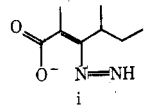
24-9; **6d**, 15250-29-0; **6e**, 91-47-4; **7**, 60065-25-0; **8**, 60065-26-1; **9**, 60132-36-7; **10**, 60132-37-8.

References and Notes

(1) Part 3 of a series on pheromone synthesis. For part 2 see P. J. Kocienski and G. J. Cernigliaro, *J. Org. Chem.*, **41**, 2927 (1976).
(2) H. M. Fales, M. S. Blum, R. M. Crewe, and J. M. Brand, *J. Insect Physiol.*, **18**, 1077 (1972).
(3) J. A. Katzenellenbogen and T. Utawanit, *J. Am. Chem. Soc.*, **96**, 6153 (1974).
(4) L. A. Carpino, *J. Am. Chem. Soc.*, **80**, 601 (1958); L. A. Carpino, P. H. Terry, and S. D. Thatte, *J. Org. Chem.*, **31**, 2867 (1966).
(5) L. A. Carpino and E. G. S. Rundberg, *J. Org. Chem.*, **34**, 1717 (1969), investigated some bicyclic halopyrazolinones in which R_1 and R_2 were alkyl groups which formed part of a ring. In these cases, the *E* isomer was the exclusive product.
(6) For a review see D. J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York, N.Y., 1965, pp 130–135.
(7) The procedure used for the preparation of **7** was derived from A. P. Krapcho, J. Diamanti, C. Cayen, and R. Bingham, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 198: bp 102–105 °C (20 mm); ir (CCl_4) 1750, 1720 cm^{-1}; NMR (CCl_4) δ 3.7 (s, 3 H), 3.7 (q, 1 H), 2.7 (quintet, 1 H), 1.6 (m, 2 H), 1.3 (d, 3 H), 1.1 (d, 3 H), 0.9 (t, 3 H).
(8) The vinyl proton of the *E* isomers **5** were consistently shifted downfield ~1.0 ppm from the corresponding *Z* isomers **6**: G. Büchi and H. Wüest, *Helv. Chim. Acta*, **50**, 2440 (1967).
(9) An alternative to the Scheme I mechanism entails hydrolytic cleavage of **2** to the vinyl diimide i which may then undergo radical decomposition to the observed products. ESR studies have shown that vinyl radicals invert



i

rapidly at −180 °C: O. Simamura, *Top. Stereochem.*, **4**, 21 (1969). The insensitivity of the **5b:6b** ratio to substitution at C-3 lends support to the notion of a linear radical or rapid inversion of a trigonal vinyl radical relative to the rate of capture by a hydrogen atom.
(10) Infrared and NMR spectra were recorded in CCl_4 solution with Perkin-Elmer 457 and Varian HA-100 instruments, respectively. Mass spectra were obtained with a Du Pont 29-491B spectrometer.

A Convenient Synthesis of Quinones from Hydroquinone Dimethyl Ethers. Oxidative Demethylation with Ceric Ammonium Nitrate

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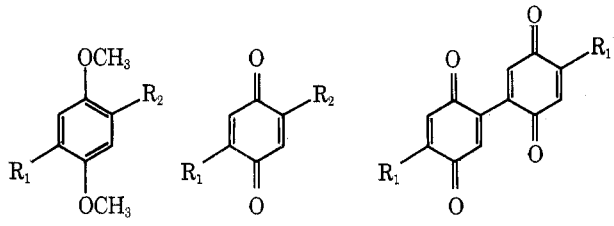
Received March 22, 1976

The oxidation of *p*-dimethoxybenzene derivatives to the corresponding benzoquinones has been accomplished using a variety of oxidizing agents,[1] particularly nitric acid[1] and argentic oxide.[2] Nitric acid works well for highly substituted 1,4-dimethoxybenzene derivatives, but in some instances nitration of the aromatic ring occurs in addition to or instead of demethylation. Argentic oxide appears to be quite broad in its application, but the reagent is relatively expensive and may be inconvenient for large scale preparations. Both nitric acid and argentic oxide require strongly acidic media, and acid labile functional groups may not be tolerated.

