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Alkylthiylation of triquinphosphoranes by disulfides: an entry to chiral thiatriquinphosphoranes

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Abstract

Triquinphosphoranes **1** undergo alkylthiylation reactions, even in the dark, with methyl and *n*-butyl disulfides to give the corresponding thiaphosphoranes with high yields. Chiral triquinphosphorane **2**, by this reaction, gives rise to chiral thiatriquinphosphorane **4**. The reaction with *t*-BuSSBu-*t* preferably gave the thiophosphoramide. An increased reactivity was observed when the experiments were conducted under UV irradiation. © 2000 Elsevier Science Ltd. All rights reserved.

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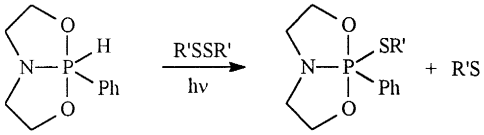
Hydridophosphoranes can be prepared by an exchange reaction involving alcoholysis or aminolysis of the P^{III}–OR or P^{III}–NR_2 bonds.[1] Under UV- or X-irradiation, they could give phosphoranyl radicals, the structure of which has been extensively investigated.[2] These radicals were suggested to be intermediates in the reaction of hydridophosphoranes with free radicals, such as alkoxy, alkyl or, more recently, alkylthiyl radicals.[3] Indeed, Bentrude et al. have shown that a bicyclic phenylhydridophosphorane undergoes UV-light-induced alkylthiylation reactions with a series of alkyl disulfides (R′SSR′, R′=Me, *n*-Bu, neopentyl, *sec*-Bu and *t*-Bu) to give the corresponding isolable thiaphosphoranes in high yield (61–100%, except for *t*-BuSSBu-*t*) (Scheme 1). The reactivity of phosphoranyl radicals toward disulfides was demonstrated to depend both on steric factors and on the sulfur–sulfur bond strength.



Scheme 1.

As far as we are aware, chiral hydridophosphoranes[4] have not yet been reacted with alkyl disulfides. We previously reported the synthesis of a new class of chiral tricyclic hydridophosphoranes, the triquin-

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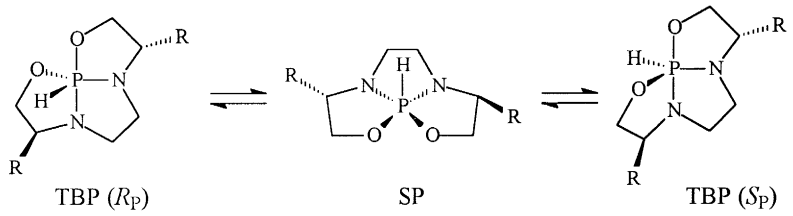
phosphoranes, from chiral enantiopure diaminodiols that present a C_2 symmetry axis.[5] We showed that the structure of these phosphoranes is best represented by two trigonal bipyramids (TBP) with opposite absolute configurations at the phosphorus atom, R_P and S_P, in fast equilibrium by a Berry pseudorotation process via a square pyramid (SP) transition state (Scheme 2).[4b]

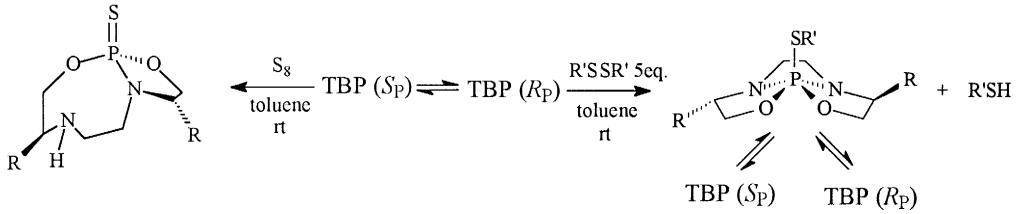


1 : R=H; **2** : R=Bn

Scheme 2.

