; H, 5.92.

The same compound was obtained also by the reaction of *trans*-4-phenyl-3-buten-2-one with benzaldehyde in the presence of PPSE in 43% yield.

**5-(2-Methylcinnamoyl)-*cis*-2,*cis*-4,*cis*-6-triphenyl-1,3-dioxane (6b).** A solution of PPSE (3 g) was added to a mixture of 2-butanone (72 mg, 1.0 mmol) and benzaldehyde (424 mg, 4 mmol) at room temperature. After stirring for 3 h at room temperature, the mixture was treated with saturated $NaHCO_3$ solution (30 mL) and extracted with dichloromethane. The combined extracts were dried over $Na_2SO_4$ and evaporated. The unreacted benzaldehyde was removed in vacuo at 60~70 °C and the residue was subjected to preparative TLC (silica gel, benzene) to yield **6b** (180 mg, 39%). This product was further purified by recrystallization from ethanol–chloroform: mp 174–176 °C; IR (KBr) 1650 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.30 (d, 3 H, $J$ = 1.5 Hz), 4.05 (t, 1 H, $J$ = 3.0 Hz), 5.37 (d, 2 H, $J$ = 3.0 Hz), 5.95 (s, 1 H), 6.65~8.05 (m, 21 H). Anal. Calcd for $C_{32}H_{28}O_3$: C, 83.45; H, 6.13. Found: C, 83.23; H, 6.19.

**Preparation of *meso*-Keto Diol 9 and *d,l*-Keto Diol 10.** A solution of 1,3-diphenyl-3-hydroxypropan-1-one (7) (679 mg, 3.0 mmol) in 5 mL of dry THF was added at −78 °C to a solution of lithium diisopropylamide which was prepared from diisopropylamine (0.93 mL, 6.0 mmol) and butyllithium (6.6 mmol) in 18 mL of THF. After 30 min, anhydrous zinc chloride (1.10 g, 8.1 mmol) was added and stirring was continued for 30 min at the same temperature. Then a solution of benzaldehyde (359 mg, 3.39 mmol) in THF (3 mL) was added. After keeping the temperature at −78 °C for 1.5 h, the mixture was treated with water (50 mL) containing 1 mL of acetic acid and was extracted with ether. The combined extracts were dried over $Na_2SO_4$ and evaporated. The residual oil was subjected to preparative TLC (silica gel, benzene–ethyl acetate, 15:1) to give **9** (253 mg, 25%) and **10** (273 mg, 27%).

The compound **9** was an unstable oil and decomposed during shipment for microanalysis: IR (neat), 1670, 3440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.5 (1 H, br s), 4.69 (1 H, s), 4.12 (t, 1 H, $J$ = 6.0 Hz), 4.69 (1 H, s), 5.03 (d, 2 H, $J$ = 6.0 Hz), 7.1~7.7 (m, 15 H).

The compound **10** was obtained as white crystals: mp 108.0–110.5 °C; IR (KBr) 1705 and 3385 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.47 (br s, 1 H), 4.15 (dd, 1 H, $J$ = 7.0 Hz, 2.5 Hz), 4.55 (br s, 1 H), 5.39 (m, 2 H), 7.05~7.51 (m, 15 H). Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.26; H, 6.17.

These keto diols were then converted into their trimethylsilyl derivatives **11** and **12** in 15% and 20% yields, respectively, by treatment with chlorotrimethylsilane and triethylamine in the presence of 4-(dimethylamino)pyridine (DAMP).

Compound **11**:[26] IR (KBr) 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) −0.21 (s, 18 H), 4.23 (t, 1 H, $J$ = 8.0 Hz), 4.93 (d, 2 H, $J$ = 8.0 Hz), 6.94~7.74 (m, 15 H).

Compound **12**:[26] IR (KBr) 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ −0.21 (s, 18 H), 4.35 (t, 1 H, $J$ = 7.5 Hz), 5.01 (d, 1 H, $J$ = 7.5 Hz), 5.27 (d, 1 H, $J$ = 7.5 Hz), 6.96–7.54 (m, 15 H).

