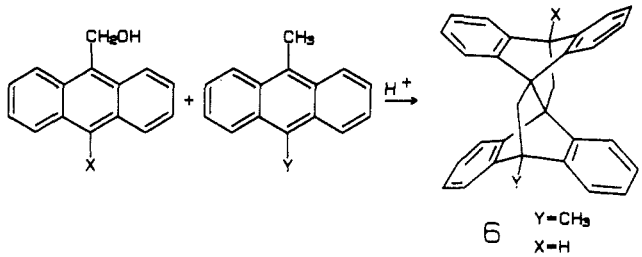


react as described above. This resulted in the isolation of **6** in 28% yield. Thus, the synthesis of a series of unsymmetrical lepidopterenes appears to be possible.

Experimental Section

Lepidopterene (1). Method I. 9-Methylanthracene (0.10 g, 0.52 mmol), ammonium peroxydisulfate (0.10 g, 0.46 mmol), copper(II) acetate (0.03 g, 0.15 mmol), and 5 mL of 0.02 M sodium acetate in acetonitrile/acetic acid (7/3, v/v) were combined and heated at 90 °C for 1 h under argon. A 1-mL aliquot of 0.05 M phenanthrene was added as an internal GC standard. The reaction mixture was poured into 50 mL of water and extracted four times with methylene chloride. The combined extracts (50 mL) were dried over sodium sulfate. GC and NMR indicated an 80% yield of **1** (based on **3** consumed).

Method II. 9-Anthracenemethanol (0.10 g, 0.5 mmol) and 9-methylanthracene (0.19 g, 1.0 mmol) were heated at 90 °C under argon in 0.1 M perchloric acid in acetonitrile/water (7/3, v/v) for 1 h. The reaction mixture was then worked up as above. Gas chromatography showed the absence of 9-anthracenemethanol and the disappearance of 0.52 mmol of **3**. After solvent removal, NMR of the residue indicated only **3** and **1** present. Addition of benzene to the residue and filtering gave 0.13 g (70%) of **1** as a white solid: mp 330–335 °C (lit.[3b] mp 317–323 °C); HRMS, *m/e* calcd for $C_{30}H_{22}$ (M^+) 382.17215, found 382.1731; ^1H NMR (300 MHz, $CDCl_3$) δ 2.91 (d, J = 2.7 Hz, 4 H), 4.65 (t, J = 2.7 Hz, 2 H), 6.74 (d, J = 7.5 Hz, 4 H), 6.82 (td, J = 7.5, 1.5 Hz, 4 H), 7.01 (td, J = 7.5, 1.5 Hz, 4 H), 7.35 (d, J = 7.5 Hz, 4 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 143.59, 143.59, 125.48, 125.22, 122.64, 122.35, 54.01, 45.58, 28.93; IR (KBr) 3080, 3020, 2990, 2980, 2950, 1460, 990, 760, 740, 635, 585 cm^{-1}; UV–vis [cyclohexane; λ_{max}, nm ($\epsilon \times 10^{-3}$)] 272 (2), 264 (1.9), 257 (1.7), 253 (1.7).

10-Methyl-9-anthracenemethanol. 10-Methyl-9-anthraldehyde (0.13 g, 1.4 mmol) in 50 mL of anhydrous ether was added in portions to a stirred suspension of 0.57 g (1.5 mmol) of lithium aluminum hydride in 15 mL of ether. After 2 h, the reaction was quenched by the slow addition of water. The reaction mixture was poured into 50 mL of dilute H_2SO_4 and extracted with methylene chloride. The organic phase was washed with aqueous sodium bicarbonate and water and dried over sodium sulfate. Solvent was removed under reduced pressure and the residue recrystallized from benzene/hexane to give 0.24 g (77%) of yellow crystals, mp 224–228 °C (lit.[10] mp 222.5–223 °C).

