Stereochemistry of Thiono–Thiolo Rearrangement of Phosphorothioic Esters. 2[1]

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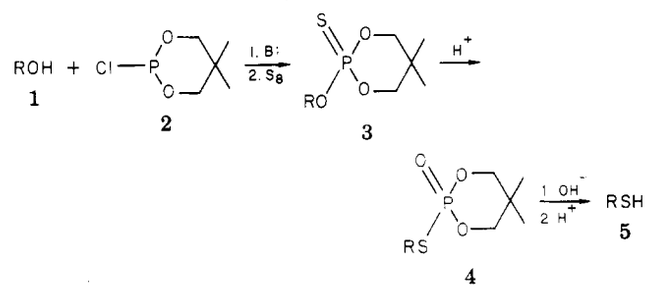
1-Methylbenzyl group migration proceeds with 65% retention when (*R*)-(+)-2-[(1-methylbenzyl)oxy]-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane undergoes thiono–thiolo rearrangement in acetic acid solution. This rearrangement in trifluoroacetic acid medium occurs with much lower stereospecificity (3.5%) and net inversion of configuration at the migrating carbon. Rearrangement of (*R*)-(−)-2-(benzyloxy-1-*d*)-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane in CF_3COOH/CH_2Cl_2 medium proceeds with inversion of configuration (58.3%). These facts are rationalized in terms of an ion-pair mechanism. The diverse stereochemistry is explained by solvation effects in the reaction medium influencing the reactivity and equilibrium between tight ion-pair, solvent-separated ion-pair, and free ions. Base hydrolysis of (*S*)-(−)-2-[(1-methylbenzyl)thio]-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane and (*S*)-(+)-2-(benzylthio-1-*d*)-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane affords (*S*)-(−)-1-methylbenzylthiol and (*S*)-(+)-benzylthiol-*1*-*d*, respectively.

Recently we described the facile protic-acid-catalyzed thiono–thiolo (selenono–selenolo) rearrangement of *O*-alkyl esters of phosphorothioic (-selenoic) acid to their *S*(*Se*)-alkyl isomers. Besides generating a theoretical interest in its mechanism, this rearrangement offers an easy route for conversion of alcohols into corresponding thiols (selenols) due to the simplicity of P–S (P–Se) bond cleavage.[2] This approach is represented in Scheme I. Moreover, it was of interest to know whether this overall procedure can be applied to the stereospecific synthesis of alkylthiols.

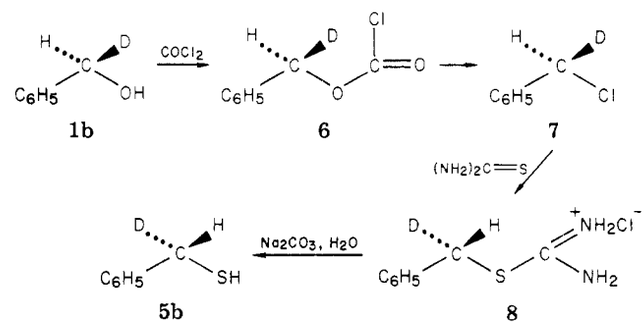
In this report we describe the results of our studies on the stereospecificity of the rearrangement of 2-alkoxy-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinanes (**3**) to 2-(alkylthio)-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinanes (**4**). As model systems the derivatives of (*R*)-(+)-1-methylbenzyl alcohol (**1a**) and (*R*)-(−)-benzyl-1-*d* alcohol (**1b**) were investigated. The optical purities of **1a** and **1b** were calculated on the basis of values described in the literature.[3] The stereospecificities of **3** → **4** conversion were calculated as the ratios of optical purities of alkylthiols **5** obtained from stereospecific degradations of phosphorothiolates **4** to those of starting alcohols **1**. Because, to our knowledge, optically active benzylthiol-*1*-*d* (**5b**) was not known, it was necessary to obtain it in an independent way to determine its optical purity and to assign its absolute configuration. (*R*)-(−)-Benzyl-1-*d* alcohol (**1b**, $[\alpha]^{20}_D$ −0.324 ± 0.005°, deuterium content 36%, optical purity 56.3%)[4] was converted into benzyl-1-*d* chloroformate (**6**) and subsequently to (*R*)-(−)-benzyl-1-*d* chloride ($[\alpha]^{20}_D$ −0.274 ± 0.005°, **7**). It was believed that both reactions proceed with retention of configuration.[5] Reaction of **7** with thiourea gave (*S*)-(+)-*S*-benzylisothiuronium-1-*d* chloride (**8**, $[\alpha]^{20}_D$ +0.350 ± 0.005° (*c* 34, acetone)) which after alkaline hydrolysis gave (*S*)-(+)-benzylthiol-1-*d* (**5b**, $[\alpha]^{20}_{436}$ +0.695 ± 0.005°, deuterium content 32%).

