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.

Acknowledgment is gratefully made to the Robert A. Welch Foundation, the Research Corporation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this research.

References and Notes

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(6) This amine was prepared by catalytic reduction[7] of the *N*-amino derivative,[8] and resolved via the salts with mandelic acid. Clearly distinct methyl adsorptions were observed in the ^1H NMR for the diastereomeric salts. The (+) amine, obtained with (−)-mandelic acid, had $[\alpha]^{25}_{D}$ +10.6° (*c* 1, EtOH), while the (−) amine, obtained using (+)-mandelic acid, had $[\alpha]^{25}_{D}$ −11.5°. Each amine was obtained from salts judged pure by NMR. The (+) amine is drawn with the *S,S* configuration based solely on the results of alkylation. A single-crystal x-ray analysis on the mandelic acid salt is currently underway.
(7) C. G. Overberger, L. C. Palmer, B. S. Marks, and N. R. Byrd, *J. Am. Chem. Soc.*, **77,** 4100 (1955).
(8) P. B. Dervan and T. Uyehara, *J. Am. Chem. Soc.*, **98,** 2003 (1976); we are indebted to Professor Dervan for a detailed experimental procedure for the preparation of the *N*-aminopyrrolidine.
(9) The formation of this enamine is impractically sluggish under most normal conditions. We have observed, however, that with type 3-Å molecular sieves, enamine formation is at least ten times faster than with 4-Å sieves.
(10) C. Beard, C. Djerassi, J. Sicher, F. Sipos, and M. Tichy, *Tetrahedron*, **19,** 919 (1963).
(11) K. Hiroi, K. Achiwa, and S. Yamada, *Chem. Pharm. Bull.*, **20,** 246 (1972).
(12) W. D. Gurowitz and M. A. Joseph, *J. Org. Chem.*, **32,** 3289 (1967).
(13) Enantiomeric excess 0 ± 1%; for an interesting, analogous case where induction was observed see H. Matsushita, M. Noguchi, and S. Yoshikawa, *Chem. Lett.*, 1313 (1975).
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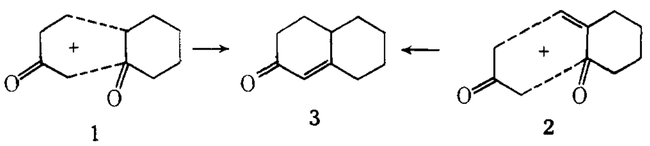
2-Ethoxyallylidene Triphenylphosphorane. A New Reagent for Cyclohexenone Annulation

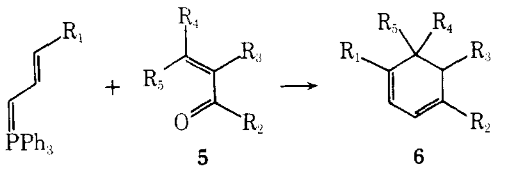
Summary. 2-Ethoxyallylidene triphenylphosphorane is a new, convenient reagent for the annulation of cyclohexenones onto a variety of α,β-unsaturated ketones, thereby allowing the construction of monocyclic, fused bicyclic, and spiro bicyclic ring systems.

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 methodology for the formation of cyclohexenones from two structural units, each containing three carbon atoms (2 → 3).[2]


1 3 2

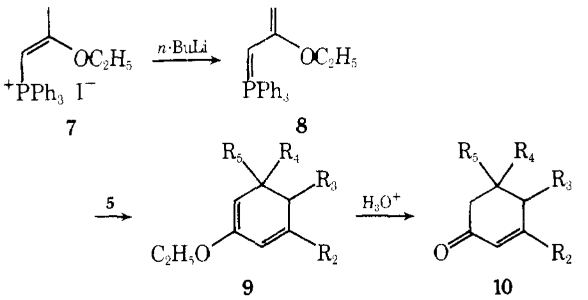
Moreover, virtually all of the procedures for the annulation of these six-membered rings produce cyclohexenones as the final step in an aldol–cyclodehydration sequence from 1,5-dicarbonyl compounds, and a wide variety of useful reagents and techniques have been developed for the homologation of the ketones 1 and the α,β-unsaturated ketones 2 to these crucial intermediates. Undoubtedly owing to the paucity of methodology for their preparation, 2-alkoxy-1,3-cyclohexadienes, which contain the enone moiety as a latent functional group, have rarely been employed as precursors to cyclohexenones.[3] Since 2-alkoxy-1,3-cyclohexadienes might also serve as useful dienes in Diels–Alder reactions[4] as well as masked cyclohexenones, a simple procedure for the annulation of such functionalized cyclohexadienes onto pre-existing ketones would possess considerable synthetic utility. Consequently, we now wish to report a general procedure for the facile construction of 2-alkoxy-1,3-cyclohexadienes from starting materials containing three carbon atoms and for their subsequent conversion in situ to cyclohexenones.