9-Methyllepidopterene (6). Method 1. 9,10-Dimethylanthracene (0.052 g, 0.025 mmol), 9-anthracenemethanol (0.052 g, 0.25 mmol), and a catalytic (1-mg) amount of p-toluenesulfonic acid were refluxed in 10 mL of deoxygenated benzene for 45 min. The reaction mixture was poured into 50 mL of water, and the layers were separated. The aqueous phase was extracted three times with 15-mL volumes of CH_2Cl_2. The organic phases were combined, dried over Na_2SO_4, and then evaporated to give a solid residue. Attempts to isolate **6** in pure form from this material were unsuccessful. However, liquid chromatography performed by adsorbing the material to silica gel (Fisher grade 150, 60–100 mesh) and eluting with hexane through a 1 × 14 cm column of silica gel provided a fraction that consisted mainly of **6** and unreacted **7** (by ^1H NMR). Integration of the methyl NMR peaks for **6** and **7** showed the ratio of **6**/**7** to be ca. 1/2.

Method 2. 10-Methyl-9-anthracenemethanol (0.067 g, 0.3 mmol), 9-methylanthracene (0.048 g, 0.25 mmol), and a catalytic amount (ca. 2–3 mg) of p-toluenesulfonic acid were combined with 5 mL of deoxygenated benzene. The resultant suspension was heated to reflux under argon. After 40 min, an additional 0.02 g (0.09 mmol) of the alcohol and 5 mL of benzene were added. After an additional 2 h at reflux, the solution was allowed to cool. The reaction mixture was filtered and the solvent removed. The yellow residue was taken up in methylene chloride and chromatographed on a short column of silica gel, eluting with 10% CH_2Cl_2/hexane and neat CH_2Cl_2. The hexane eluates were combined, the solvent was removed, and the residue was recrystallized from benzene/hexane (2 days at ca. 0 °C) to give 0.028 g (28%) of **6** as yellow crystals: mp 261–263 °C (uncorrected); ^1H NMR (79.5 MHz, $CDCl_3$) δ 7.4–6.6 (ArH, 16 H), 4.60 (t, J = 2.8 Hz, 1 H), 2.91 (d, J = 2.8 Hz, 2 H), 2.68 (s, 2 H), 2.21 (s, 3 H). Anal. Calcd for $C_{31}H_{24}$: C, 93.9; H, 6.1. Found: C, 93.62; H, 6.02.

Acknowledgment. We thank Dr. David C. Lankin (Varian Associates) for obtaining the high-field ^1H and ^{13}C NMR spectra and Dr. Edward Chess (BNW) for performing the high-resolution mass spectral analyses reported here.

Registry No. **1**, 55614-27-2; **3**, 779-02-2; **3** (alcohol), 1468-95-7; **6**, 103692-67-7; **7**, 781-43-1; 10-methyl-9-anthraldehyde, 7072-00-6; 10-methyl-9-anthracenemethanol, 71339-55-4.

(10) Southern, P. F.; Waters, W. A. *J. Chem. Soc.* **1960**, 4340–4346.

Functionalization of Aromatic Systems: A Highly Chemoselective Synthesis of [(Trimethylsilyl)methyl]nitroarenes

Giuseppe Bartoli,* Marcella Bosco, Renato Dalpozzo, and Paolo E. Todesco

Istituto di Chimica Organica, Viale Risorgimento 4, I-40136 Bologna, Italy

Received March 11, 1986

In spite of the ready availability of aromatic nitro compounds, only few methods to introduce alkyl side chains, carrying useful functional groups, into these compounds have been developed. Makosza et al.[1] succeeded in realizing a "vicarious" substitution of hydrogen with α-cyano-, sulfonyl-, and carbalkoxy-substituted alkyl groups, by using weakly basic carbanions bearing a good leaving group on the anionic carbon. Although the occasional competitive displacement of substituents bound to one of the reactive positions of the aromatic ring may occur, this method showed interesting applications in organic synthesis.[2]

The discovery of the irreversible conjugate addition of highly basic carbanions such as Grignard reagents[3] provided a general and efficient tool to introduce regio-[4] and chemoselectively[5] alkyl groups into an aromatic ring. The Grignard reagent addition method shows a greater versatility than Makosza's vicarious substitution, since, in ethereal solution, the nitronate adducts are stable enough to be treated in situ with a large variety of selective reducing,[6]

(1) (a) Makosza, M.; Golinski, J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 451. (b) Makosza, M. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon: Oxford, 1983; p 401. (c) Makosza, M.; Winiarski, J. *J. Org. Chem.* **1984**, *49*, 1494.

(2) (a) Stahly, G. P.; Stahly, B. C.; Lilje, K. C. *J. Org. Chem.* **1984**, *49*, 578. (b) Makosza, M.; Golinsky, J.; Baran, J. *J. Org. Chem.* **1984**, *49*, 1488.