Because the conversion of the chloride **7** to the isothiuronium chloride **8** proceeds with inversion of configuration,[6] the absolute configuration of (+)-benzylthiol-1-*d* must be (*S*)-(+). Attempts to assign optical purity of (S)-(+)-**5b** by means of the formation of diastereoisomeric thiolo esters with (−)-2-phenyl-2-methoxy-2-(trifluoromethyl)acetic acid[7] have failed. Assuming that conversions **1b** → **7** → **8** → **5b** are fully stereospecific,[5,6] the calculated value of the optical rotation of the pure enantiomer of **5b** should be at least $[\alpha]^{20}_{436}$ +3.86 ± 0.1° (neat). The conversion of **1b** → **5b** is depicted in Scheme II.

Scheme I



Scheme II



The above correlation and the assumption of full stereospecificity for all processes shown in Scheme II allowed us to assign the stereospecificity of the conversion of ROH (**1**) → RSH (**5**) via the phosphorothioate pathway (vide infra). The model compounds **3a** and **3b** were obtained by condensation of 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane (**2**) with **1a** and **1b**, respectively, and addition of elemental sulfur to the unisolated intermediate 2-alkoxy-5,5-dimethyl-1,3,2-dioxaphosphorinane. Both **3a**

(1) Part 1: W. J. Stec, B. Uznanski, K. Bruzik, and J. Michalski, *J. Org. Chem.*, **41**, 1291 (1976).
(2) (a) A. J. Kirby and S. G. Warren, "Organic Chemistry of Phosphorus", Elsevier, Amsterdam, 1967; (b) G. R. Norman, W. M. LeSuer, and T. W. Mastin, *J. Am. Chem. Soc.*, **74**, 161 (1952).
(3) (a) E. Downer and J. Kenyon, *J. Chem. Soc.*, 1156 (1939); (b) V. E. Althouse, D. M. Feigl, W. A. Sanderson, and H. S. Mosher, *J. Am. Chem. Soc.*, **88**, 3595 (1966).
(4) A. Streitwieser, Jr., and J. R. Wolfe, *J. Am. Chem. Soc.*, **79**, 903 (1957).
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(6) H. M. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, 1252 (1964).
(7) (a) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969); (b) J. A. Dale and H. S. Mosher, *J. Am. Chem. Soc.*, **95**, 512 (1973).

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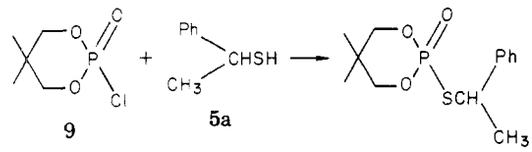
and **3b** were isolated by means of column chromatography and/or crystallization from an appropriate solvent. The rearrangements of **3** to **4** were carried out in a mixture of trifluoroacetic acid–methylene chloride (1:1 (v/v)) and, in the case of **3a** only, in CH_3COOH, CF_3COOH, and $(CF_3)_2CHOH$ solutions. The rearrangement was followed by means of ^{31}P NMR spectroscopy. Products **4** were isolated, after neutralization of the reaction mixture, by means of column chromatography. All starting **3** and products of their rearrangement (**4**) were chromatographically pure compounds and their characteristics, as well as reaction conditions, are collected in Table I. Thiolo esters **4** were treated with aqueous KOH, and alkylthiols **5a** and **5b** were isolated. The optical purity and absolute configuration of **5a** were known from the literature[8,3a] and those of **5b** are tentatively assigned in this work (vide supra). Thus, the optical purity of **5a**, $[\alpha]^{20}_{436}$ −2.99° (neat), corresponds to 1.22% ee and that of **5b**, $[\alpha]^{20}_{436}$ +1.102 ± 0.005° (neat, deuterium content 87%), corresponds to 32.8% ee.

The cleavage of the P–S bond under the described conditions should, in principle, proceed without racemization at the carbon atom of the alkylthio group. This assumption was validated by the following cross-experiment: **5a** resulting from alkaline degradation of **4a** was condensed with 2-chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (**9**), and **4a′** obtained from this reaction was



9 **5a** **4a′**

shown to have the same optical rotation (as well as other colligative data) as the compound obtained from the **3a** → **4a** rearrangement. This result allowed us to draw a conclusion about the stereospecificity of the **3** → **4** conversion on the basis of the ratio of the optical purity of thiol **5** to that of corresponding substrate **3** (see the last column of Table I).