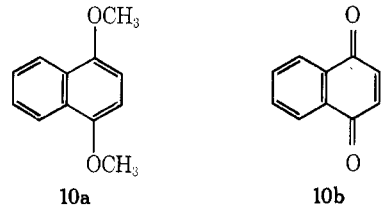
As a part of our studies on the metabolism and mechanism of action of psychotomimetic 1-phenyl-2-aminopropanes, we required a mild method for the oxidative demethylation of *p*-dimethoxybenzene derivatives. We have found that ceric ammonium nitrate [$Ce(NH_4)_2(NO_3)_6$, CAN] in aqueous acetonitrile will oxidize a variety of hydroquinone dimethyl ethers (**a**) to the corresponding quinones (**b**) often in high yield. The reaction can be carried out in the absence of strong acid, and is generally quite fast, requiring only a few minutes reaction time at room temperature. The selectivity and mildness of the reaction is illustrated by the fact that a variety of functional groups are tolerated. For example, the acid labile *tert*-butoxycarbonyl function survived the oxidation of **6a** to **6b**. Especially noteworthy is the facile conversion of the benzyl alcohol **3a** to the quinone **3b**, since CAN has been reported to oxidize benzylic alcohols to the corresponding benzaldehydes.[4]



a b c

Compd	R_1	R_2
1	H	H
2	CH_3	CH_3
3	CH_3	CH_2OH
4	CH_3	$CH{=}C(CH_3)NO_2$
5	CH_3	$CH_2CH(CH_3)NHCOCH_3$
6	CH_3	$CH_2CH(CH_3)NHCO_2C(CH_3)_3$
7	OCH_3	$CH_2CH(CH_3)NHCOC_6H_5$
8	CH_3	H
9	OCH_3	H

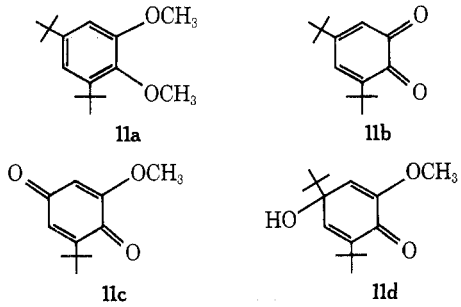
Generally, good yields of *p*-benzoquinones were obtained from 2,5-disubstituted 1,4-dimethoxybenzene derivatives. With the monosubstituted derivative 2,5-dimethoxytoluene (**8a**), however, the major product was a dimer, 4,4′-dimethylbiphenyl-2,5,2′,5′-diquinone (**8c**).[3,5] Similar results were obtained with 1,2,4-trimethoxybenzene (**9a**). In the case of the completely unsubstituted *p*-dimethoxybenzene (**1a**) a moderate (57%) yield of benzoquinone (**1b**) was obtained. Apparently, the yield was reduced by competitive dimerization, although no attempt to characterize side products was made. As an example of naphthoquinone formation, oxidation of



10a **10b**

1,4-dimethoxynaphthalene (**10a**) to naphthoquinone (**10b**) was achieved in nearly quantitative yield.

Our success in the synthesis of *p*-quinones encouraged us to attempt to extend the reaction to the synthesis of *o*-quinones. Attempted oxidation of 1,2-dimethoxybenzene to *o*-benzoquinone was unsuccessful, presumably owing to oxidative coupling reactions and/or the instability of the product. On the assumption that bulky substituents might inhibit coupling reactions and stabilize the product, we carried out the oxidation of 3,5-di-*tert*-butyl-1,2-dimethoxybenzene (**11a**). This reaction produced the desired *o*-quinone **11b**, as well as a second product, *p*-quinone **11c**, which must result from cleavage of a *tert*-butyl group from the aromatic ring. This rather remarkable transformation can be rationalized

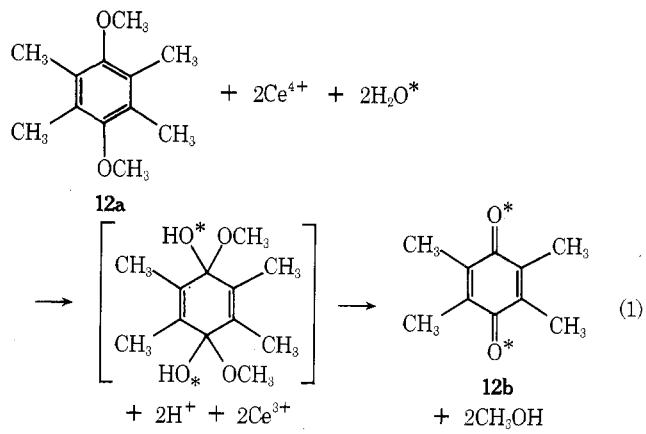


11a **11b**

11c **11d**

by postulating the intermediacy of carbinol **11d**, which undergoes oxidation with loss of a *tert*-butyl group to give quinone **11c**. It is well known that tertiary alcohols similar in structure to proposed intermediate **11d** are cleaved to ketones by CAN.[7]