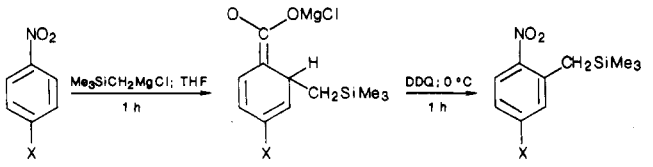
(3) (a) Bartoli, G.; Rosini, G. *Synthesis* **1976**, 270. (b) Bartoli, G.; Leardini, R.; Medici, A.; Rosini, G. *J. Chem. Soc., Perkin Trans. 1*, **1978**, 692.

(4) Bartoli, G. *Acc. Chem. Res.* **1984**, *17*, 109.

(5) Bartoli, G.; Bosco, M.; Dalpozzo, R.; *Tetrahedron Lett.* **1985**, *26*, 115.

0022-3263/86/1951-3694$01.50/0

Table I. Addition of Peterson Reagent to Para-Substituted Nitrobenzenes, Followed by In Situ Treatment with DDQ



1a-i 2a-i 3a-h,i

a, X = Cl; b, X = I; c, X = CN; d, X = CHO; e, X = COOMe; f, X = COPh; g, X = CH_2Cl; h, X = $CH_2CH_2COCH_3$; i, X = $OSiMe_3$; j, X = OH

substrate	product	reacn temp, °C	yield, %[a]
1a	3a	0	58
1b	3b	−70	95
1c	3c	−70	70
1d	3d	−70	53[b]
1e	3e	−70	65
1f	3f	−70	80
1g	3g	−70	73
1h	3h	−70	78
1i	3j	0	76

[a] Yields of pure isolated products; in all cases trace amounts of unreacted starting material were isolated. [b] A 3% of 2,4-bis[(trimethylsilyl)methyl]nitrobenzene was isolated.

oxidizing,[7] and dehydrating agents.[8]

Other types of functionalized carbanionic species can successfully be used, as shown by the recently reported addition of silyl enol ethers, activated by a fluoride ion source,[9] and of lithium dithianes.[10]

In this paper we report the results of an addition of [(trimethylsilyl)methyl]magnesium chloride (Peterson reagent) to nitroarenes in THF. Oxidation in situ of the resulting cyclohexadiene nitronate intermediate gives *o*- or *p*-[(trimethylsilyl)methyl]nitroarenes, a new class of potential functionalized benzyl carbanions.

In Table I the reaction sequence, products, yields, and reaction temperatures are summarized for para-substituted nitrobenzenes.

An appropriate reaction temperature and a stoichiometric amount of Peterson reagent with respect to nitroarene are essential for ensuring a high chemoselectivity degree to the reaction. Nitroarenic substrates containing chlorine and silyloxy groups can be selectively alkylated at 0 °C. In the presence of iodo, cyano, carbonyl, and chlorobenzylic groups, which are highly reactive toward Grignard reagents, lower temperatures are required.

Various oxidizing agents were tested to convert nitronate adducts into the corresponding aromatic nitro compounds. Best results were obtained with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

Only hydroxy groups need protection, e.g., as trimethylsilyl ether. This type of protecting group is advantageous due to its ease of removal on aqueous workup.

The great efficiency and the wide applicability of the present reaction is confirmed by the good results obtained with various hetero and homo polycyclic systems (Table II) by employing the same experimental procedure as used for substituted nitrobenzenes. The only exception was the synthesis of 9-nitro-10-[(trimethylsilyl)methyl]anthracene. In this case, better yields were obtained using a larger excess of Peterson reagent and lead(IV) acetate (LTA) as the oxidizing agent.[7c]

In all cases examined, high regioselectivity was observed, which is not surprising, since it has been established that carbanionic nucleophiles show a high kinetic preference to attack at unsubstituted positions.[4,11,2b] Thus, in reactions with compounds which give irreversible addition to unsubstituted positions of a nitroarenic system, a satisfactory control of the orientation of the alkylation at a unique position can be achieved by placing heterosubstituents in the other reactive positions (Table I and Table II, entry 1). Obviously, this expedient is not necessary in bi- and polycyclic systems which have a single reactive position (Table II, entry 2–5).[4]

Furthermore, this reaction proceeds with high chemoselectivity. Functions highly reactive toward Grignard reagents such as iodo, nitrile, chloromethyl, and carbonyl groups of ketones, esters, and aldehydes are not affected if some trivial experimental expedients are employed; i.e., low temperatures and equimolecular amounts of Peterson reagent and substrate. In all cases examined of functionalized nitroarenes, only the products arising from attack to the nitroarenic system were obtained.