An inspection of Table I demonstrates that the thiono–thiolo rearrangement in trifluoroacetic acid proceeds with inversion of configuration accompanied by considerable racemization. However, the change of reaction medium to acetic acid strongly alters the stereochemistry of the investigated process, and the optical rotation of **4a** clearly shows that the rearrangement **3a** → **4a** performed in CH_3COOH solution occurs with 65.0% retention of configuration. The above results disfavor the protic-acid-catalyzed thiono–thiolo rearrangement of phosphorothioic acid esters as a route for stereospecific conversion of alcohols into corresponding alkylthiols. However, these results deliver the essential information about the mechanism of the **3** → **4** rearrangement. In our previous work[1] we have described the protic-acid-catalyzed rearrangement of *O*-(primary alkyl)phosphorothioates (-phosphinothioates), and by the choise of inappropriate model compounds we have limited protic-acid-catalyzed thiono–thiolo rearrangements to *O*-(primary alkyl) esters of phosphoro- (phosphino)thioic acids. We have found since[9] that secondary alkyl esters also isomerize under the influence of trifluoroacetic acid. Other highly ionizing media, like hexafluoro-2-propanol, also cause the rearrangement of 2-[(1-methylbenzyl)oxy]-2-thiono-5,5-di-

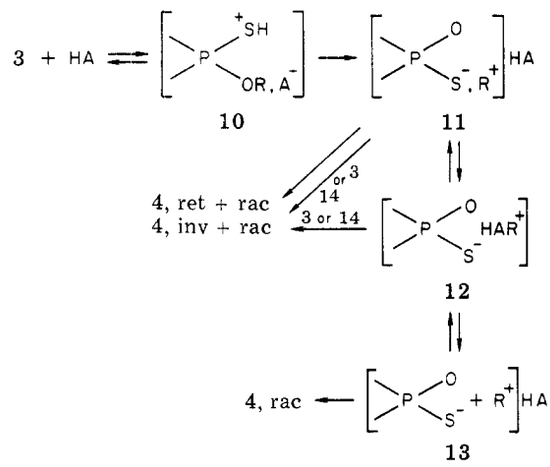
(8) M. Isola, E. Ciufarin, and L. Sagramora, *Synthesis*, 326 (1976); H. M. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, 1244 (1964).
(9) W. J. Stec and K. Bruzik, unpublished results.

Table I. Physical and Stereochemical Characteristics of 3 and the Product of Its Rearrangement (4)

migrating group R	reacn medium[a]	substrate 3			product 4				% stereospecificity of 3 → 4 convrsn
		absolute config	$[\alpha]^{20}_D$,[b] deg (optical purity, % ee)	mp, °C	absolute config	$[\alpha]^{20}_{436}$,[b] deg (optical purity, % ee)	mp, °C	% yield of 4	
PhCHD	CF_3COOH/CH_2Cl_2 (1:1 (v/v))	*R*	−0.25 ± 0.005 (56.3)[c]	43–44[i]	*S*	+0.182 ± 0.005[e] (32.8)[d]	70–72[j]	71	58.3[f] (inv)
$PhCH(CH_3)$	CF_3COOH/CH_2Cl_2 (1:1 (v/v))	*R*	+5.3 (16)	95–100[k]	*S*	−2.47[e] (1.22)	57–59[j]	85	7.6[g] (inv)
$PhCH(CH_3)$	CF_3COOH (0.1 M)	*R*	+33.1 (100)	102–103[k]	*S*	−7.03[e] (3.5)	56–58[j]	75	3.5[h,m] (inv)
$PhCH(CH_3)$	CH_3COOH (0.1 M)	*R*	+33.1 (100)	102–103[k]	*R*	+131.7[e] (65.0)	64–65[j]	56	65.0[h] (ret)
$PhCH(CH_3)$	$(CF_3)_2CHOH$ (0.2 M)	*R*	+33.1 (100)	102–103[k]	*S*	−0.5[e] (0.4)	58–60[j]	71	0.4[h] (inv)

[a] The reactions were carried out at 23 °C. [b] Optical rotations were measured in acetone solution. [c] Deuterium content 82.8%. [d] Deuterium content 83.4%. [e] Enantiomeric excess for **4a,b** is derived from % ee of **5a,b**. [f] Calculated as the ratio of the optical purity of **5b** to that of **1b**. [g] Calculated as the ratio of the optical purity of **5a** to the optical purity of **3a**. [h] Calculated as the ratio of the optical purity of **4a** to the optical purity of **3a**. [i] $\delta_{^{31}P} = +61.6$ ($CHCl_3$). [j] $\delta_{^{31}P} = +59.6$ ($CHCl_3$). [k] $\delta_{^{31}P} = +19.6$ ($CHCl_3$). [m] We have found that **4a** racemizes in CF_3COOH medium (concentration 0.05 M) at 22.4 °C with the rate constant $k_{rac} = 8.3 \times 10^{-5}$. Because $k_{rearr} >> k_{rac}$ the influence of the product racemization on the stereospecificity of **3a** → **4a** rearrangement may be neglected.