Although a detailed mechanistic study was beyond the scope of the present work, we felt that it would be worthwhile to determine whether the quinone formation involves alkyl–or aryl–oxygen bond cleavage. Oxidation of 1,4-dimethoxy-2,3,5,6-tetramethylbenzene (**12a**) in the presence of $H_2{}^{18}O$



(1)

(95% isotopic enrichment) provided doubly labeled duroquinone (**12b**) (90% isotopic enrichment by chemical ionization mass spectral analysis). A control experiment showed that duroquinone (**12b**) exchanges relatively slowly with $H_2{}^{18}O$ under the reaction conditions.[8] Consequently, the oxidation must proceed by aryl–oxygen bond cleavage with the net formation of the quinone and 2 mol of methanol (eq 1). An identical mechanism has been established for analogous oxidations with argentic oxide.[2]

The ready availability of CAN, the mild and convenient reaction conditions required, and the good to excellent yields obtained for a variety of compounds suggest that the reaction should find broad application.

Experimental Section

Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. NMR spectra were recorded on a Varian A-60A or Perkin-Elmer R-12B instrument. Chemical shifts are reported in parts per million relative to Me_4Si as an internal standard. The uv spectra were recorded on a Cary 15 spectrophotometer. The chemical ionization mass spectra (CIMS) were recorded on an AEI MS-902 spectrometer using isobutane as the reagent gas. Sublimations were carried out using a Büchi Kugelrohr oven. Microanalyses were performed by the Microanalytical Laboratory, University of California, Berkeley.

General Procedure for Oxidative Demethylation. Unless otherwise noted, the dimethoxy compound was dissolved in acetonitrile, and an aqueous solution of ceric ammonium nitrate (2–3 equiv Ce^{IV}) was added portionwise over 5 min. In most cases a transient blue-black color was observed. After stirring for 30 min at room temperature, the reaction mixture was extracted with chloroform. The chloroform extract was concentrated on a rotary evaporator and the crude product was purified by sublimation or recrystallization.

***p*-Benzoquinone (1b).** To a solution of *p*-dimethoxybenzene (**1a**, 1.38 g, 10 mmol) in acetonitrile (25 ml) was added a solution of CAN (16.5 g, 30 mmol) in H_2O (25 ml). The mixture was extracted with chloroform, the extract was concentrated under reduced pressure, and the residue was sublimed (160 °C, 20 mm) to give the yellow quinone **1b** (0.61 g, 5.7 mmol, 57%), mp 111.5–112.5 °C (lit.[10] mp 114.5 °C).

2,5-Dimethyl-1,4-benzoquinone (2b). The dimethyl ether **2a**[11] (1.0 g, 6.0 mmol) in acetonitrile was treated with aqueous CAN (8.8 g, 16 mmol) to yield the bright yellow quinone **2b** which after sublimation (145 °C, 4 mm) gave 0.78 g (5.70 mmol, 95%) of pure product, mp 122.5–123.5 °C (lit.[12] mp 123.5–125 °C).

2-Hydroxymethyl-5-methyl-1,4-benzoquinone (3b). The reaction of alcohol **3a**[13] (0.17 g, 0.93 mmol) and CAN (1.1 g, 2 mmol) provided 0.1 g (73%) of crude product, mp 72–74 °C. The analytical sample was obtained by sublimation (50 °C, 0.5 mm): mp 90–93 °C; NMR ($CDCl_3$) δ 2.05 (d, J = 1.5 Hz, 3 H, CH_3), 4.55 (bd, 2 H, CH_2), 6.60 (q, J = 1.5 Hz, 1 H), 6.80 (t, J = 1.5 Hz, 1 H).

Anal. Calcd for $C_8H_8O_3$: C, 63.15; H, 5.30. Found: C, 62.93; H, 5.32.

