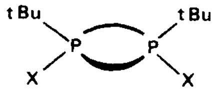
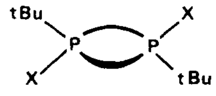
the chiral phosphorus center. Molecule **3** itself was not isolated but its thiono methoxy derivative was characterized by the usual techniques (elemental analysis; ^{1}H, ^{13}C, ^{31}P NMR spectra; mass spectrometry). After completion of the dithiol addition, the reaction mixture exhibits in the ^{31}P (^{1}H) NMR spectrum the following peaks, where the chemical shifts are given in parts per million downfield from H_3PO_4 as the external reference: M (97.3), D$_2$ (104.0), P (115.5), D$_1$ (121.0 ppm).

A silica column chromatography performed under nitrogen of the final reaction mixture using hexane–benzene (3:1) as eluent allows separation of a first and third pure fraction, each showing one peak in the ^{31}P (^{1}H) NMR spectrum, D$_1$ (121.0) and M (97.3 ppm), respectively. A second fraction shows two peaks at D$_2$ (104.0) and M (97.3 ppm).

By NMR spectral analysis (^{1}H, ^{13}C, ^{31}P) (Tables I and II), elemental analysis, and mass spectrometry, the species corresponding to peaks M, D$_1$, and D$_2$ are unambiguously assigned to 2-*tert*-butyl-1,3,2-dithiaphosphorinane (**1**) and the corresponding twelve-membered-ring dimers **2** and **2′** (mp 119–121 °C), respectively. These dimers differ by the relative orientation of the *tert*-butyl group with respect to the mean plane of the molecule. Up to now, we have been unsuccessful in obtaining a pure sample of **2**, which is always contaminated by **1**. Peak P (115.5 ppm) corresponds to higher polymeric species which are now under investigation.



2, X = lone pair
2S, X = S

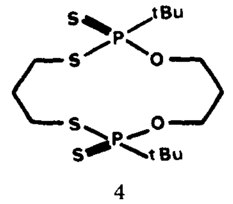


2′, X = lone pair
2′S, X = S

Addition of elemental sulfur[7] to a mixture containing **1**, **2**, and **2′** gives rise to the expected thiono derivatives **1S** (mp 77–78 °C), **2S** (mp 162–164 °C), and **2′S** (mp 250–252 °C). These compounds, separated by silica column chromatography with benzene as eluent, have been characterized by elemental analysis, mass spectroscopy, molecular weight measurement (osmometry), and ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy (Tables I and II). In the ^{1}H NMR spectrum, the protons attached to carbons 5 and 5′ are equivalent in **2′S** and nonequivalent in **2S**. Thus, **2′** and **2′S** correspond to the stereoisomers in which the *tert*-butyl groups are in a trans relationship with respect to the mean plane of the twelve-membered ring (presence of an inversion center i).

When a solution of pure dimer **2′** is left in a sealed NMR tube, it shows additional ^{31}P NMR peaks which appear with time. After a few hours at 80 °C, a mixture of both isomers **2** and **2′** is observed. If the tube is heated at 160 °C, a mixture of the two dimers **2** and **2′** (3:1) with the monomeric species **1** is obtained. The equilibrium ratio of the three species **2′**, **2**, and **1** at 160 °C is 3:1:6. A mixture of the species **2** and **1** leads to a similar equilibrium. Thus, the trans isomer **2′** is thermodynamically more stable than **2**. Different kinetics rates are obtained in nonsealed tubes, probably owing to the presence of catalytic reagents which accelerate the reaction.

Besides the synthesis of a new category of heterocyclic phosphorus molecules, one of the interesting point of the reaction described in this paper is the existence of **3** as a stable intermediate. Thus **3** can react with various difunctional compounds (diols, diamines, dithiols, etc.) leading to various large-membered-ring molecules. As an example, the twelve-membered-ring **4** has been prepared.



4

The synthesis of various rings which differ by the size (11, 12, 13) and the nature of their heteroatoms is being actively continued.

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(8) Faculty member of the Université Scientifique et Médicale de Grenoble.

Jean-Pierre Dutasta, Jean Martin
Jean-Bernard Robert*[8]
Laboratoire de Chimie Organique Physique
Département de Recherche Fondamentale
Centre d'Etudes Nucléaires de Grenoble 85 X
F.38041 Grenoble Cedex, France

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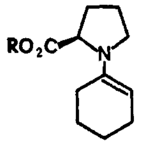
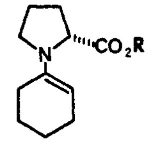
Asymmetric Induction. 2.[1] Enantioselective Alkylation of Cyclohexanone via a Chiral Enamine[†]

Summary: Asymmetric induction was observed in the alkylation of the cyclohexanone enamine prepared from (+)-*trans*-2,5-dimethylpyrrolidine. Alkylation with methyl iodide, *n*-propyl bromide, and allyl bromide afforded the corresponding 2-*n*-alkylcyclohexanones with optical purities of 83, 93, and 82%, respectively. Very low levels of dialkylation product formation were observed.