Scheme III



methyl-1,3,2-dioxaphosphorinane [(*R*)-(+)-**3a**)] to its (1-methylbenzyl)thio isomer [(*S*)-(−)-**4a**)], and this process is accompanied by a very high degree of racemization (0.4% net inversion). These results can not be rationalized in terms of previously proposed S_N2-type mechanisms.[1] As pointed out in our earlier work,[1] the first step most probably involves the proton transfer toward the sulfur atom of the phosphorothioyl moiety.[10] S-protonated species **10** possess strong alkylating properties toward unprotonated phosphorothionates and in the case of primary alkyl esters, e.g., $(EtO)_3PS$ and $(MeO)_3PS$, an intermolecular character of alkyl transfer has been demonstrated.[1] However, this mechanistic pathway, when applied to **4a** and **4b**, should result in inversion of configuration at the carbon atom of the migrating alkyl group. The diverse stereospecificity as well as the pronounced influence of the reaction medium on the stereochemistry of the thiono–thiolo rearrangement speak strongly for a dissociative-type mechanism, most probably involving ion-pair intermediates **11**, **12**, and **13** (Scheme III).

In CF_3COOH and in CF_3COOH/CH_2Cl_2 media, due to strong solvation of the leaving group,[11] nucleophilic attack of either the dialkylphosphorothioate anion >POS$^-$ (**14**) or the unprotonated *O*-alkylphosphorothioate **3** occurs most probably from the rear side of the ion pair, resulting in predominant inversion at the carbon of the migrating alkyl group. The known lower tendency of the benzyl group, as compared with the methylbenzyl group, to form a carbonium ion[12] explains the higher degree of racemization of **4a** over that of **4b**.

The change of the solvent to acetic acid causes the formation of a tight ion pair (**11**), and the product results either solely from recombination of **11** or from competition between predominant recombination of the ion pair **11** and nucleophilic attack of **3**/**14** from the rear side of the ion pair. Such a reaction pathway must occur with retention accompanied by racemization.[13]

Further arguments speaking for the ion-pair mechanism (solvolysis, elimination, skeletal rearrangement of the migrating alkyl group) of protic-acid-catalyzed thiono–thiolo rearrangement will be published.

Experimental Section

All melting and boiling points are uncorrected. Solvents and commercial reagents were distilled and dried by conventional methods before use. Methylene chloride was rigorously purified as described by Cheradame and Sigwalt[14] and was stored in sealed ampules over a sodium mirror. Commercial trifluoroacetic acid (Fluka) was refluxed for 24 h in the presence of 10 wt % of trifluoroacetic anhydride and its rectification on a spinning-band column was followed by distillation through a 30-in. helix-packed column. Acetic acid was refluxed for 7 days with the 10 wt % of acetic anhydride and distilled through a 30-in. helix-packed column. Both acids were stored under vacuum to avoid contact with moisture. Hexafluoro-2-propanol (Merck) was rectified on a helix-packed column and was stored in a sealed ampule.

^1H NMR spectra were recorded at 60 MHz with a Perkin-Elmer R12B spectrometer. ^{31}P NMR spectra were obtained on a JEOL FX-60 spectrometer operating at 24.3 MHz with external H_3PO_4 as the reference. Negative chemical shifts are assigned for compounds absorbing at higher field than H_3PO_4. Mass spectra were obtained on an LKB-2091 spectrometer at a 70-eV ionizing energy. GC analyses were performed on a Varian Aerograph 1520 chromatograph. Product purities were also determined by TLC (silica gel F_{254}, standard glass plates). Optical activity measurements were made with a Perkin-Elmer 241 MC photopolarimeter. In the cases of compounds possessing low optical rotations the reported values of rotation are the mean values of at least ten repetitive readings. Measurements of deuterium content in labeled compounds were accomplished by using mass fragmentography.[15]

Starting Materials. 2-Chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane (**2**) and 2-chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (**9**) were obtained according to methods described in the literature.[16]

1-Methylbenzyl alcohol (1a) was resolved into enantiomers by the method of Kenyon and Downer:[3a] (*S*)-(−)-**1a**, $[\alpha]^{20}_D$ −44.1° (neat), pure enantiomer; (*R*)-(+)-**1a**, $[\alpha]^{20}_D$ +25.4° (neat), 57.6% ee.