2-(2-Nitro-1-propenyl)-5-methyl-1,4-benzoquinone (4b). A solution of CAN (50 g, 90 mmol) in 150 ml of H_2O was added portionwise, with stirring, to a solution of **4a**[14] (10 g, 42 mmol) in 300 ml of glacial acetic acid over 10 min. The mixture was stirred for 1 h at room temperature, poured into 1 l. of ice water, and filtered to collect the precipitated product. The product was washed with 200 ml of H_2O and vacuum dried to give 5.65 g (27.3 mmol, 65%) of a bright yellow powder, mp 90–91.5 °C. The analytical sample was recrystallized from methanol as long orange needles: mp 91–92 °C; NMR ($CDCl_3$) δ 2.15 (d, J = 1.5 Hz, 3 H, CH_3), 2.45 (d, J = 1.5 Hz, 3 H, CH_3), 6.75 (d, J = 1.5 Hz, 1 H), 6.85 (m, 1 H), 7.90 (m, 1 H).

Anal. Calcd for $C_{10}H_9NO_4$: C, 57.97; H, 4.38; N, 6.71. Found: C, 57.95; H, 4.38; N, 6.63.

2-(2-Acetamido-1-propyl)-5-methyl-1,4-benzoquinone (5b). The reaction of amide **5a**[15] (0.5 g, 2 mmol) with CAN (2.5 g, 4.6 mmol) in aqueous acetonitrile gave 0.43 g (97%) of crude **5b**, mp 132.5–133.5 °C. Recrystallization from a small amount of ethanol–hexane gave the pure quinone (0.28 g, 1.28 mmol, 64%) as fine yellow needles: mp 134–135 °C; NMR ($CDCl_3$) δ 1.25 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.90 (s, 3 H, $NHCOCH_3$), 2.15 (d, J = 1.5 Hz, 3 H, $CH{=}CCH_3$), 2.60 (m, 2 H, CH_2), 3.9–4.5 (1 H, CH), 6.0–6.5 (1 H, NH), 6.65 (2 H, C=CH); uv (H_2O) λ_{max} 256 nm (ϵ 16 800).

Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.14; H, 6.66; N, 6.28.

1-(2,5-Dimethoxy-4-methylphenyl)-2-*tert*-butoxycarbonylaminopropane (6a). To a solution of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane[14] (1.04 g, 5 mmol) and triethylamine (1.0 g, 10 mmol) in 25 ml of THF was added *tert*-butoxycarbonyl azide (0.86 g, 6 mmol).[25] The solution was stirred for 30 min at room temperature and then heated under reflux for 30 min. After cooling to room temperature the solution was poured into 50 ml of H_2O and extracted with ether (2 × 50 ml). The combined extracts were washed with H_2O (25 ml) and concentrated under reduced pressure to give 1.6 g of white solid, mp 116–120 °C. Recrystallization from ethanol–water gave 1.1 g (71%) of white needles: mp 124–125 °C; NMR ($CDCl_3$) δ 1.15 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.42 [s, 9 H, $C(CH_3)_3$], 2.25 (s, 3 H, $ArCH_3$), 2.76 (d, J = 6.5 Hz, 2 H, CH_2), 3.82 (s, 6 H, OCH_3), 6.70 (s, 1 H, ArH), 6.76 (s, 1 H, ArH).

Anal. Calcd for $C_{17}H_{27}NO_4$: C, 65.99; H; 8.80; N, 4.53. Found: C, 65.87; H, 8.62; N, 4.71.

2-(2-*tert*-Butoxycarbonylamino-1-propyl)-5-methyl-1,4-benzoquinone (6b). A solution of ceric ammonium nitrate (1.2 g, 2.2 mmol) in 20 ml of H_2O was added to a solution of **6a** (0.30 g, 1 mmol) in 20 ml of acetonitrile over 3 min. After stirring for 15 min the deep yellow solution was diluted with 100 ml of H_2O which resulted in precipitation of the product. The precipitate was collected by filtration and air dried to give 0.17 g (61%) of yellow solid, mp 133.5–134.5 °C. The analytical sample was recrystallized from methanol as yellow needles: mp 134–134.5 °C; NMR ($CDCl_3$) δ 1.23 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.36 [s, 9 H, $C(CH_3)_3$], 2.04 (d, J = 1.5 Hz, 3 H, $CH{=}CCH_3$), 2.3–2.8 (m, 2 H, CH_2), 4.3–4.8 (br, 1 H, CH), 6.55–6.75 (m, 2 H, CH=C).

