626-05-1; 2,6-dichloropyridine, 2402-78-0; 2,6-dihydroxy-2,6-dimethyl-4-heptanone, 3682-91-5.

References and Notes

(1) (a) Supported by National Science Foundation Grant MPS 74-20520. (b) Presented in part at the 172nd National Meeting of the American Chemical Society, San Francisco, Calif., Aug 30–Sept 3, 1976, Abstract No. ORGN-19.
(2) J. V. Hay and J. F. Wolfe, *J. Am. Chem. Soc.*, **97**, 3702 (1975).
(3) J. V. Hay, T. Hudlicky, and J. F. Wolfe, *J. Am. Chem. Soc.*, **97**, 374 (1975).
(4) N. Kornblum, *Angew. Chem., Int. Ed. Engl.*, **14**, 734 (1975).
(5) (a) R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **38**, 1407 (1973); (b) *ibid.*, **37**, 36
0 (1972); (c) J. F. Bunnett and B. F. Gloor, *ibid.*, **38**, 4156 (1973); (d) *ibid.*, **39**, 382 (1974); (e) J. F. Bunnett and X. Creary, *ibid.*, **39**, 3612 (1974); (f) *ibid.*, **39**, 3173 (1974); (g) R. A. Rossi, R. H. deRossi, and A. F. López, *J. Am. Chem. Soc.*, **98**, 1252 (1976).
(6) J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463, 7464 (1970).
(7) J. F. Wolfe, J. C. Greene, and T. Hudlicky, *J. Org. Chem.*, **37**, 3199 (1972).
(8) R. A. Rossi, R. H. deRossi, and A. F. López, *J. Org. Chem.*, **41**, 3371 (1976).
(9) J. A. Zoltewicz, T. M. Oestreich, and A/ A. Sale, *J. Am. Chem. Soc.*, **97**, 5889 (1975).
(10) A. K. Hoffman, A. M. Feldman, E. Gelblum, and W. G. Hodgson, *J. Am. Chem. Soc.*, **86**, 639 (1964).
(11) J. F. Bunnett and J. E. Sundberg, *J. Org. Chem.*, **41**, 1702 (1976).
(12) R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **38**, 3020 (1973).
(13) A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, *J. Chem. Soc. A*, 666 (1969).
(14) J. F. Bunnett and X. Creary, *J. Org. Chem.*, **39**, 3611 (1974).
(15) R. A. Rossi and J. F. Bunnett, *J. Am. Chem. Soc.*, **94**, 683 (1972).
(16) A ketone enolate to halopyridine ratio of 2:1 is required for ketones having two or more α hydrogens, since 1 equiv of ketone enolate is necessary to ionize the pyridyl ketone product. Ketones with only one α hydrogen would need a ketone enolate to halopyridine ratio of 1:1.
(17) A. K. Hoffmann, A. M. Feldman, E. Gelblum, and A. Henderson, "Organic Syntheses", Collect. Vol. V, H. E. Baumbarten, Ed., Wiley, New York, N.Y., 1973, p 355.
(18) N. Kornblum, R. J. Clutter, and W. J. Jones, *J. Am. Chem. Soc.*, **78**, 4003 (1956).
(19) The enol content of the pyridyl ketones prepared in this study was estimated by comparison of the integrated intensities of the ^{1}H NMR signals arising from H-6 of the pyridine nucleus in each tautomeric form, or by comparing the intensity of proton signals (saturated and vinylic) arising from the hydrogens α to the pyridine ring with the intensity of the remaining nonenolizable protons of the side chain.
(20) No attempt has been made to optimize the isolated yield of **16**. We are pleased to acknowledge the assistance of Mr. Richard Goehring in carrying out this experiment.
(21) J. P. Wibant, C. C. Kloppenburg, and M. G. J. Beets, *Recl. Trav. Chim. Pays-Bas*, **63**, 134 (1940).
(22) J. B. Conant and N. Tuttle, "Organic Syntheses", Collect. Vol. I, H. Gilman and A. H. Blatt, Ed., Wiley, New York, N.Y., 1941, p 199.
(23) E. E. Connolly, *J. Chem. Soc.*, 338 (1944).
(24) H. C. Brown, J. D. Brady, M. Grayson, and W. H. Bonner, *J. Am. Chem. Soc.*, **79**, 1897 (1957).

