Inorganica Chimica Acta, 61 (1982) 129–133

Asymmetric Catalyses. 7. (+) and (−) MeNorphos as Ligands in Rh Catalyzed Asymmetric Olefin Hydrogenation

HENRI BRUNNER* and MANFRED PRÖBSTER

Institut für Anorganische Chemie der Universität Regensburg, Universitätsstr. 31, D-8400 Regensburg, F.R.G.

Received October 20, 1981

(±)MeNorphosO is resolved into its optically pure components (+) and (−)MeNorphosO by (−)-L-dibenzoyltartaric acid monohydrate. The racemic mixture of (±)MeNorphosO is obtained by the Diels–Alder reaction of methylcyclopentadiene and trans-$(C_6H_5)_2P(O)CH{=}CHP(O)(C_6H_5)_2$. *(+) and (−) MeNorphosO are reduced by* $SiHCl_3$ *to give (+) and (−)MeNorphos. The* ^1H *NMR spectra of NorphosO and Norphos, as well as MeNorphosO and MeNorphos, are assigned with respect to the norbornene skeleton. (+) and (−)MeNorphos are used as optically active ligands in asymmetric hydrogenation catalysts. (Z)-α[N-acetamido] cinnamic acid and itaconic acid are hydrogenated with 92 and 60% ee.*

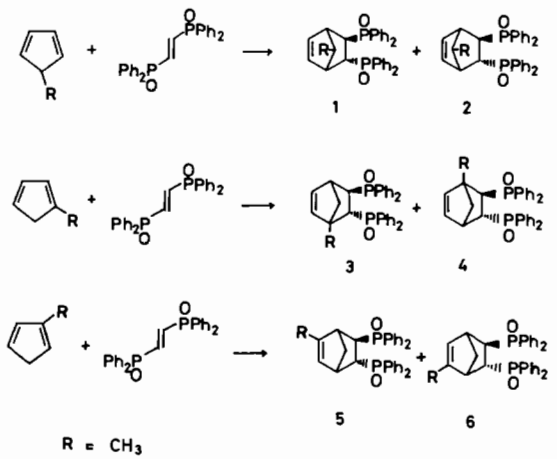
Introduction

Asymmetric hydrogenation of prochiral substrates with transition metal complexes of optically active phosphine ligands is of continuing interest [1–7]. With (+) and (−) Norphos (bicyclo-[2.2.1] hept-5-ene-2,3-diylbis(diphenylphosphine) we introduced a new optically active chelate ligand which gave high optical yields in different kinds of asymmetric catalyses [8–10]. It is well known that small variations in the optically active ligands can lead to drastic changes in the magnitude and direction of optical induction, as demonstrated for the Diop derivatives with *o*- and *m*-methyl groups in the phenyl rings [11]. Therefore, we synthesized the methyl derivatives of (+) and (−) Norphos, abbreviated (+) and (−) MeNorphos, and investigated their potential as chiral ligands in asymmetric hydrogenation catalysts [12].

Results and Discussion

Synthesis of (±) MeNorphosO

The synthetic procedure for (±) MeNorphos is similar to that for (±) Norphos [8, 9]. The Diels–Alder reaction of methylcyclopentadiene (which consists of the three isomers [13–15] shown in Scheme 1) with *trans*-1,2-ethenediylbis(diphenylphosphineoxide) [16] gives high yields of racemic MeNorphosO [12]. If *trans* orientation of the $PO(C_6H_5)_2$ groups at the norbornene skeleton is assumed, 6 diastereoisomers, each of which forms a pair of enantiomers, are possible. Only one of the enantiomers is shown in Scheme 1 for each pair of enantiomers.



Scheme I

The ^1H NMR spectra of (±) MeNorphosO and (±) MeNorphos, obtained by reduction, contain in the methyl area only one doublet (J = 1.4 Hz) in accord with structures 5 or 6 for MeNorphosO, the coupling being assigned to an allylic coupling $HC{=}C{-}CH_3$. In agreement with these results only one unsaturated proton (δ = 5.3 ppm) is found. On this basis structures 1–4 are excluded. We assign structure 5 to the (±) MeNorphosO obtained, because the steric hindrance between the methyl group and the *exo*-$PO(C_6H_5)_2$ group is less than it would be in isomer 6 with a methyl/*endo*-$PO(C_6H_5)_2$ interaction. (+) and (−) MeNorphos are correlated to the absolute configurations b and a in Scheme 2 on the basis of the arguments given for (+) and (−) Norphos [8, 9].