We wish now to report the first addition of various alkyl disulfides to the parent triquinphosphorane **1** (R=H) and to the chiral triquinphosphorane **2** (R=Bn).[6]

The triquinphosphorane **1** (R=H) reacted rapidly with methyl disulfide, at room temperature in toluene solution, to give the methylthiophosphorane **3a** in a good yield (70% after distillation) (Scheme 3).[7] ^{31}P NMR monitoring of the reaction showed after 7 min the disappearance of the hydridophosphorane highfield signal at −37.3 ppm and of the $^{1}J_{P-H}$ coupling, together with the appearance of a signal at −14.3 ppm, which suggests the conservation of the pentacoordinated structure. The spectral data were in accordance either with an achiral SP structure or with two enantiomeric TBP in fast equilibrium. The same reaction was conducted with *n*-butyl disulfide and *t*-butyl disulfide. Although reaction times were increased up to several hours, we obtained *n*-butylthiaphosphorane **3b** and *t*-butylthiaphosphorane **3c**, characterised by their ^{31}P NMR signals at −14.3 and −12.5 ppm, respectively. In the latter case, *t*-butylthiaphosphorane **3c** was only a minor product of the reaction. The major compound, exhibiting a ^{31}P NMR signal at 53.9 ppm, was identified as the thiophosphoramide **5**.[8] Compound **3c** could be obtained in a 80% chemical yield, by reacting triquinphosphorane **1** with *t*-butyl disulfide under irradiation, for 24 h at −50°C.[9] When raising the solution temperature, we observed a slow transformation of **3c** into **5**. A similar evolution was observed by Bentrude with the bicyclic phenylhydridophosphorane (Scheme 1) and *t*-BuSSBu-*t*.[3b] We propose a mechanism for this fragmentation (Scheme 4), that should proceed via a cyclic six-membered transition state (Ei mechanism), in which the basic apical nitrogen atom abstracts the β-hydrogen atom of *t*-Bu group to afford isobutene and **5**.



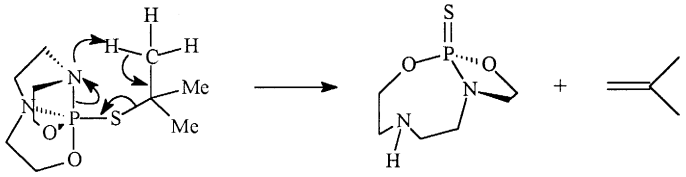
5 : R=H

1 : R=H
2 : R=Bn

3a : R=H, R'=Me
3b : R=H, R'=*n*-Bu
3c : R=H, R'=*t*-Bu
4 : R=Bn, R'= Me

Scheme 3.

Chiral triquinphosphorane **2** was reacted with methyl disulfide in the absence of irradiation. Probably because of the steric hindrance of the two benzyl substituents, the reaction required 44 h to go to



Scheme 4.

completion instead of a few min in the case of the parent compound **1**. As previously observed, ^{31}P NMR spectrum showed the disappearance of the hydridophosphorane signal at −36.7 ppm and the loss of the $^{1}J_{P-H}$ coupling, together with the appearance of a signal at −12.9 ppm (Scheme 3). The NMR data for compound **4** are consistent either with an enantiopure SP or with the diastereomeric TBP in fast equilibrium.[10] As already observed by Bentrude et al.,[3b] steric strains seem to play an important role in the reactivity of triquinphosphoranes toward alkyl disulfides, requiring increased reaction times.

Then we compared the reactivity of the parent triquinphosphorane **1** with alkyl disulfides under irradiation and in the dark at room temperature for 7 min (Table 1).

Table 1
Comparison of the reactivity of **1** varying the conditions of light[a]

Entry	Alkyl disulfide	Without light[b]		Under irradiation[c]	
		Yield (%)[d]	^{31}P NMR (ppm)	Yield (%)[d]	^{31}P NMR (ppm)
1	MeSSMe	100	-14.3	100	-14.3
2	*n*-BuSSBu-*n*	20	-14.3	100	-14.3
3	*t*-BuSSBu-*t*	-	-	80	-12.5, 53.9

a : 7 min., r.t., toluene. b : these reactions were realised with a protection from any light. c : see ref. 10. d : yields were determined by integration of the ^{31}P NMR signals.

In the case of methyl disulfide (entry 1), a rapid reaction occurred in these conditions, even in the dark. In contrast, in the case of *n*-butyl disulfide (entry 2) and *t*-butyl disulfide (entry 3), we observed a significant increase of the reactivity when the reactions were conducted under irradiation. These results strongly suggest that the alkylthiylation of triquinphosphoranes does involve free radical species.

Since we previously demonstrated that chiral triquinphosphoranes can undergo asymmetric discrimination,[4] discrimination of the enantiomers of unsymmetrical disulfides such as MeSSR* is currently investigated.