Recently simple allylidene triphenylphosphoranes 4 have been found to react with α,β-unsaturated ketones 5 to give substituted cyclohexadienes 6 (eq 1).[5,6] We reasoned, therefore, that the introduction of a heteroatom substituent such as an alkoxy group onto the allylidene phosphorane would allow the construction of alkoxy-functionalized cyclohexadienes which would afford cyclohexenones upon acid-catalyzed hydrolysis.



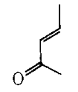
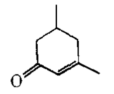
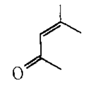
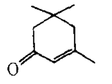
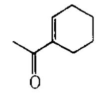
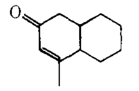
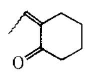
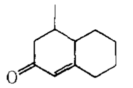
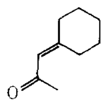
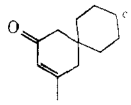
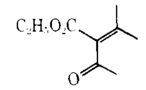
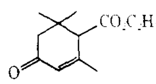
4 5 6 (1)

Although there are no known alkoxyallylidene triphenylphosphoranes, we found that 2-ethoxyallylidene triphenylphosphorane (8) could be easily generated by treating (2-ethoxy-1-propenyl)triphenylphosphonium iodide (7)[7] with n-butyllithium. This new functionalized allylidene triphenylphosphorane was found to react smoothly with a variety of structurally different α,β-unsaturated ketones 5 to give, upon acid-catalyzed hydrolysis of the intermediate 2-ethoxy-1,3-cyclohexadienes 9, the cyclohexenones 10[8] (eq 2) in generally fair to good overall yields (Table I). An examination of the entries in Table I reveals that this synthetic procedure, which may be conveniently executed without the isolation of the intermediate 2-ethoxy-1,3-cyclohexadienes 9, may be employed for the construction of monocyclic, fused bicyclic, and spiro bicyclic ring systems. Moreover, since 4-carboethoxy-3,5,5-trimethylcyclohexenone (see entry 6) has recently been used as an intermediate in the synthesis of α-damascones,[9] the potential application of this new synthetic methodology to the total synthesis of natural products is readily apparent.



7 8 9 10 (2)

Table I. Annulation of Cyclohexenones

Entry	Starting enone 5	Product cyclohexenone 10[a]	% yield[b]
1			48
2			61
3			34
4			36
5		[c]	56
6			26

[a] All compounds gave satisfactory IR, MS, and NMR spectral data. [b] Overall yield based on starting enone 5, but not optimized. [c] Exact mass calcd for $C_{12}H_{18}O$, 178.1358. Found, 178.1354.

The following experimental procedure is representative of this conversion. To a well-stirred suspension of the phosphonium salt 7 (15 mmol) in anhydrous THF (75 mL) cooled to −50 °C under dry nitrogen, n-butyllithium in hexane (15 mmol) was slowly added. When the addition had been completed, the red-orange mixture was allowed to warm to about −25 °C, and the stirring was continued at that temperature for 2 h. After the solution of the allylidene phosphorane 8 was again cooled to −50 °C, a solution of the appropriate α,β-unsaturated ketone 5 (10 mmol) in anhydrous THF (5 mL) was added slowly dropwise. The resulting orange-brown reaction mixture was then stirred at room temperature for 18 h, whereupon 1 N HCl (75 mL) was added and the mixture stirred vigorously at room temperature for an additional 6 h. The crude cyclohexenones 10 were isolated by an extractive work-up and purified by vacuum distillation.

Further investigations to explore the synthetic utility of this and other functionalized allylidene triphenylphosphoranes are under active investigation and will be reported independently.