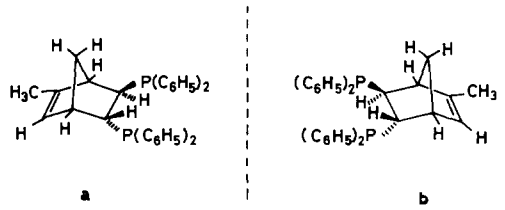
*Author to whom all correspondence should be addressed.
† For part 6 see ref. 10.

0020-1693/82/0000-0000/$02.75

TABLE I. ^{1}H NMR Spectra of (±) NorphosO, (±) MeNorphosO, (±) Norphos, and (±) MeNorphos: τ Values in ppm (relative intensity); $CDCl_3$ (int. TMS); Bruker WH 90.

	NorphosO	MeNorphosO	Norphos	MeNorphos
H1 (or H4)	7.08 (1)	7.10 (1)	7.13 (1)	7.26 (1)
H2	6.24 (1)	6.26 (1)	7.03 (1)	7.09 (1)
H3	6.77 (1)	6.78 (1)	7.73 (1)	7.83 (1)
H4 (or H1)	7.08 (1)	7.35 (1)	7.13 (1)	7.48 (1)
H5	3.71 (1)[a,b]		3.72 (1)[a,d]	
H6	4.21 (1)[a,c]	4.70 (1)	3.93 (1)[a,e]	4.40 (1)
H7a	7.82 (1)	7.86 (1)	9.07 (1)	9.14 (1)
H7s	8.74 (1)	8.70 (1)	8.92 (1)	8.89 (1)
CH_3		8.21 (3)[f]		8.15 (3)[f]
C_6H_5	1.97–3.09 (20)	2.06–3.08 (20)	2.96–2.35 (20)	2.88–2.36 (20)

[a] Center of a 4-line-multiplet. [b] Between 3.62 and 3.79 τ. [c] Between 4.12 and 4.29 τ. [d] Between 3.65 and 3.81 τ. [e] Between 3.87 and 4.03 τ. [f] Doublet with J = 1.4 Hz.



Scheme II

^{1}H NMR Spectra

The assignment of the phenyl and methyl protons in (±) MeNorphosO and (±) MeNorphos is straightforward (Table I). The vinyl proton in (±) MeNorphosO and (±) MeNorphos forms a broad signal of intensity 1 at τ 4.70 and 4.40, respectively. The two olefinic protons of (±) NorphosO and (±) Norphos give rise to an AB system of doublets (Table I). For the identification of the signals of the other protons of (±) MeNorphosO and (±) MeNorphos, which couple with each other and with the *exo* and *endo* P atoms, a comparison with (±) NorphosO and (±) Norphos was carried out.

The signals in the ^{1}H NMR spectrum of (±) NorphosO (Fig. 1) are assigned using the numbering scheme shown in the formula. The methylene protons H7s and H7a give rise to the multiplets at 8.74 and 7.82 τ, both with relative intensity 1. The doublet structure of H7a is due to a coupling with H7s, the two lines are broadened by coupling with the bridgehead protons H1 and H4, which are not equivalent. As H7s, in addition to the coupling with H7a also exhibits W-coupling [17] with the *endo* substituents H3 and P_{endo}, it forms a broad multiplet. The two different bridgehead protons H1 and H4 give overlapping multiplets of intensity 2 at 7.08 τ because they couple with all the substituents at the norbornene skeleton, except H3 and P_{endo} [18]. The *endo* proton H3 at 6.77 τ (intensity 1) couples with H2 and P_{exo} but not with H4, giving a doublet of

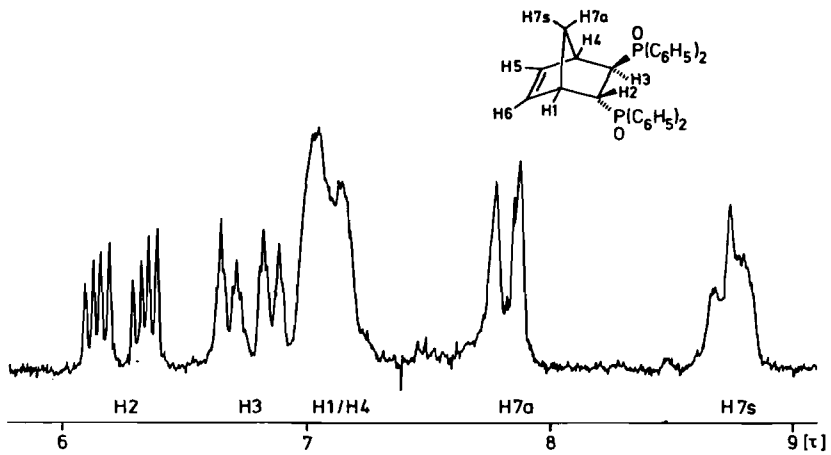


Fig. 1. ^{1}H NMR spectrum of (±) NorphosO in $CDCl_3$ (90 MHz, Bruker WH 90).