(*R*)-(−)-Benzyl-1-*d* alcohol (1b) was prepared from benzaldehyde-1-*d*[4] via its asymmetric reduction with (isobornyloxy)magnesium bromide. Its isolation and purification were performed in a way slightly different from that described by Streitwieser.[4] Steam distillation was applied for removal of isoborneol and camphor from the crude reaction mixture. The distillate was treated with K_2CO_3 and extracted with ether. The organic layer was dried over anhydrous $MgSO_4$, and solvent was evaporated. Purification was carried out by means of column chromatography on silica gel (100–200 mesh; benzene–acetone–chloroform–*n*-hexane, 9:1:1:9 developing system). Distillation gave chromatographically pure (GC assay) **1b**: bp 77 °C (5 mm); $[\alpha]^{20}_D$ −0.729 ± 0.005°; 56.3% ee; yield 4.9 g (33%); deuterium content 82%, MS M$^+$· *m*/*z* 109 (100%).

(*R*)-(+)-2-[(1-Methylbenzyl)oxy]-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane (3a). To the solution of **2** (11 g, 0.0653 mol) in benzene (150 mL) a mixture of triethylamine (8 g, 0.08 mol) and (*R*)-(+)-1-methylbenzyl alcohol (**1a**, 8 g, 0.0655 mol, $[\alpha]^{20}_D$ +5.3° (neat)) in benzene (50 mL) was added at 5 °C with vigorous stirring. Stirring was continued for 1 h. Triethylamine hydro-

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(13) The recombination of the ion pair with retention accompanied by racemization was demonstrated by R. A. Moss, *Acc. Chem. Res.*, **7**, 421 (1974).

(14) H. Cheradame, M. Mazza, Ng. A. Hung, and P. Sigwalt, *Eur. Polym. J.*, **9**, 375 (1973).

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(16) (a) R. S. Edmundson, *Tetrahedron*, **21**, 2379 (1965); (b) *Chem. Ind. (London)*, 1220 (1965).

chloride was filtered off and solvent was removed from the filtrate under reduced pressure. The crude product was distilled, yielding 2-[(1-methylbenzyl)oxy]-5,5-dimethyl-1,3,2-dioxaphosphorinane: 12 g (75%); bp 96–100 °C (0.01 mm). This compound was diluted with benzene (100 mL), and elemental sulfur was added with stirring at 10 °C. After 2 h the reaction with sulfur was completed (TLC assay). Solvent was evaporated and the residual solid was crystallized three times from ethyl ether to a constant optical rotation value: yield of (*R*)-(+)-**3a** 0.9 g (11%); mp 102–103 °C; $[\alpha]^{20}_D$ + 33.14° (*c* 6.3, acetone); MS $M^{+\cdot}$ *m/z* 286 (4.5%), base peak *m/z* 104.

Anal. Calcd for $C_{13}H_{19}O_3PS$: C, 54.5; H, 6.7; P, 10.8; S, 11.2. Found: C, 54.78; H, 7.04; P, 11.10; S, 10.80.

This product is assumed to have 100% optical purity. The assumption is proved by the synthesis of **3a** from optically pure alcohol (*S*)-(−)-**1a**, $[\alpha]^{20}_D$ −44.1° (neat). **3a** prepared from optically pure **1a** had an optical rotation value $[\alpha]^{20}_D$ −32.04° (*c* 10, acetone).

(*R*)-(−)-2-(Benzyloxy-1-*d*)-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane (3b). This compound was obtained in a way similar to that of **3a** but the isolation of the intermediate phosphite was omitted. After sulfur addition **3b** was purified by column chromatography on silica gel (benzene–*n*-heptane–acetone, 10:10:1). Starting from (*R*)-(−)-benzyl-1-*d* alcohol (3.6 g, 0.033 mol) pure **3b** (8.15 g, 90.5%; mp 43–44 °C, $[\alpha]^{20}_D$ −0.250 ± 0.005° (*c* 50, acetone); 56.3% ee) was obtained: deuterium content 82.8%, MS $M^{+\cdot}$ *m/z* 273 (29%), base peak *m/z* 92.

Anal. Calcd for $C_{12}H_{18}O_3PS$: C, 52.8; H, 6.5; P, 11.4. Found: C, 53.15; H, 6.53; P, 11.52.

(*S*)-(−)-2-[(1-Methylbenzyl)thio]-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (4a). (a) (*R*)-(+)-**3a** (10.5 g, 0.0367 mol; $[\alpha]^{20}_D$ +5.3° (*c* 14, acetone)) was placed in a flask connected with a vacuum line. CH_2Cl_2 (7.15 mL) and CF_3COOH (10.8 g, 7.15 mL) were introduced after evacuation. After 5 min at 23 °C solvent and an excess of CF_3COOH were evaporated under vacuum. The residue was dissolved in CH_2Cl_2, and gaseous NH_3 was introduced for neutralization of CF_3COOH involved in the complex of **4a** with CF_3COOH. The precipitate of ammonium trifluoroacetate was filtered off and an excess of NH_3 and solvent were removed. The crude product was purified on a column with silica gel (100–200 mesh, benzene–petroleum ether–acetone, 10:10:1, as eluent), yielding 8.9 g of an oily product which solidified when stored at room temperature: yield of **4a** 85%; mp 57–59 °C, $[\alpha]^{20}_{436}$ −2.47° (*c* 13, acetone); MS $M^{+\cdot}$ *m/z* 286 (15%), base peak *m/z* 105.