Heterodienophiles. 8.[1] Acid-Catalyzed Reactions of Benzal- and Methylenebisurethanes with α-Phellandrene. Structural and Stereochemical Studies

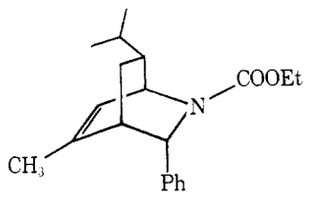
Grant R. Krow,* Kalyani M. Damodaran, Der Min Fan, Ron Rodebaugh, Anthony Gaspari, and Upendir K. Nadir

Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

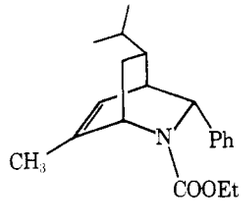
Received February 2, 1977

The boron trifluoride/copper bromide catalyzed reactions of benzal- and methylenebisurethane with α-phellandrene (**3**) have been investigated. Benzalbisurethane (**4**) affords a 37/63 mixture of 3-*endo*- and -*exo*-phenyl-5-methyl-7-isopropylisoquinuclidines (**1** and **6**), the products of regiospecific 1,4-cycloaddition of benzaliminourethane (**5**) to α-phellandrene (**3**). Methylenebisurethane **17** and α-phellandrene (**3**), however, afford *N*-carbethoxy-1-methyl-4-isopropenyl-6-azabicyclo[3.2.1]octane (**19**) and *N*-carbethoxy-3,7,7-trimethyl-9-azabicyclo-[4.3.0]non-2-ene (**20**), products derived by formal 1,3-cycloaddition of iminourethane to *p*-menthadiene isomers of α-phellandrene (**4**); thus, methylenebisurethane **17** and α-terpinene also afforded **19** and **20**. Ozonolysis of **19** completed a two-step synthesis of *N*-carbethoxy-1-methyl-6-azabicyclo[3.2.1]oct-4-one (**21**). Camphene (**29**) and **17** afforded amidoalkylation product **31**.

The Diels–Alder cycloaddition of imines with conjugated dienes offers a convenient synthetic route to diverse azacyclic and azabicyclic molecules.[1-4] Surprisingly, however, questions of regiochemistry and stereochemistry in these additions have been little explored.[3] In one study by Harter and Liisberg[3g] a regioisomeric mixture of *anti*-isopropyl, *endo*-phenylisoquinuclidines **1** and **2** of unspecified relative amounts has been



1



2

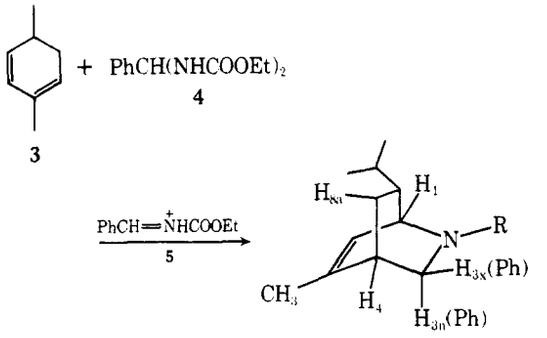
reported from the reaction of α-phellandrene (**3**) with benzalbisurethane (**4**), a precursor of the iminourethane **5**.

We decided to continue the study of alkylidenebisurethane reactions with cyclic terpenes for several reasons. We doubted the regiochemical and stereochemical assignments given to the mixture of **1** and **2**. Cycloaddition reactions of iminourethane **5** with cyclohexa-1,3-diene do not afford 3-*endo*-phenylisoquinuclidine (**7**) only; they afford a 3-*endo*/*exo*-phenylisoquinuclidine **7**/**8** mixture with the 3-*exo*-phenyl isomer **8** predominating.[1g] Also, considerations of relative carbonium ion stabilities in a stepwise addition of an immonium ion[1b,f,g] to α-phellandrene might favor regioisomer **1** to the exclusion of **2**. Cyclic terpenes are readily available and facile synthetic access to the ring skeletons of several alkaloid[5,6] systems is available by direct cycloaddition[2i] or rearrangement[4] of initially formed adducts. We hoped to extend the scope of these syntheses.