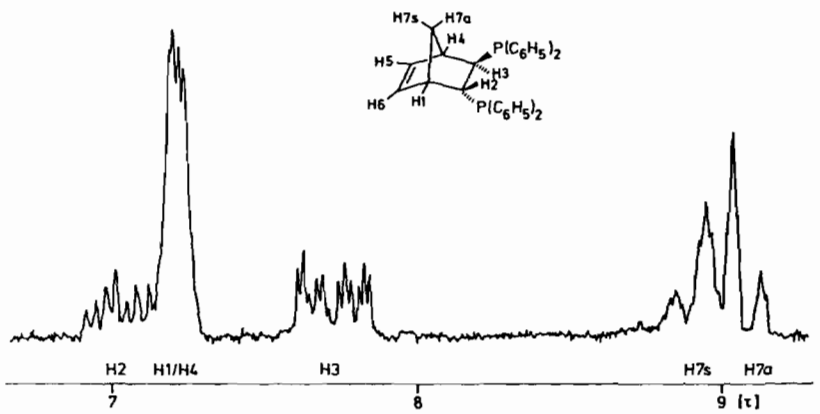


Fig. 2. ^{1}H NMR spectrum of (±) Norphos in $CDCl_3$ (90 MHz, Bruker WH 90).

doublets broadened by the W-coupling with H7s and other small couplings. For the *exo* proton H2 the W-coupling with the methylene proton H7s is absent. The coupling with H1, H3 and P_{endo} therefore leads to a 8-line-spectrum centered at 6.24 τ of intensity 1 (Table I).

The ^{1}H NMR spectrum of the norbornene skeleton of (±) MeNorphosO is similar to that of (±) NorphosO except for the following points: the two bridgehead protons exhibit different chemical shifts, one forming a broad singlet, the other a broad doublet (Table I).

The ^{1}H NMR spectrum of (±) Norphos, obtained by (±) NorphosO reduction [8, 9], is shown in Fig. 2. A comparison with Fig. 1 reveals that in (±) Norphos all of the norbornene protons at sp^3 carbon atoms are shifted highfield with respect to (±) NorphosO: the protons H7s, H1/H4 (far away from the $P(C_6H_5)_2$ and $PO(C_6H_5)_2$ substituents) a little, and the protons H7a, H3, H2 (close to the $P(C_6H_5)_2$ and $PO(C_6H_5)_2$ substituents) very much (Table I). For H7a this upfield shift is so large that it appears in (±) Norphos at higher field than H7s. For (±) MeNorphos the same large upfield shifts for H2, H3 and especially H7a compared to (±) MeNorphosO are observed (Table I). Similar to (±) MeNorphosO in (±) MeNorphos, the two bridgehead protons H1 and H4 form two separated multiplets.

Optical Resolution and Reduction

Similar to the resolution of (±) NorphosO, (–)-L-dibenzoyltartaric acid, abbreviated (–) DBT, is used for the formation of the two hydrogen-bonded diastereoisomers (+) MeNorphosO/(–) DBT and (–) MeNorphosO/(–) DBT differing in solubility [9]. As the diastereoisomer separation with MeNorphosO is more difficult than with NorphosO, two modifications of the NorphosO resolution [8, 9] are necessary.

(–) DBT forms with (–) MeNorphosO the less soluble diastereomer and with (+) MeNorphosO the more soluble diastereomer. According to the Marckwald principle [19], the situation is reversed if (+) DBT is used instead of (–) DBT. So, a change from (–) DBT to (+) DBT in different separation steps inverts the solubility of the diastereoisomer with a given enantiomer of MeNorphosO from more soluble to less soluble and *vice versa.* Furthermore, in some resolution steps substoichiometric quantities of DBT give better results than do stoichiometric amounts.