Anal. Calcd for $C_{13}H_{19}O_3PS$: C, 54.5; H, 6.7; P, 10.8; S, 11.2. Found: C, 54.21; H, 6.95; P, 11.15; S, 11.42.

(b) A solution of 153 mg of (*R*)-(+)-**3a**, $[\alpha]^{20}_D$ +33.14°, in 2.6 mL of hexafluoro-2-propanol was prepared under vacuum-line conditions. After 5 min at 23 °C, the solvent was removed under vacuum, and residual oil was treated with a solution of methylamine in benzene. The mixture was concentrated and pure phosphorothiolate **4a** was obtained after chromatography on silica gel: yield 108 mg (71%); mp 58–60 °C; $[\alpha]^{20}_{436}$ −0.5° (*c* 5, acetone); 0.4% ee.

(c) Finely powdered (*R*)-(+)-**3a** (500 mg, 1.76 mmol; $[\alpha]^{20}_D$ +33.14°) was dissolved in CF_3COOH (17.6 mL) at 23 °C under vacuum-line conditions. Solvent was then evaporated under vacuum and the residual oil was diluted with benzene. Gaseous dry ammonia was introduced into this solution, and after solvent removal the concentrated raw product was introduced on a silica gel column. The product (*S*)-(−)-**4a** was obtained in 70% yield (350 mg; $[\alpha]^{20}_{436}$ −7.03° (*c* 6, acetone); 3.5% ee).

(*R*)-(+)-2-[(1-Methylbenzyl)thio]-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (4a). A solution of (*R*)-(+)-**3a** (300 mg, 1.05 mmol; $[\alpha]^{20}_D$ +33.14°) in CH_3COOH (10.5 mL) was prepared in a 10-mm NMR tube under vacuum-line conditions and was kept at room temperature. The rearrangement progress was monitored by ^{31}P NMR spectroscopy. After 150 h 82% of **3a** → **4a** conversion was determined, CH_3COOH was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 and treated with an excess of gaseous ammonia. Crude product was purified chromatographically to give (*R*)-(+)-**4a**: 167 mg (56%); mp 64–65 °C; $[\alpha]^{20}_{436}$ +131.7° (*c* 2.5, acetone). Except for its optical rotation this product was identical with the sample of **4a** described above (^{31}P NMR, MS, TLC).

2-(Benzylthio-1-*d*)-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (4b). The rearrangement of **3b** → **4b** was performed essentially as described for **3a**. **3b** (8.0 g, 0.0294 mol) was dissolved in CH_2Cl_2 (6.7 mL) and CF_3COOH (10 g, 0.088 mol). A small part of the reaction mixture was transferred under vacuum into a 10-mm NMR tube. The rearrangement was followed by ^{31}P NMR spectroscopy. After 5 days at room temperature 96% conversion was established. The reaction was quenched as described for the conversion **3a** → **4a**. After column chromatography **4b** was isolated: 5.7 g (71%); mp 70–72 °C; $[\alpha]^{20}_{436}$ +0.182 ± 0.005° (*c* 50, acetone); deuterium content 83.4%; MS $M^{+\cdot}$ *m/z* 273 (40%), base peak *m/z* 92.

Anal. Calcd for $C_{12}H_{18}O_3PS$: C, 52.8; P, 11.36. Found: C, 53.05; P, 11.70.

Hydrolysis of 4a. **4a** (8.9 g, 0.031 mol) was treated under argon with aqueous KOH (12 g in 50 mL of water). The reaction mixture was heated for 1 h at 70 °C with vigorous stirring. After the mixture was cooled, an aqueous HCl solution was added to obtain pH 7. The product was extracted with ether and the organic layer after drying over anhydrous $MgSO_4$ was concentrated. The oily residue was distilled under reduced pressure yielding **5a**: 2.6 g (60%); bp 84–88 °C (17 mm); $[\alpha]^{20}_D$ −1.308°, $[\alpha]^{20}_{436}$ −2.99° (neat); 1.22% ee; MS $M^{+\cdot}$ *m/z* 138 (20%), base peak *m/z* 105.