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.02. Found: C, 64.18; H, 7.55; N, 5.18.

1-(2,4,5-Trimethoxyphenyl)-2-benzamidopropane (7a). A solution of 5 g of potassium bicarbonate in 50 ml of H_2O was added to a suspension of 1-(2,4,5-trimethoxyphenyl)-2-aminopropane hydrochloride[16] (2 g, 7.7 mmol) and benzoyl chloride (2.8 g, 20 mmol) in 50 ml of ether. The mixture was stirred for 3 h at room temperature during which a flocculent precipitate formed. The ether was removed under reduced pressure, and the crude product was recrystallized from ethanol to provide 1.97 g (6.0 mmol, 78%) of fluffy white solid: mp 156–157 °C; NMR ($CDCl_3$) δ 1.30 (d, J = 7 Hz, 3 H, $CHCH_3$), 2.86 (d, J = 7 Hz, 2 H, $ArCH_2$), 3.80 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.1–4.5 (m, 1 H, CH), 6.60 (s, 1 H, ArH), 6.79 (s, 1 H, ArH), 6.92 (br, s, 1 H, NH) 7.3–7.9 (m, 5 H, C_6H_5CO).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.12; H, 7.04; N, 4.23.

2-(2-Benzamido-1-propyl)-5-methoxy-1,4-benzoquinone (7b). Amide **7a** (0.7 g, 2.12 mmol) and CAN (3.3 g, 6.0 mmol) gave an orange solid that was crystallized from ethanol–hexane to yield 0.22 g (0.735 mmol, 35%) of pure **7b**: mp 158–159 °C; NMR ($CDCl_3$) δ 1.35 (d, J = 7 Hz, 3 H, $CHCH_3$), 2.70 (bd, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 5.97 (s, 1 H, C=CH), 6.42–6.83 (1 H, NH), 6.62 (s, 1 H, C=CH), 7.27–7.94 (5 H, ArH); uv ($CHCl_3$) λ_{max} 263 nm (ϵ 15 100).

Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.73; N, 4.68. Found: C, 67.89; H, 5.78; N, 4.60.

Oxidation of 2,5-Dimethoxytoluene (8a). The oxidation of **8a** (1.52 g, 10 mmol) with CAN (16.5 g, 30 mmol) was carried out in the usual manner. Sublimation of the crude product at 180 °C (30 mm) provided 0.1 g (0.8 mmol, 8%) of 2-methyl-1,4-benzoquinone (**8b**), mp 65–66.5 °C (lit.[5] mp 64–65 °C). The pressure was reduced to 0.05 mm and 1.02 g (8.5 mmol, 85%) of the dimeric quinone **8c** (mp 180–184 °C) was collected. Recrystallization from isopropyl alcohol–toluene gave pure **8c**, mp 189–190 °C (lit.[6] mp 189–190 °C).

Oxidation of 1,2,4-Trimethoxybenzene (9a). The reaction mixture of **9a** (0.82 g, 5 mmol) with CAN (8.3 g, 15 mmol) was worked up by addition to ice water (100 ml) followed by filtration to collect the crude orange product **9c** (0.2 g, 1.45 mmol, 29%), mp 225–227 °C dec (lit.[17] mp 205–240 °C dec).

1,4-Naphthoquinone (10b). Oxidation of 1,4-dimethoxynaphthalene[18] (**10a**, 1 g, 5.3 mmol) with CAN (8.8 g, 16 mmol) in the usual manner followed by sublimation (135 °C, 0.1 mm) of the crude product provided 0.79 g (4.98 mmol, 94%), mp 122.5–123.5 °C (lit.[19] mp 124–125 °C).

Oxidation of 3,5-Di-*tert*-butyl-1,2-dimethoxybenzene (11a). The crude product obtained from the reaction of **11a**[20] (3 g, 12 mmol) and CAN (26 g, 48 mmol) was chromatographed on a 30 × 250 mm silica gel column. Three 50-ml fractions using 30:70 ether–hexane as the eluent were collected. A fourth fraction (50 ml) using ether as the eluent was obtained. Evaporation of the solvent from fraction 2 gave a dark red residue that was recrystallized from hexane to give 0.1 g of *o*-quinone **11b**: mp 112–113 °C (lit.[21] mp 113–114 °C); uv ($CHCl_3$) λ_{max} 254 nm (sh, ϵ 2960), 402 (1690). Fraction 4 was evaporated and sublimed (120 °C, 0.1 mm) to give 0.76 g of yellow solid. Recrystallization from hexane provided pure quinone **11c** as long yellow needles: mp 81–82 °C (lit.[22] mp 84–85 °C); chemical ionization mass spectrum *m/e* 195 (MH^+, base peak); uv ($CHCl_3$) λ_{max} 268 nm (ϵ 16 400).