First step: the racemic mixture of MeNorphosO is dissolved in ethanol/chloroform (4:1) and a stoichiometric quantity of (–) DBT in ethanol is added. In the resulting precipitate the less soluble diastereoisomer (–) MeNorphosO/(–) DBT (and in the mother liquor the more soluble diastereoisomer (+) MeNorphosO/(–) DBT) are enriched. After KOH-treatment from the less soluble portion (–) MeNorphosO, $[\alpha]_{578}$ –19°, and from the more soluble portion (+) MeNorphosO, $[\alpha]_{578}$ +34°, are obtained.

Second step: the (–) MeNorphosO fraction is treated with half of the stoichiometric amount of (+) DBT. After separation of the precipitate, from the more soluble fraction (–) MeNorphosO is obtained with $[\alpha]_{578}$ –51°. Similar to step 1 the enrichment of the (+) MeNorphosO fraction is improved by using half of the stoichiometric quantity (–) DBT, $[\alpha]_{578}$ +44°.

Third step: the rotation of (–) MeNorphosO is increased to $[\alpha]_{578}$ –64° by using 1 equivalent of (–) DBT *via* the less soluble diastereoisomer. Similarly the optical rotation of (+) MeNorphosO rises to $[\alpha]_{578}$ +66° after precipitating (+) MeNorphosO/(+) DBT with 1 equivalent of (+) DBT. Sometimes a repetition of this step is necessary to obtain optically pure (+) and (–) MeNorphosO of the optical rotations indicated.

In the resolution procedure described both enantiomers (+) and (–) MeNorphosO alternatively appear in the more and less soluble fractions, making the resolution most efficient and allowing the separation of all impurities.

The optically pure phosphine oxides (+) and (−)MeNorphosO are reduced with $SiHCl_3$ [20, 21], as described for (+) and (−)NorphosO [8, 9], giving (+)MeNorphos, $[\alpha]_{578}$ +31°, and (−)MeNorphos, $[\alpha]_{578}$ −32°. The reduction can be monitored by the strong ν(P = O) band at 1180 cm^{-1} in the IR spectrum of MeNorphosO which must be absent in MeNorphos.

In the mass spectra of MeNorphosO and MeNorphos the molecular ions and the ions due to the Retro-Diels–Alder reactions appear with high intensity. The base peaks are $[M-PO(C_6H_5)_2]^+$ and $[M-P(C_6H_5)_2]^+$, respectively.

Hydrogenation of (Z)-α-[N-acetamido] cinnamic Acid and Itaconic Acid

The hydrogenation of (Z)-α-[N-acetamido]cinnamic acid according to Scheme 3a is carried out at room temperature in methanol using hydrogen at atmospheric pressure. The components of the catalyst are $[RhCl(COD\text{-}1.5)]_2$ and MeNorphos, (+)MeNorphos giving (−)-N-acetylphenylalanine and (−)MeNorphos giving (+)-N-acetylphenylalanine. The procedure and the work up, as well as the determination of the degree of hydrogenation by NMR spectroscopy and the degree of optical induction by polarimetry, has been described in detail previously [8, 9, 22, 23]. For the quantitative hydrogenation of 500 mg AAZ in 10 h 14 mg $[RhCl(COD\text{-}1.5)]_2$ and 29 mg (+) or (−)Me-Norphos were used, corresponding to a pro-catalyst: co-catalyst: substrate ratio of 1:2.1:40. Several experiments were also carried out with a ratio 1:2.1:65, giving the same chemical and optical yields. The enantiomeric excess obtained with the MeNorphos containing catalyst was 92% in more than a dozen runs. This value shows that the optical induction in reaction 3a is a little smaller for the catalyst with the methyl substituted Norphos than for the catalyst with the unsubstituted Norphos.

Similar trends were observed in the asymmetric hydrogenation of itaconic acid with the same catalysts (Scheme 3b). The optical yields obtained were about 60% for the MeNorphos containing catalyst and 62% for the Norphos based catalyst. These values compare favourably with most of the results obtained in the asymmetric hydrogenation of itaconic acid [24–28], although more than 90% ee have been reported recently with Rh/BPPM systems [29]. The rate of hydrogenation of itaconic acid increases in the presence of amines [12, 29].