Acknowledgment. We wish to thank the Robert A. Welch Foundation for partial support of this work.

References and Notes

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(2) For some examples of methods for the construction of functionalized cyclohexanones from two three carbon structural units, see (a) A. V. Logan, E. N. Marvell, R. La Pore, and D. C. Bush, *J. Am. Chem. Soc.*, **76**, 4127 (1954); (b) Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, **38**, 3244 (1973); (c) G. Stork and J. d'Angelo, *J. Am. Chem. Soc.*, **96**, 7114 (1974); (d) D. J. Dunham and R. G. Lawton, *ibid.*, **93**, 2074 (1971); and (e) H. Stetter and K. Elfert, *Synthesis*, 36 (1974).

(3) On the other hand, 1-alkoxy-1,4-cyclohexadienes are readily available from aromatic ethers by dissolving metal reduction, and their subsequent conversion to cyclohexenones is well documented. For example, see (a) A. J. Birch, *J. Chem. Soc.*, 593 (1946); (b) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5360, 5366 (1953); and (c) H. L. Dryden, Jr., G. M. Webber, R. R. Burtner, and J. A. Cella, *J. Org. Chem.*, **26**, 3237 (1961).

(4) For related examples involving 1-alkoxy-1,3-cyclohexadienes, see (a) D. A. Evans, W. L. Scott, and L. K. Truesdale, *Tetrahedron Lett.*, 121 (1972); (b) A. J. Birch and K. P. Dastur, *ibid.*, 1009 (1974); and (c) R. G. F. Giles and G. H. P. Roos, *J. Chem. Soc., Perkin Trans. 1*, 2057 (1976).

(5) G. Büchi and H. Wüest, *Helv. Chim. Acta*, **54**, 1767 (1971).

(6) (a) W. G. Dauben, D. J. Hart, J. Ipaktschi, and A. P. Kozikowski, *Tetrahedron Lett.*, 4425 (1973); (b) W. G. Dauben and J. Ipaktschi, *J. Am. Chem. Soc.*, **95**, 5088 (1973).

(7) The phosphonium salt **7** was prepared in ~60% overall yield from chloroacetone by modifying the literature procedure of F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957).

(8) All compounds were adequately characterized by spectral methods (IR, NMR, and MS), and the new compound (entry 5) gave satisfactory high resolution mass spectral data.

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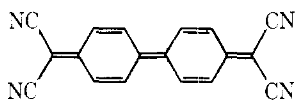
Tetracyanoquinoquinazolinoquinazoline†

Summary: The title compound was prepared as a dianionic salt whose physical properties and electrochemical behavior are reported.

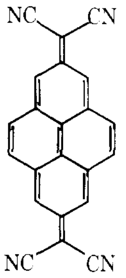
Sir: Since the discovery of the unusual solid state transport properties of TTF,[1] several new donors based on the TTF skeleton have been prepared.[2–4] On the other hand, no new acceptors, except perhaps TNAP,[5] endowed with the crucial characteristic formation of stable mixed valence anionic arrays (i.e., partially filled bands) sui generis to TCNQ have appeared in the literature. For example, tetrafluoro TCNQ,[6] TCM,[7,8] TMCP,[9] and TCNDQ[10] do not appear to fulfill the above requirements.

While TCNDQ tends to polymerize, a pyrene analogue (B) would be expected to be more stable because biphenyl inter-ring hydrogen repulsions are eliminated.