$H_2{}^{18}O$ Studies. CAN (155 mg, 0.283 mmol) and $H_2{}^{18}O$ (0.1 g, 5.5 mmol, 95% ^{18}O) were added to a small, oven-dried vial. 1,4-Dimethoxy-2,3,5,6-tetramethylbenzene[23] (**12a**, 16.8 mg, 0.087 mmol) in 0.3 ml of dry acetonitrile was added, the vial was capped, and the mixture was shaken occasionally over a 15-min period. The upper (organic) layer was separated, the solvent was evaporated under reduced pressure, and the residue was sublimed (130 °C, 0.5 mm) to give 5 mg of yellow solid. Chemical ionization mass spectral analysis indicated 90% bis-^{18}O-**12b** MH^+ *m/e* (rel intensity) 169 (100), 167 (8.7), 165 (2.0). As a control, a solution of duroquinone[24] (**12b**, 7.7 mg, 0.047 mmol) and 2,5-dimethyl-1,4-dimethoxybenzene (**2a**, 14.2 mg, 0.085 mmol) in 0.4 ml of acetonitrile was treated with CAN (178 mg, 0.325 mmol) in $H_2{}^{18}O$ (0.1 g, 5.5 mmol, 95% ^{18}O). The quinones were isolated by sublimation and analyzed by chemical ionization mass spectrometry: MH^+ *m/e* (rel intensity) 169 (19), 167 (54), 165 (100).

Acknowledgments. The authors are grateful to Professor Robert Weinkam for the mass spectral data. This research was supported by Public Health Service Research Grant MH 21219 and a NIH postdoctoral research fellowship to P.J.

Registry No.—**1a**, 150-78-7; **1b**, 106-51-4; **2a**, 2674-32-0; **2b**, 137-18-8; **3a**, 5600-82-8; **3b**, 40870-52-8; **4a**, 29907-72-0; **4b**, 59953-56-9; **5a**, 30784-23-7; **5b**, 59953-57-0; **6a**, 59953-58-1; **6b**, 59953-59-2; **7a**, 59953-60-5; **7b**, 59953-61-6; **8a**, 24599-58-4; **8b**, 553-97-9; **8c**, 4388-07-2; **9a**, 135-77-3; **9c**, 43042-33-7; **10a**, 10075-62-4; **10b**, 130-15-4; **11a**, 22385-74-6; **11b**, 3383-21-9; **11c**, 2300-74-5; **12a**, 13199-54-7; **12b**, 527-17-3; CAN, 16774-21-3; 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane, 15588-95-1; *tert*-butoxycarbonyl azide, 1070-19-5; 1-(2,4,5-trimethoxyphenyl)-2-aminopropane hydrochloride, 15995-72-9; benzoyl chloride, 98-88-4.