Experimental

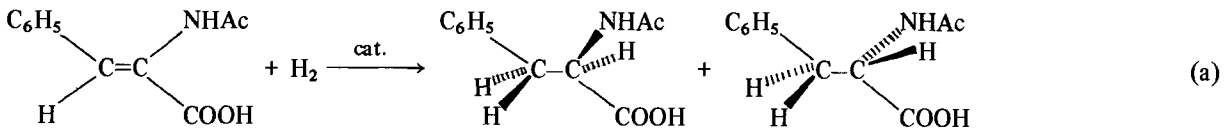
Diels–Alder Reaction of Methylcyclopentadiene with Trans-*1, 2-ethenediylbis(diphenylphosphineoxide) = EPO*

20 ml (200 mmol) methylcyclopentadiene and 5 g (11.7 mmol) EPO in 300 ml benzene are heated in an autoclave to 150–160 °C for 2.5 h. After evaporation of the solvent a white residue is obtained which is stirred with petrolether, filtered and washed with petrolether. Yield 5.5 g (±)MeNorphosO (85% with respect to EPO). *Anal.* Found, C, 75.72; H, 5.80; Calcd. for $C_{32}H_{30}O_2P_2$ (508.5), C, 75.58; H, 5.95%.

Optical Resolution of Methyl-bicyclo[2.2.1]hept-5-ene-2,3-diylbis(diphenylphosphineoxide) = (±)MeNorphosO

Step 1: 15 g (29.5 mmol) (±)MeNorphosO are dissolved in 150 ml ethanol/chloroform 4:1, (thereafter called "solvent"). A solution of 11.4 g (30.3 mmol) L-(−)-dibenzoyl tartaric acid monohydrate = (−)DBT in 13 ml 99% EtOH is added. After two hours the crystals formed are separated from the mother liquor. *a*) Crystalline fraction 15.7 g, enriched in (−)MeNorphosO/(−)DBT. *b*) Fraction obtained from the mother liquor 10.5 g, enriched in (+)MeNorphosO/(−)DBT. The less soluble fraction *a*) is dissolved in 140 ml $CHCl_3$. This solution is shaken with 150 ml 2.5% aqueous KOH. The water phase is washed three times with 30 ml $CHCl_3$. The combined $CHCl_3$ phases contain 10.0 g (−)MeNorphosO, $[\alpha]_{578}^{20}$ −19° (c = 1, $CHCl_3$). Similarly the KOH-cleavage of the more soluble fraction *b*) is carried out with reduced solvent and reagent quantities according to the smaller quantity of *b*). 5.0 g (+)MeNorphosO, $[\alpha]_{578}^{20}$ +34°.

Scheme 3



Step 2a: 10 g (–) MeNorphosO are dissolved in 100 ml solvent. A solution of 3.8 g (+) DBT in 4 ml EtOH is added. After two hours, filtration gives 7 g less soluble (+) MeNorphosO/(+) DBT and the mother liquor 6.4 g more soluble (–) MeNorphosO/(+) DBT. Yield of (–) MeNorphosO after KOH-cleavage 4.7 g, $[\alpha]_{578}^{20}$ –51°.

Step 3a: 4.7 g (–) MeNorphosO in 47 ml solvent are treated with 3.7 g (–) DBT in 4 ml EtOH. Crystalline fraction 6.5 g (–) MeNorphosO/(–) DBT, which give after KOH-cleavage 4.3 g (–) MeNorphosO, $[\alpha]_{578}^{20}$ –64°.

Step 2b: 5.0 g (+) MeNorphosO in 50 ml solvent are treated with 1.9 g (–) DBT in 2 ml EtOH. Crystalline fraction 1.5 g (–) MeNorphosO/(–) DBT. The mother liquor contains 4.6 g (+) MeNorphosO/(–) DBT, which after KOH-cleavage gives 2.6 g (+) MeNorphosO, $[\alpha]_{578}^{20}$ +44°.

Step 3b: 2.6 g (+) MeNorphosO in 25 ml solvent and 2 g (+) DBT in 2.2 ml EtOH give 1.5 g crystals of (–) MeNorphosO/(+) DBT and 2.9 g (+) MeNorphosO/(–) DBT in the mother liquor. KOH-cleavage of the more soluble fraction yields 1.9 g (+) MeNorphosO, $[\alpha]_{578}^{20}$ +66°.