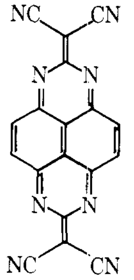


A

TCNDQ



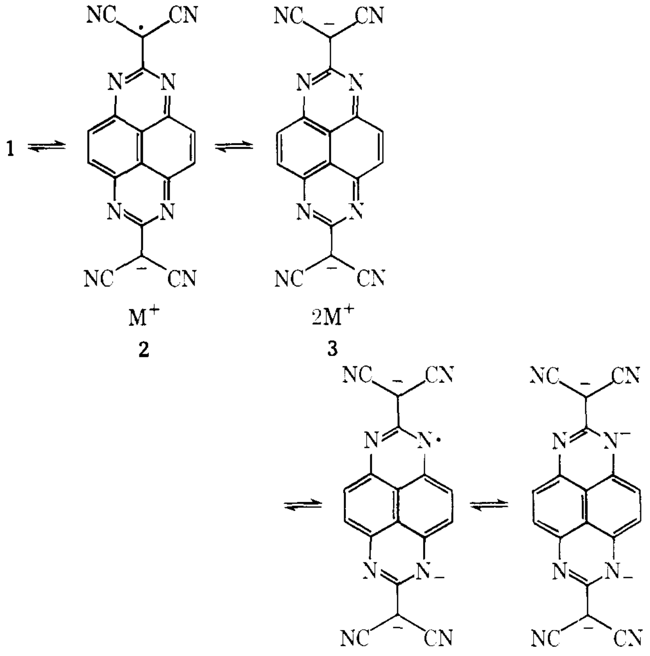
B



TCQQ

1

Rather than attempting a synthesis of B, we decided to prepare 1 for the following reasons: (a) projected syntheses of 1 appeared more straightforward than those of B, and (b) substitution of N for C was expected to enhance the electron affinity of the acceptor and also increase the number of available oxidation states (cf. 1–5). Thus, by increasing the valence, we expected to enhance the probability for formation of partially filled bands.



M^+ 2

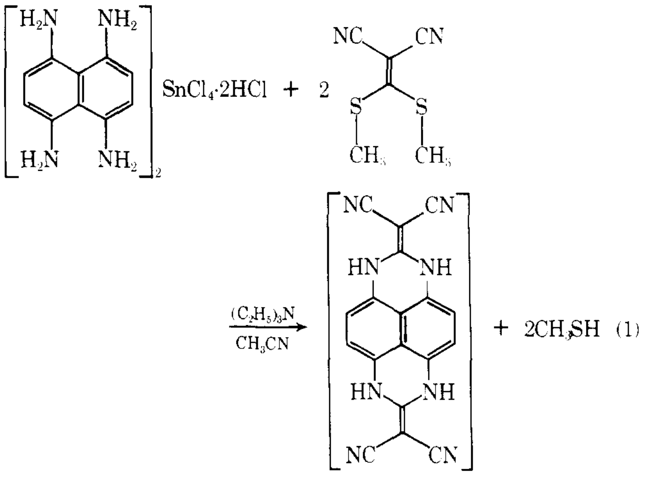
$2M^+$ 3

$3M^+$ 4

$4M^+$ 5

3a, $M^+ = Ph_4As^+$
b, $M^+ = Bu_4N^+$

Here we report on the preparation of **3a,b** and some of its properties. The dianion was prepared by the sequence of reactions depicted below:[11]



C (1)

$$C + 2NaH + \left\{\begin{matrix} Ph_4AsCl \\ \text{or} \\ Bu_4NCl \end{matrix}\right\} \longrightarrow 3a \text{ or } 3b \quad (2)$$

Since attempts to purify the crude reaction mixture obtained from reaction 1 failed, it was treated with base in acetonitrile in the presence of either tetrabutylammonium or tetraphenylarsonium chloride. Even when both reactions (1 and 2) were carried out under strictly anaerobic conditions, **3a(b)** was the only characterizable product isolated. The physical properties of **3a** are given below: **3a** UV (CH_2Cl_2) 680 nm (ϵ 690), 640 (770), 368 (1×10^5), 350 (sh, 4.8×10^4), 323 (3.6×10^4), 310 (3.8×10^4), 297 (3×10^4), 272 (2×10^4), 265 (1.8×10^4), 259 (1.6×10^4). The last three bands were due to the tetraphenylarsonium cation. For **3a,** IR (KBr) ν, 2180, 2170 (d, s), 1550 (s), 1470 (m), 1430 (m), 1380 (s), 1320 (sh), 1300 (m), 1270 (sh), 1180 (w), 1160 (w), 1080 (sh), 1070 (m), 1000 (w), 970 (w), 840 (m), 750 (s), 690 cm^{-1} (s). For **3b,** NMR (CD_3CN) δ 7.8 (s, 4 H), 3.02 (br t, 16 H), 1.4 (br m), 0.9 (s), the

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† A systematic name would be 2,7-bisdicyanoquinomethano-2,7,*H*,*H*-quinazolino[6,5,4-*def*]quinazoline (TCQQ).