To our knowledge, this represents the first example of reaction of a Grignard-type reagent proceeding without affecting an aldehyde group present in the molecule.

The high potential of silyl derivatives in organic synthesis is well-known.[12] In particular, [(trimethylsilyl)methyl]nitroarenes can act as benzylic carbanions in the presence of a fluoride ion source.[13]

In fact, when compounds **3a** and **5** were allowed to react in dry THF with benzaldehyde in the presence of tetrabutylammonium fluoride (TBAF), at room temperature, alcohols **15** and **16** were obtained in good yields (see Scheme I).

No products were obtained from self-reaction of **3a** and **5** nor from addition of **3a** and **5** to **15** and **16**, thus indicating that the reaction proceeds with high chemoselectivity without affecting the strongly electrophilic nitroarenic function.

In conclusion a facile, efficient, chemo- and regioselective method of synthesis of previously unknown [(trimethylsilyl)methyl]nitroarenes is now available. The potential usefulness of these compounds in organic synthesis is suggested by the preliminary studies reported on the fluoride-mediated addition to benzaldehyde. Further aspects of the reactivity of [(trimethylsilyl)methyl]nitroarenes will be reported later.

Experimental Section

Melting points are uncorrected and were determined with a Büchi apparatus. NMR spectra were recorded at 60 MHz with a Varian EM-306-L instrument. IR spectra were recorded with a Perkin-Elmer 983 spectrophotometer.

THF, dried over sodium and distilled, was redistilled from $LiAlH_4$ immediately before use. Commercial nitro compounds were recrystallized before use.

Commercial Peterson reagent (Aldrich Co.) was titrated by using the Bergbreiter's method.[14] 2-Methoxy-1-nitro-

(6) (a) Bartoli, G.; Medici, A.; Rosini, G.; Tavernari, D. *Synthesis* **1978**, 436. (b) Bartoli, G.; Bosco, M.; Cantagalli, G.; Dalpozzo, R.; *Tetrahedron* **1984**, *40*, 3437.

(7) (a) Kienzle, F. *Helv. Chim. Acta* **1978**, *61*, 449. (b) Bartoli, G.; Bosco, M.; Baccolini, G. *J. Org. Chem.* **1980**, *45*, 522. (c) Armillotta, N.; Bartoli, G.; Bosco, M.; Dalpozzo, R. *Synthesis* **1982**, 836.

(8) Bartoli, G.; Bosco, M.; Boicelli, A. C. *J. Org. Chem.* **1979**, *44*, 2087.

(9) RajanBabu, T. V.; Reddy, G. S.; Fukunaga, T. *J. Am. Chem. Soc.* **1985**, *107*, 5473.

(10) Bartoli, G.; Dalpozzo, R.; Grossi, L.; Todesco, P. E. *Tetrahedron* **1986**, *42*, 2563.

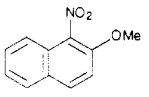
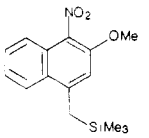
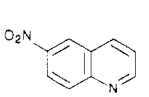
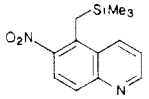
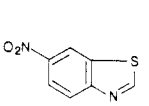
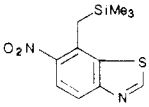
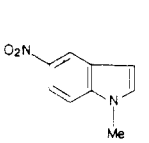
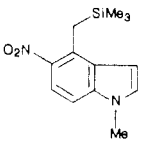
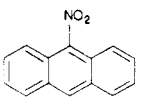
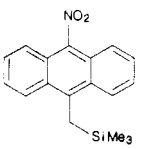
(11) Artamkina, G. A.; Egorov, M. P.; Beletskaya, I. P. *Chem. Rev.* **1982**, *82*, 427.

(12) Magnus, P. D.; Sarkar, T.; Djuric, S. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1982; Chapter 48.