Reduction of (+)- and (–)-Methyl-bicyclo[2.2.1]-hept-5-ene-2,3-diylbis(diphenylphosphinoxide) = (±) MeNorphosO

4.8 g (9.4 mmol) (+) and (–) MeNorphosO, respectively, and 15 g (0.11 mol) $SiHCl_3$ in 300 ml benzene, are heated to 100 °C for 15–20 hours in an autoclave excluding air and moisture. Solvent and excess $SiHCl_3$ are evaporated. The residue is dissolved in benzene. After cooling to 5 °C 70 ml 25% NaOH are added slowly. The water phase is washed with 50 ml benzene. The combined benzene solutions are passed through a 3 cm layer of dry Al_2O_3. Yield 3.8 g (79%) (+) and (–) MeNorphos, respectively. (+) MeNorphos, $[\alpha]_{578}^{20}$ +31°. (–) MeNorphos, $[\alpha]_{578}^{20}$ –32° (c = 1, $CHCl_3$). *Anal.* Found, C, 80.20; H 6.47%; Calcd.: for (–) $C_{32}H_{30}P_2$ (476.5), C, 80.65; H, 6.35%. mp. 129–130 °C.

Acknowledgement

We thank the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the BASF AG for support of this work.

References

1 H. B. Kagan, *Ann. N. Y. Acad. Sci., 333,* 1 (1980).
2 K. E. Koenig, M. J. Sabacky, G. L. Bachman, W. C. Christopfel, H. D. Barnstorff, R. B. Friedman, W. S. Knowles, B. R. Stults, B. D. Vineyard and D. J. Weinkauff, *Ann. N. Y. Acad. Sci., 333,* 16 (1980).
3 B. R. James, *Adv. Organomet. Chem., 17,* 319 (1979).
4 W. S. Knowles, B. D. Vineyard, M. J. Sabacky and B. R. Stults in 'Fundamental Research in Homogeneous Catalysis', Vol. 3, M. Tsutsui, Ed., Plenum Press, New York (1979) p. 537.
5 D. Valentine Jr. and J. W. Scott, *Synthesis, 5,* 329 (1978).
6 H. B. Kagan and J. C. Fiaud, *Top. Stereochem., 10,* 175 (1978).
7 V. Caplar, G. Comisso and V. Sunjic, *Synthesis, 2,* 85 (1981).
8 H. Brunner and W. Pieronczyk, *Angew. Chem., 91,* 655 (1979); *Angew. Chem. Int. Ed. Engl., 18,* 620 (1979).
9 H. Brunner, W. Pieronczyk, B. Schönhammer, K. Streng, I. Bernal and J. Korp, *Chem. Ber., 114,* 1137 (1981).
10 H. Brunner and M. Pröbster, *J. Organometal. Chem., 209,* C1 (1981).
11 T. P. Dang, J.-C. Poulin and H. B. Kagan, *J. Organometal. Chem., 91,* 105 (1975).
12 M. Pröbster, *Diplomarbeit, Universität Regensburg,* 1979.
13 S. M. Csicsery, *J. Org. Chem., 25,* 518 (1960).
14 V. A. Mironov, E. V. Sobolev and A. N. Elizarowa, *Tetrahedron, 19,* 1939 (1963).
15 S. McLean and P. Haynes, *Tetrahedron, 21,* 2329 (1965).
16 A. M. Aguiar and D. Daigle, *J. Amer. Chem. Soc., 86,* 2299 (1964).
17 J. Meinwald and Y. C. Meinwald, *J. Amer. Chem. Soc., 85,* 2514 (1963).
18 M. Karplus, *J. Chem. Phys., 30,* 11 (1959).
19 W. Marckwald, *Ber. dtsch. chem. Ges., 29,* 43 (1896).
20 K. Naumann, G. Zon and K. Mislow, *J. Amer. Chem. Soc., 91,* 7012 (1969).
21 L. Horner and W. D. Balzer, *Tetrahedron Lett.,* 1157 (1965).
22 H. Brunner and W. Pieronczyk, *J. Chem. Res. (S),* 76 (1980); *J. Chem. Res. (M),* 1251 (1980).
23 H. Brunner and G. Agrifoglio, *Monatsh. Chem., 111,* 275 (1980).
24 K. Achiwa, *Chem. Lett.,* 561 (1978).
25 W. C. Christopfel and B. C. Vineyard, *J. Amer. Chem. Soc., 101,* 4406 (1979).
26 B. R. James and D. Mahajan, *Canad. J. Chem., 57,* 180 (1979).
27 K. Ohkubo, K. Fujimori and K. Yoshinaga, *Inorg. Nucl. Chem. Lett., 15,* 231 (1979).
28 M. Fiorini and G. M. Giongo, *J. Mol. Catal., 7,* 411 (1980).
29 I. Ojima, T. Kogure and N. Yoda, *J. Org. Chem., 45,* 4728 (1980).