**Preparation of *d,l*-5-Benzoyl-*cis*-2,*cis*-4,*trans*-6-triphenyl-1,3-dioxane (13).** To a mixture of **10** (138 mg, 0.416 mmol), benzaldehyde (137 mg, 1.29 mmol), and dichloromethane (0.5 mL) was added PPSE (3 g) at 0 °C. After stirring for 1.5 h at the same temperature, the mixture was treated with saturated aqueous $NaHCO_3$ solution (25 mL), and extracted with chloroform. The combined extracts were dried over $Na_2SO_4$ and evaporated. The residue was subjected to preparative TLC (silica gel, benzene) to give **13** (70 mg, 40%): mp 120–122 °C; IR (KBr) 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.62 (t, 1 H, $J$ = 4.3 Hz), 5.47 (d, 1 H, $J$ = 4.3 Hz), 5.64 (d, 1 H, $J$ = 4.3 Hz), 6.11 (s, 1 H), 7.1–7.8 (m, 20 H); $^{13}C$ NMR ($CDCl_3$) δ 49.9, 73.3, 75.4, 97.3, 126.1, 126.5, 126.7, 127.5, 127.8, 128.0, 128.28, 128.34, 129.0, 137.8, 138.5, 139.1, 197.7. Anal. Calcd for $C_{29}H_{24}O_3$: C, 82.83; H, 5.75. Found: C, 82.39; H, 5.85.

**General Procedure for the Cross-Coupling of Aldols (14a–d) with Benzaldehyde.** To a mixture of aldol (**14a–d**) (1.0 mmol) and benzaldehyde (2.5~2.7 mmol) was added 3 g of a solution of PPSE in dichloromethane at 0 °C. The mixture was stirred in an ice bath for several hours until starting aldol was consumed. The reaction mixture was worked up in the usual manner and the product was isolated by preparative TLC. The yields and spectral data of the products are summarized in Table III.

**X-ray Crystallographic Analysis of 5f.** A large, well-shaped monoclinic crystal of **5f** was obtained by recrystallization from chloroform–ethanol: $C_{29}H_{20}Cl_4O_3$; space group $C2/c$-$C^6_{2h}$; cell constants $a$ = 36.870 (12) Å, $b$ = 10.357 (15) Å, $c$ = 14.437 (8) Å; β = 107.09; $z$ = 8. Lattice constants and intensity data for **5f** were measured by using graphite-monochromated Cu $K_\alpha$ radiation on a Rigaku AFC-5 diffractometer. A total of 2751 unique reflections

(26) The compound was unstable and did not give satisfactory elemental analyses.

with $F_0 > 4\sigma(F_0)$ were obtained by using the $\omega - 2\theta$ scanning method with a $2\theta$ scan speed of 4°/min to 150°. The structure was solved by the RASA-II system (Rigaku Corp.) on the basis of the direct method (MULTAN)[27] and refined to a final $R$ value of 0.091. The program was executed on a 16 bit/word minicomputer with a 64 Kbyte 1C memory and 10 Mbytes on magnetic disk. Further crystallographic details can be found in the supplemental material described in the paragraph at the end of this paper.

**Registry No.** 1, 84140-51-2; 2, 84140-50-1; 3, 32284-31-4; 4, 18395-45-4; 5a, 82959-04-4; 5b, 82959-05-5; 5c, 82959-06-6; 5d, 82959-07-7; 5e, 82959-08-8; 5f, 82959-09-9; 5g, 82959-10-2; 5h, 82959-11-3; 5i, 82959-12-4; 5j, 88704-56-7; 5k, 88704-57-8; 6a, 88764-10-7; 6b, 88704-65-8; 7, 42052-51-7; 9, 88764-11-8; 10, 88704-61-4; 11, 88704-62-5; 12, 88764-12-9; 13, 88704-63-6; 14a, 82959-14-6; 14b, 88704-64-7; 14c, 57548-41-1; 14d, 60669-64-9; 15a, 82959-15-7; 15b, 88704-58-9; 15c, 82959-16-8; 15d, 88704-59-0; 16b, 88764-08-3; 16c, 82978-52-7; 16d, 88764-09-4; 26, 88704-60-3; $C_6H_5COCH_3$, 98-86-2; $p$-$ClC_6H_4COCH_3$, 99-91-2; $\beta$-$C_{10}H_7COCH_3$, 93-08-3; $p$-$CH_3OC_6H_4COCH_3$, 100-06-1; $p$-$IC_6H_4COCH_3$, 13329-40-3; 2-$C_4H_3SCOCH_3$, 88-15-3; $C_6H_5CHO$, 100-52-7; $p$-$ClC_6H_4CHO$, 104-88-1; $o$-$ClC_6H_4CHO$, 89-98-5; acetone, 67-64-1; *trans*-4-phenyl-3-buten-2-one, 1896-62-4; 2-butanone, 78-93-3.