References and Notes

(1) O. C. Musgrave, *Chem. Rev.*, **69**, 499 (1969).
(2) C. D. Snyder and H. Rapoport, *J. Am. Chem. Soc.*, **94**, 227 (1972).
(3) Y.-H. C. Giza, K. A. Kun, and H. G. Cassidy, *J. Org. Chem.*, **27**, 679 (1962).
(4) W. S. Trahanovsky and L. B. Young, *J. Chem. Soc.*, 5777 (1965).
(5) Argentic oxide oxidation of 2,5-dimethoxytoluene also gives **8c** as the major product.[6]
(6) D. V. Rao, H. Ulrich, and A. A. R. Sayigh, *J. Org. Chem.*, **40**, 2548 (1975).
(7) W. S. Trahanovsky and D. B. Macaulay, *J. Org. Chem.*, **38**, 1497 (1973).
(8) In contrast to duroquinone (**12b**), it was found that 2,5-dimethyl-1,4-benzoquinone (**2b**) and 1,4-napthoquinone (**10b**) underwent relatively rapid exchange with $H_2{}^{18}O$. This finding is in accord with the results of Snyder and Rapoport that alkyl substitution adjacent to the carbonyl function greatly reduces the rate of ^{18}O exchange in naphthoquinone derivatives.[9]
(9) C. D. Snyder and H. Rapoport, *Biochemistry*, **7**, 2318 (1968).
(10) R. Craven and W. A. T. Duncan, *J. Chem. Soc.*, **127**, 1489 (1925).
(11) L. I. Smith and J. W. Opie, *J. Org. Chem.*, **6**, 427 (1941).
(12) L. I. Smith, J. W. Opie, S. Wawzonek, and W. W. Prichard, *J. Org. Chem.*, **4**, 318 (1939).
(13) L. D. Taylor and H. S. Kolesinski, *J. Polym. Sci., Part B*, **1**, 117 (1963).
(14) A. T. Shulgin, U.S. Patent 3 547 999 (1970).
(15) B. J. Ho and L. W. Tansey, *J. Med. Chem.*, **14**, 156 (1971).
(16) A. T. Shulgin, *J. Med. Chem.*, **9**, 445 (1966).
(17) A. Schüler, *Arch. Pharm. (Weinheim, Ger.)*, **245**, 262 (1907).
(18) A. Inoue, N. Kuroki, and K. Konishi, *Bull. Univ. Osaka Prefect., Ser. A*, **8**, 31 (1959); *Chem. Abstr.*, **55**, 13853e (1961).
(19) E. A. Braude and J. S. Fawcett, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 698.
(20) D. H. R. Barton, P. G. Gordon, and D. G. Hewitt, *J. Chem. Soc. C*, 1206 (1971).
(21) K. Ley and E. Müller, *Chem. Ber.*, **89**, 1402 (1956).
(22) F. R. Hewgill, B. R. Kennedy, and D. Kilpin, *J. Chem. Soc.*, 2904 (1965).
(23) K. A. Kun and H. G. Cassidy, *J. Org. Chem.*, **26**, 3223 (1961).
(24) L. I. Smith, *Org. Synth.*, **10**, 40 (1930).
(25) K. D. Polzhofer, *Tetrahedron Lett.*, 2305 (1969).

A Regiospecific Synthesis of Functionalized Vinylcyclopropanes via Cyclopropyl Cuprates

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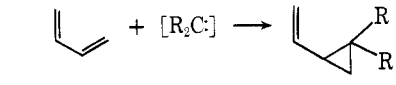
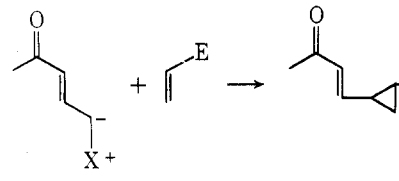
Received May 17, 1976

The synthetic utility of the vinylcyclopropane unit in the construction of cyclopentenes has been hampered by the lack of mild, efficient, and regiospecific routes to this class of compounds. One of the earliest approaches to vinylcyclopropanes involved the addition of carbenes to dienes[1] (route A).

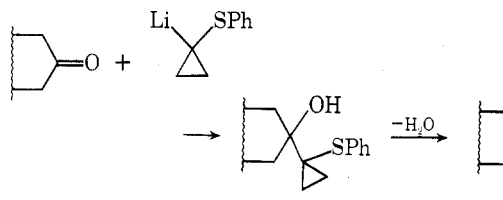


(A)

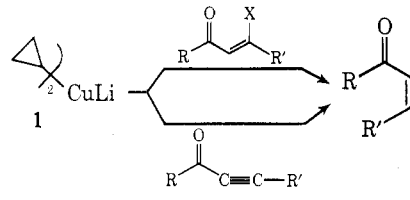


(B)

This route usually suffers from lack of regiospecificity and generality. More recently, the addition of allyl ylides to Michael acceptors has provided a mild and efficient route to functionalized vinylcyclopropanes[2] (B); the recent work of Trost and co-workers[3] also offers a number of solutions to the synthesis of vinylcyclopropanes from cyclopropyllithium reagents (C). In this note, we wish to report the facile construction of functionalized vinylcyclopropanes utilizing the conjugate addition reactions of cyclopropyl cuprates to α,β-unsaturated carbonyl compounds (D).



(C)



(D)