(13) (a) Garland, R. B.; Palmer, J. R.; Shultz, J. A.; Sollman, P. B.; Pappo, R. *Tetrahedron Lett.* **1978**, 3669. (b) Coughlin, D. J.; Salomon, R. G *J. Org. Chem.* **1979**, *44*, 3784. (c) Djuric, S.; Sarkar, T.; Magnus, P. D. *J. Am. Chem. Soc.* **1980**, *102*, 6885.

(14) Bergbreiter, D. E.; Pendergrass, E. *J. Org. Chem.* **1981**, *46*, 219.

Table II. Addition of Peterson Reagent to Homo- and Heteropolycyclic Aromatic Systems

entry	substrate	product	reacn temp, °C	yield, %[a]
1	 4	 5	−30	65[b]
2	 6	 7	−30	74[b]
3	 8	 9	0	76[b]
4	 10	 11	0	70[b]
5	 12	 13	0	65[c]

[a] Yields of pure isolated products. [b] Using DDQ in THF at 0 °C to oxidize in situ the nitronate intermediate into the nitro derivative. [c] The reaction was complete in 2 h, a larger excess of Peterson reagent was required and the oxidation was carried out with LTA; a 10% of unreacted starting material was isolated.

naphthalene,[15] 4-(4-nitrophenyl)butan-2-one,[16] 6-nitrobenzothiazole,[17] 4-nitrophenoxytrimethylsilane,[18] were synthesized by the reported methods.

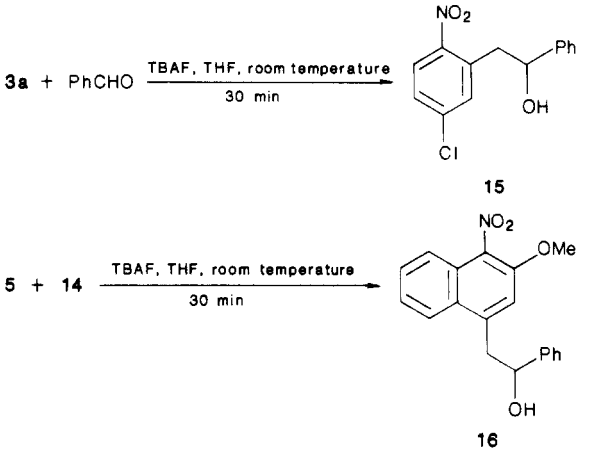
1-Methyl-5-nitroindole was prepared by adding an equimolar amount of methyl iodide to a THF solution of commercial 5-nitroindole and sodium hydride, at room temperature.

Preparation of [(Trimethylsilyl)methyl]nitroarenes 3a–h,j, 5, 7, 9, and 11 from the Corresponding Nitroarenes 1a–i, 4, 6, 8, and 10. General Procedure. Peterson reagent (5 mmol) was added dropwise to a stirred THF solution (20 mL) of 5 mmol of nitroarene under nitrogen atmosphere at the appropriate temperature (Tables I and II). The reaction mixture was stirred for 1 h, then a THF solution (15 mL) of 6 mmol of DDQ was added dropwise, and the temperature was allowed to rise at 0 °C, under stirring. After 1 h, the reaction mixture was poured in 30 mL of 5% acetic acid and extracted with methylene chloride. The organic layer was washed with a saturated solution of $NaHCO_3$ and then with water, dried over Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with an appropriate eluant.

Yields are reported in Table I and II.

This procedure was modified in the case of 9-nitroanthracene (**12**) as follows: 10 mmol of Peterson reagent was added dropwise to a stirred THF solution (20 mL) of 5 mmol of **12** under nitrogen atmosphere at 0 °C. The mixture was stirred for 2 h, and then glacial acetic acid (10 mmol) was added dropwise with stirring. To this mixture, a solution of LTA (6 mmol) in dichloromethane (30 mL) containing acetic acid (0.5 mL) was added dropwise at room temperature. Stirring was continued for 10 min and the solid inorganic material then filtered off. A few drops of ethylene glycol were added, and stirring was continued for 15 min. The resultant mixture was washed with water and with a saturated $NaHCO_3$ solution, dried with Na_2SO_4, and evaporated under reduced pressure. 9-Nitro-10-[(trimethylsilyl)methyl]anthracene was separated from starting material **12** (ca. 10%) by flash chromatography on silica gel (20:1 light petroleum (bp 40–60 °C)–ethyl acetate as eluant). The yield is reported in Table II.