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6. Triquinphosphoranes **1**: 2,11-dioxa-5,8-diaza-1λ^5-phosphatricyclo[6.3.0.0^{1,5}]undecane and **2**: (4*S*,9*S*)-4,9-dibenzyl-2,11-dioxa-5,8-diaza-1λ^5-phosphatricyclo[6.3.0.0^{1,5}]undecane were synthesised from diaminodiols *N*,*N*′-(bis(hydroxyethyl)-ethylenediamine and (2*S*,7*S*)-2,7-dibenzyl-3,6-diazaocta-1,8-diol, respectively, see: Ref. 4b.
7. Compound **3a**: yield: 70%, b.p.145°C/0.01 mmHg, ^{1}H NMR (C_7D_8): δ 3.80–3.50 (m, 4H, CH_2O), 2.90–2.40 (m, 8H, CH_2N), 2.12 (d, $^3J_{P-H}$=14.7 Hz, 3H, CH_3S), ^{13}C NMR (C_7D_8): δ 59.4 (d, $^2J_{P-C}$=2.3 Hz, CH_2O), 45.0 (d, $^2J_{P-C}$=13.4 Hz, CH_2N), 43.9 (d, $^2J_{P-C}$=11.3 Hz, CH_2N), 15.6 (d, $^2J_{P-C}$=5.6 Hz, CH_3S), ^{31}P NMR (C_7D_8): δ −14.3 ppm.
8. Treatment of phosphorane **1** with S_8 gave directly compound **5**: crystallised from benzene, yield: 90%, m.p. 148°C, elemental analysis for $C_6H_{13}N_2O_2PS$: calcd: C 34.61, H 6.29, N 13.45, found: C 34.94, H 6.63, N 13.01. IR: 3360 cm^{-1}, ^{1}H NMR (C_7D_8, 400 MHz): δ 4.24–4.10 (m, 3H, CH_2O), 4.09–3.95 (m, 1H, CH_2O), 3.38–3.22 (m, 5H, CH_2N), 3.07–2.94 (m, 1H, CH_2N), 2.60–2.51 (m, 2H, CH_2N), 2.46 (s, 1H, NH), ^{13}C NMR (C_7D_8): δ 66.7 (d, $^2J_{P-C}$=7.9 Hz, CH_2O), 62.8 (d, $^2J_{P-C}$=1.8 Hz, CH_2O), 48.8 (d, $^3J_{P-C}$=3.0 Hz, CH_2N), 48.3 (d, $^2J_{P-C}$=14.7 Hz, CH_2N), 47.5 (d, $^3J_{P-C}$=4.0 Hz, CH_2N), 46.6 (d, $^2J_{P-C}$=1.9 Hz, CH_2N), ^{31}P NMR (C_7D_8): δ 53.9 ppm.
9. Original Hanau system, with a Hg lamp.
10. Compound **4**: yield: 90%, colourless oil. IR: 3400, 3061–2929, 1604, 1495, 1455, 1034, 794, 734, 700, 638 cm^{-1}, ^{1}H NMR ($CDCl_3$): δ 3.87 (dd, J_{H-H}=6.63 Hz, J_{H-H}=8.88 Hz, 1H, CHN), 3.72 (dd, J_{H-H}=6.67 Hz, J_{H-H}=8.88 Hz, 1H, CHN), 3.61–3.51 (m, 4H, CH_2O), 3.06–2.64 (m, 4H, CH_2N), 2.59–2.40 (m, 4H, CH_2Ph), 2.25 (s, 3H, CH_3S), ^{13}C NMR ($CDCl_3$): δ 138.0, 137.7, 129.0, 128.9, 128.4, 128.3, 128.1 (12C, ArC), 64.9 (d, $^2J_{P-C}$=2.5 Hz, CH_2O), 63.3 (CH_2O), 59.7 (d, $^2J_{P-C}$=7.7 Hz, CHN), 53.8 (d, $^2J_{P-C}$=16.0 Hz, CHN), 44.7 (d, $^2J_{P-C}$=5.9 Hz, CH_2N), 41.5 (d, $^2J_{P-C}$=10.5 Hz, CH_2N), 40.4 (CH_2Ph), 39.7 (d, $^2J_{P-C}$=5.7 Hz, CH_2Ph), 15.3 (d, $^2J_{P-C}$=5.7 Hz, CH_3S), ^{31}P NMR ($CDCl_3$): δ −12.9 ppm, $[\alpha]_D^{20}$=+39.8 (*c* 1.29, $CHCl_3$).