**Supplementary Material Available:** Tables of fractional atomic coordinates, bond lengths, and bond angles for 5f (3 pages). Ordering information is given on any current masthead page.

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# Stereoselective Synthesis of (±)-3,4,4a,5,6,7,8,8a-Octahydronaphthalen-1(2*H*)-ones via Homogeneous Hydrogenation of (±)-5,6,7,8-Tetrahydronaphthalenones

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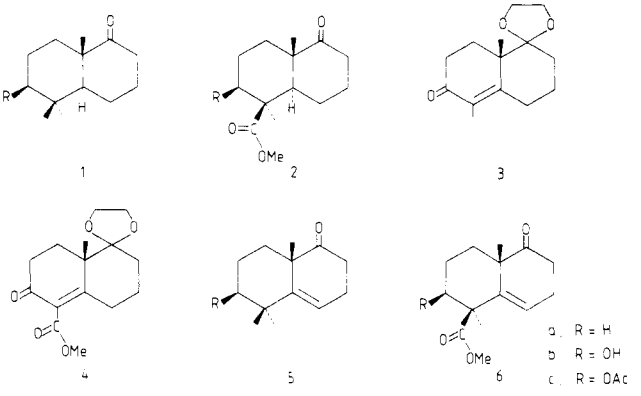
Homogeneous hydrogenation of 5,6,7,8-tetrahydronaphthalenone derivatives **7a,c** and **9b** using tris(triphenylphosphine)rhodium(I) chloride gave (±)-5,5,8aβ-trimethyl-3,4,4aα,5,6,7,8,8a-octahydronaphthalen-1(2*H*)-one (**1a**) and (±)-methyl 1-oxo-5α,8aβ-dimethyl-6β-hydroxy-1,2,3,4,4aα,5,6,7,8,8a-decahydronaphthalene-5β-carboxylate (**2b**) in good yields.

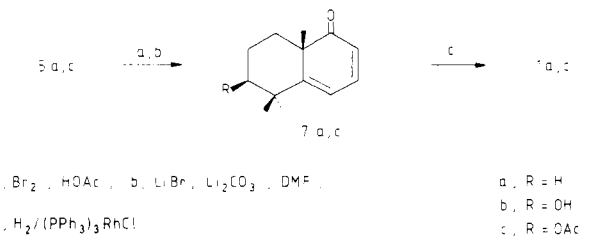
In connection with several planned terpene syntheses in our laboratory, convenient stereocontroled preparations of the trans-fused bicyclic ketones **1** and **2** were required. The obvious procedures for the preparation of these compounds, i.e., reductive alkylation of **3** and **4** or catalytic hydrogenation of **5** and **6**, respectively, turned out to be unattractive. Reductive alkylation of **3** gave good results in small-scale preparations,[1] but on a larger scale mixtures of reduced and alkylated products were obtained that required extensive purification. Reductive alkylation of **4** seemed not very promising since dissolving metal reduction of **4** gives mixtures of cis- and trans-fused reduction products[2] and methylation of the trans-fused enolate affords a methylated product with the epimeric configuration at C-5.[3] The reductive elimination developed by Coates et al.[4] and applied in the total synthesis of LLZ-1271α[5] has the disadvantage that no functionality remains in ring A, and this method is therefore unsuitable for the preparation of **2b** and **2c** (Chart I).

The catalytic hydrogenation of **5** is reported but proved to be rather irreproducible.[1b,6] Catalytic hydrogenation of **6** was unsuccessful, and moderate results were obtained when compounds related to **6** were reduced.[7]

Chart I




Scheme I




In this paper a synthesis of racemic **1** and **2** is described by using compounds **7** and **9** as key intermediates. Extension of the unsaturated system in ring B in **5** or **6** followed by homogeneous catalytic hydrogenation with

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