Hydrolysis of 4b. Alkaline hydrolysis of **4b** (5.7 g, 0.0209 mol) with aqueous KOH (7 g in 50 mL of H_2O) gave **5b**: 1.27 g (49%); bp 70–72 °C (3 mm); $[\alpha]^{20}_{436}$ +1.102 ± 0.005° (neat); deuterium content 87%; 32.8% ee (calculated with the assumption that **5b** obtained via **1b** → **6** → **7** → **8** → **5b** possesses the same optical purity as starting **1b**); ^1H NMR δ 1.78 (dt, benzylthiol-1-*d*), 3.74 (dt, benzylthiol-1-*d*), 1.78 (t) and 3.69 (d) (signals of protons from 13% of nondeuterated benzylthiol), 7.34 (br s) ($^3J_{DCSH}$ = 1.1 Hz, $^3J_{HCSH}$ = 7.7 Hz, $^2J_{HCD}$ = 0.9 Hz).

Condensation of (*S*)-(−)-5a with 2-Chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (9). A solution of sodium (*S*)-(−)-(1-methylbenzyl)thiolate prepared from (*S*)-(−)-**5a** (1.55 g, 0.0112 mol; $[\alpha]^{20}_{436}$ −2.99° (neat)) and sodium hydride (0.3 g, 0.0125 mol) in THF (50 mL) was added dropwise at 5 °C to a soltuion of **9** (2.1 g, 0.0114 mol) in the same solvent (20 mL). The reaction was maintained at room temperature for 4 h, the excess of NaH and NaCl was centrifuged, and the clear reaction mixture was concentrated. The residue was chromatographed on silica gel. (*S*)-(−)-**4a** was obtained in 60% yield (1.9 g): mp 58–60 °C; $[\alpha]^{20}_{436}$ −2.45 ± 0.005° (*c* 14, acetone).

(*R*)-(−)-Benzyl-1-*d* Chloride (7). (*R*)-(−)-Benzyl-1-*d* alcohol (**1b**: 1.21 g, 0.0112 mol; $[\alpha]^{20}_D$ −0.729 ± 0.005°; deuterium content 82%) and benzyl alcohol (1.5 g, 0.0139 mol) were diluted with toluene (10 mL). The solution was added dropwise into toluene (50 mL) saturated with phosgene. A temperature of 0 °C was maintained. After 0.5 h an excess of phosgene and solvent were evaporated, yielding almost pure benzyl-1-*d* chloroformate (**6**) (GCMS assay) which was diluted with dioxane (20 mL), and the mixture was refluxed for 30 h. The progress of the decomposition of **6** was followed by means of GC. The solvent was distilled off through a Vigreaux column and **7** was isolated via distillation: bp 68–69 °C (15 mm); $[\alpha]^{20}_D$ −0.274 ± 0.005° (neat); deuterium content 36%; 2.58 g (82%); MS $M^{+\cdot}$ *m/z* 127 (13%), 129 (3.5%), 91 (base peak), 92 (65%).

(*S*)-(+)-*S*-Benzylisothiuronium-1-*d* Chloride (8) and Its Hydrolysis to (*S*)-(+)-Benzylthiol-1-*d* (5b). The isolated (*R*)-(−)-**7** (2.58 g, 0.0204 mol) and thiourea (1.55 g, 0.0204 mol) in absolute ethanol (10 mL) were heated under reflux during 1 h. Solvent was evaporated, the solid residue was washed twice with ether, giving **8** (3.9 g, 94%; mp 170–173 °C; $[\alpha]^{20}_D$ +0.175 ± 0.005° (*c* 34, ethanol)) which was added into 1.5 N Na_2CO_3 (50 mL), and the mixture was heated at 70–80 °C for 1 h. Continuous extraction of the product with ether and the usual workup of the ethereal fraction gave **5b**: 0.8 g (33%); bp 73–75 °C (8 mm); $[\alpha]^{20}_{436}$ +0.695 ± 0.005° (neat); deuterium content 32%; MS $M^{+\cdot}$ *m/z* 125 (36%), 124 (39%), 91 (base peak), 92 (95%).

Attempts to Assign Optical Purity of (*S*)-(+)-Benzylthiol-1-*d* (5b). Into the solution of sodium benzylthiolate-1-*d* prepared from (*S*)-(+)-benzylthiol-1-*d* (125 mg, 1 mmol; $[\alpha]^{20}_D$ +0.506 ± 0.005° (neat)) and sodium (50 mg) in THF (10 mL) was added at ambient temperature with stirring a solution of (−)-2-methoxy-2-(trifluoromethyl)-2-phenylacetyl chloride[7] (280 mg, 1.1 mmol) in THF (5 mL). Stirring was continued for 12 h, the

precipitate of sodium chloride was centrifuged, and solvent was evaporated. The crude product was purified by means of preparative thin-layer chromatography on silica gel: yield 220 mg, oil (62%); $[\alpha]^{20}_D$ −122.1° (c 2.1, benzene); MS m/z 189 (base peak), 92 (60%); ^{1}H NMR (CD_3CN, external Me_4Si): 7.7 (br s), 7.44 (br s), 4.31 (br s), 3.64 (q). ^{1}H NMR spectra were also recorded in CCl_4, C_6D_6, $CDCl_3$, and CD_3COCD_3. In all cases we were unable to observe nonequivalence either of benzylic protons or of 2-methoxy protons in diastereoisomeric benzyl-*1-d*-MPTA thiolo esters.