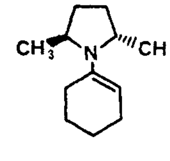
Sir: In 1968 Horeau published[2] the first enantioselective alkylation of a ketone, using the imine anion derived from isobornylamine and cyclohexanone. Recent modifications to this scheme have raised the enantiomeric ratio to greater than 9:1.[1,3] We wish to report here a complementary technique that affords similarly high degrees of enantioselectivity in the alkylation of enamines.



A



B



1

In 1969 Yamada reported[4] the first in a series of investigations[5] of the alkylation of the chiral enamines formed using various proline esters, and though the best optical yield obtained was 55%, the more typical values fell in the range from 10 to 30%. These results, taken together, are consistent with the participation of two sets of transition states differing by geometrical isomerization (represented by A and B). Of the four transition states resulting from the distinct pathways of approach of the alkylating agent (back and front on both A

[†] We wish to dedicate this paper to Professor Robert Burns Woodward on the occasion of his sixtieth birthday.

Table I

Alkylating Agent	Chemical[a] yield, %	% dialkylation[b]	$[\alpha]^{25}_{D}$ (*c*, MeOH)[c,d]	Lit. $[\alpha]^{25}_{D}$ (*c*, MeOH)	Optical purity, %
CH_3I	50 (24)	6	+11.6° (2.7)	14.0° (0.23)[10]	83
$CH_3CH_2CH_2I$	57	7	+25.9° (1.4)	−27.9° (4.5)[11]	93
$CH_2{=}CHCH_2Br$	80	4	+11.2° (1.5)	13.7° (2.2)[11]	82

[a] VPC yield, based on the crude enamine (isolated yield). [b] The extent of dialkylation was determined at conversions of greater than 90%. [c] Measured with a Perkin-Elmer Model 151 polarimeter using samples carefully purified by preparative GLC to ensure the absence of dialkylation products. Values of −11.7° for 2-methylcyclohexanone and −25.8° for 2-*n*-propylcyclohexanone were obtained using the (−) amine. [d] All of the alkylcyclohexanones were produced with the same absolute chiral sense.

and B), the carboxyl moiety would be expected to exert a significant steric interaction in only one (back on B). Assuming nearly equivalent energies for the three remaining transition states leads to the prediction that induction in this system would be limited to an enantiomeric excess of around 2:1 (34% ee). Clearly what is needed is an amine with a C_2 axis of symmetry.

In the event, the enamine **1**, derived from (+)-*trans*-2,5-dimethylpyrrolidine[6,7] and cyclohexanone,[9] underwent smooth alkylation with excess methyl iodide in refluxing acetonitrile to afford, after hydrolysis in a two-phase system consisting of pentane and buffered, aqueous acetic acid, (*S*)-2-methylcyclohexanone with an optical purity of 83%. Other results are tabulated in Table I.

With the hope of implementing this technique for the enantioselective formation of quaternary centers, we prepared the analogous enamine from racemic 2-methylcyclohexanone. Unfortunately, and contrary to a published report,[12] we found this enamine to be at least 90% the less substituted isomer, and in fact saw no evidence indicating the presence of the more substituted enamine. Hydrolysis as above provided 2-methylcyclohexanone with no measurable rotation.[13]

There appear to exist, a priori, three distinct mechanisms of induction which would explain our observed results.

(I) Both diastereomeric immonium ions are being formed in a relatively nonselective alkylation, with a subsequent, selective hydrolysis providing enantioselectivity by kinetic resolution.

(II) Unselective formation of the immonium ions, as above, with subsequent equilibration under the conditions of alkylation forming predominently one of the diastereomeric ions.

(III) Kinetic control at the point of alkylation affording mainly one of the immonium ions.

The high material balance in the alkylations with propyl iodide (80%) and allyl bromide (99%), as well as the lack of optical activity in the methylcyclohexanone recovered from the hydrolysis of the enamine, preclude the operation of a kinetic resolution (I). The latter experiment is also inconsistent with the second rationale insofar as it is clear that both diastereomeric immonium ions must have been present in this hydrolysis, and were not interconverted under those conditions. We thus conclude that we are observing the result of an enantioselective alkylation.

We would also like to draw attention to the low level of dialkylation products obtained, even at the high level of conversion (greater than 90%) to which these alkylations were taken. These results compare quite favorably with the best heretofore observed.[14]

We are currently pursuing other uses of this enantioselective alkylation as well as a variety of other asymmetric induction schemes using *trans*-2,5-dimethylpyrollidine.

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James K. Whitesell,* Steven W. Felman
Department of Chemistry
University of Texas at Austin, Austin, Texas 78712

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2-Ethoxyallylidene Triphenylphosphorane. A New Reagent for Cyclohexenone Annulation

Summary. 2-Ethoxyallylidene triphenylphosphorane is a new, convenient reagent for the annulation of cyclohexenones onto a variety of α,β-unsaturated ketones, thereby allowing the construction of monocyclic, fused bicyclic, and spiro bicyclic ring systems.

Sir: The Robinson annulation reaction and the many variants thereof are extraordinarily useful synthetic reactions for the construction of a cyclohexenone ring onto an extant ketone.[1] Most of these procedures involve the combination of a two-carbon structural unit with another possessing four carbon atoms (**1** → **3**), but there is an unfortunate lack of synthetic