Scheme I



For physical data of compounds **3a–h,j, 5, 7, 9, 11,** and **13**, see paragraph at the end of paper about supplementary material.

Preparation of 1-Phenyl-2-(5-chloro-2-nitrophenyl)ethanol (15). Commercial TBAF·$3H_2O$ (6 mmol, Fluka AC) was heated in a round-bottom flask with magnetic stirring at 40–45 °C under high vacuum (<0.1 mmHg). Heating was continued for 10 h and the sample liquified.[19] A THF solution (20 cm^3) of freshly distilled benzaldehyde (7.5 mmol) was added to the flask, at room temperature, under nitrogen atmophere. A THF solution (10 cm^3) of 5 mmol of [(trimethylsilyl)methyl]nitroarene **3a** was added dropwise at room temperature. The reaction mixture was stirred for 30 min, and then 5 cm^3 of 37% HCl was added. The reaction became discolored. The mixture was extracted with dichloromethane, washed with water, dried over Na_2SO_4, evaporated, and submitted to a flash chromatographic purification using light petroleum (bp 40–60 °C)–diethyl ether (9:1) as eluant, giving 0.93 g (67% yield) of **15**: oil, ^1H NMR ($CDCl_3$) δ 2.13 (br s, 1 H, OH), 2.9–3.6 (m, 2 H, CH_2), 4.8–5.1 (m, 1 H, CH), 7.2–7.6 and 7.8–8.1 (m, 7 H + 1 H, Ar); IR (film) ν_{OH} 3420 cm^{-1}, ν_{NO_2} 1530 and 1350 cm^{-1}.

Preparation of 1-Phenyl-2-(3-methoxy-4-nitronaphthyl)-ethanol (16). The reaction was carried out as described above, and, after flash chromatography on silica gel using light petroleum (bp 40–60 °C)–ethyl acetate (4:1) as eluant, 1.23 g (76% yield) of **16** was isolated: ^1H NMR ($CDCl_3$) δ 2.67 (br s, 1 H, OH), 3.30 (d, 2 H, CH_2, J_{CH_2-CH} = 7.0 Hz), 3.73 (s, 3 H, OMe), 4.53 (t, 1 H, CH), 6.93 (s, 1 H, H-2), 7.0–7.7 and 7.8–8.1 (m, 8 H + 1 H, Ar); IR (film) ν_{OH} 3413 cm^{-1}, ν_{NO_2} 1525 and 1360 cm^{-1}.

Registry No. **1a**, 100-00-5; **1b**, 636-98-6; **1c**, 619-72-7; **1d**, 555-16-8; **1e**, 619-50-1; **1f**, 1144-74-7; **1g**, 100-14-1; **1h**, 30780-19-9; **1i**, 1014-66-0; **3a**, 103368-87-2; **3b**, 103368-88-3; **3c**, 103368-89-4; **3d**, 103368-90-7; **3e**, 103368-91-8; **3f**, 103368-92-9; **3g**, 103368-93-0; **3h**, 103368-94-1; **3i**, 103368-95-2; **4**, 4900-66-7; **5**, 103368-96-3; **6**, 613-50-3; **7**, 103368-97-4; **8**, 2942-06-5; **9**, 103368-98-5; **10**, 29906-67-0; **11**, 103368-99-6; **12**, 954-46-1; **13**, 103369-00-2; **14**, 100-52-7; **15**, 103369-01-3; **16**, 103369-02-4; Me_3SiCH_2MgCl, 13170-43-9.

Supplementary Material Available: Melting points and full NMR data for compounds **3a–h,j, 5, 7, 9, 11,** and **13** (2 pages). Ordering information is given on any current masthead page.

(15) Baltazzi, E. *C. R. Hebd. Seances Acad. Sci.* **1950**, *230*, 2207.
(16) Mech, H. *C. R. Hebd. Seances Acad. Sci.* **1906**, *143*, 752.
(17) Ward, E. R.; Poesche, W. H. *J. Chem. Soc.* **1961**, 2825.
(18) Bassindale, A. R.; Eaborn, C.; Walton, D. R. M. *J. Chem. Soc. C* **1970**, 1577.
(19) Cox, D. P.; Terpinski, J.; Lawrynowicz, W. *J. Org. Chem.* **1984**, *49*, 3216.