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Registry No. (*S*)-(−)-**1a**, 1445-91-6; (*R*)-(+)-**1a**, 1517-69-7; (*R*)-(−)-**1b**, 4181-90-2; **2**, 2428-06-0; (*R*)-(+)-**3a**, 71719-69-2; (*R*)-(−)-**3b**, 71719-70-5; (*S*)-(−)-**4a**, 71719-71-6; (*R*)-(+)-**4a**, 71719-72-7; (*S*)-(+)-**4b**, 71719-73-8; (*S*)-(−)-**5a**, 33877-11-1; (*S*)-(+)-**5b**, 71719-74-9; (*R*)-(−)-**6**, 71719-75-0; (*R*)-(−)-**7**, 4181-91-3; (*S*)-(+)-**8**, 71719-76-1; **9**, 4090-55-5; (*R*)-(+)-2-[(1-methylbenzyl)oxy]-5,5-dimethyl-1,3,2-dioxaphosphorinane, 71719-77-2; (−)-2-methoxy-2-(trifluoromethyl)-2-phenylacetyl chloride, 39637-99-5; *S*-(phenylmethyl-*d*) α-methoxy-α-(trifluoromethyl)benzeneethanethioate, 71719-78-3; thiourea, 62-56-6.

Ruthenium-Catalyzed [2 + 2] Cross-Addition of Norbornene Derivatives and Dimethyl Acetylenedicarboxylate

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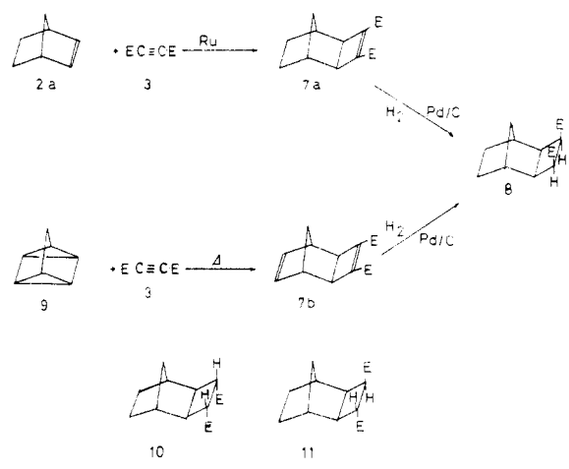
Bicyclo[2.2.1]hept-2-ene and its derivatives react with dimethyl acetylenedicarboxylate in the presence of ruthenium complex catalysts in benzene at 80–100 °C to give [2 + 2] cross adducts, *exo*-tricyclo[4.2.1.0^{2,5}]non-3-ene derivatives. $RuH_2(CO)[P(p\text{-}PhF)_3]_3$, $RuH_2(CO)(PPh_3)_3$, $RuH_2(PPh_3)_4$, and (cyclooctatriene)(cyclooctadiene)-ruthenium are effective catalysts. The reaction of 7-oxabicyclo[2.2.1]hept-2-enes affords 9-oxa-*exo*-tricyclo-[4.2.1.0^{2,5}]non-3-enes. The 1:2 mixture of cyclopentadiene or furan derivatives and dimethyl acetylenedicarboxylate also gives the corresponding tricyclo[4.2.1.0^{2,5}]nonene derivatives in the presence of the catalysts. Novel linear hexa- and heptacyclo compounds were prepared by using this reaction.

Two plus two cycloaddition of olefins and/or acetylenes is a valuable route to cyclobutane derivatives. The reaction is formally envisaged as a thermally forbidden process,[1] and the reaction is achieved photochemically[2] or by the use of transition-metal catalysts.[3]

As for the [2 + 2] cross-addition of olefins with acetylenes, inefficient photoaddition of bicyclo[2.2.1]hept-2-ene (norbornene) with dimethyl acetylenedicarboxylate[2e] (yield <10%) and a transition-metal-catalyzed addition of norborna*diene* with acetylenes[3c] have been reported. Thus there have been no reports on the efficient [2 + 2] cross-addition of norbornene with acetylenes.

On the other hand, ruthenium complexes are well-known to be excellent catalysts for hydrogen transfer reactions;[4] however, there have been only a few reports on catalytic carbon–carbon bond formation: e.g., carbonylation of olefins or acetylenes,[5] telomerization of olefins with alkyl halides,[6] polymerization and oligomerization of olefins[7] or acetylenes,[8] and homologation of methyl acetate.[9]

Scheme I



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