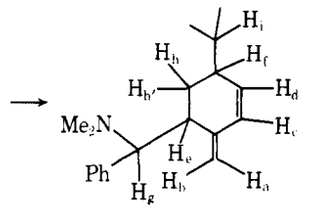
Results and Discussion

Reactions of α-Phellandrene and Benzalbisurethane. Reaction of α-phellandrene (**3**) with benzalbisurethane (**4**) in

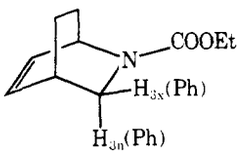
refluxing benzene or chloroform containing boron trifluoride etherate and copper bromide as catalyst[3c] gave what was shown by NMR analysis to be a mixture of 3-*endo*-phenyl adduct **1** (37%) and 3-*exo*-phenyl adduct **6** (63%). For the



1, Ph-*endo*, H_{3x}, R = COOEt
6, Ph-*exo*, H_{3n}, R = COOEt
9, Ph-*endo*, H_{3x}, R = CH_3
10, Ph-*exo*, H_{3n}, R = CH_3
11, Ph-*exo*, H_{3n}, NR = NMe_2^+



12



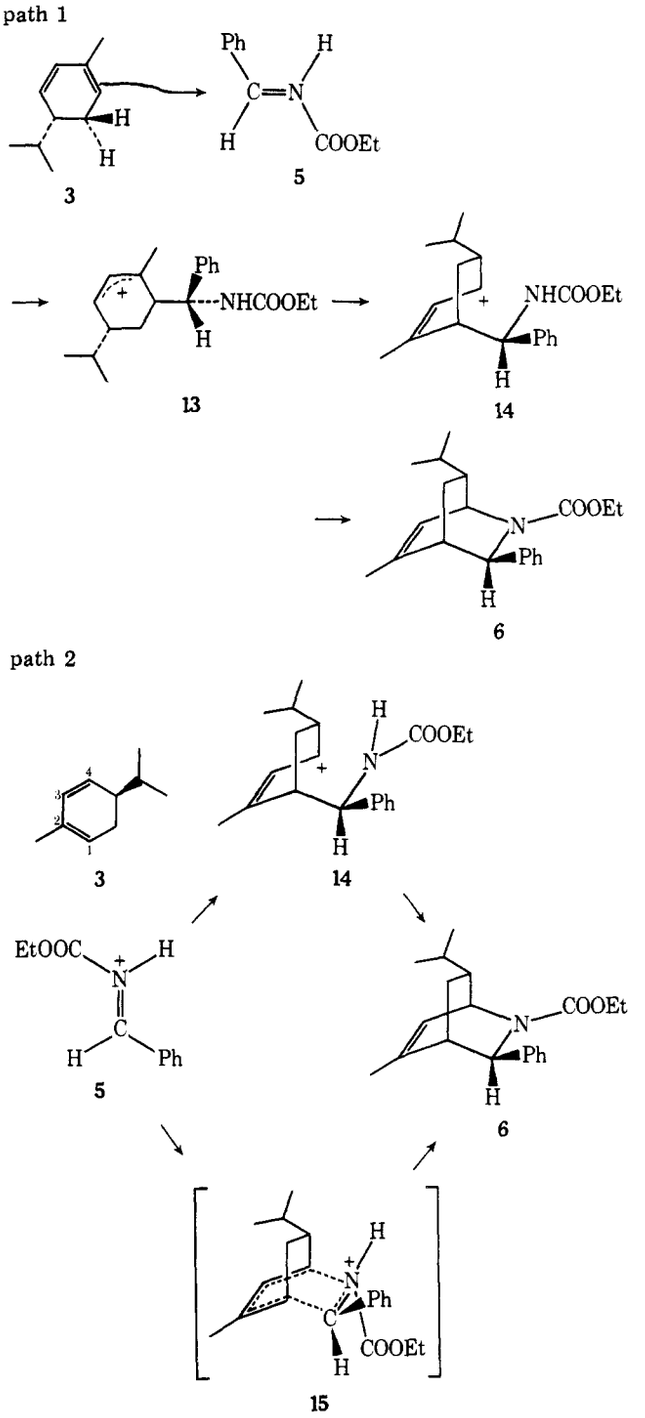
7, Ph-*endo*, H_{3x}
8, Ph-*exo*, H_{3n}

minor *endo*-phenyl isomer **1** proton H_{3x} at δ 4.60 (d, $J_{3x,4}$ = 4 Hz) coupled only with H_4 at δ 2.50. With the major *exo*-phenyl isomer **6** proton H_{3n} at δ 4.36 (m, $J_{3n,4}$ = 4.75, $J_{3n,8a}$ = 2 Hz) showed long-range W-plan coupling to H_{8a} characteristic of the 3-endo proton in isoquinuclidines.[1e,g] Absorption for allylic methyls of **1** and **6** appeared as singlets at δ 1.86 and 1.88. The downfield shift of H_{3x} (δ 4.60) of **1** relative to H_{3n} (δ 4.36) of **6** compares favorably with the chemical shifts (acetone-d_6) of *N*-carbethoxy-*endo*- and *exo*-3-phenylisoquinuclidines (**7** and **8**) for H_{3x} (δ 4.70) and H_{3n} (δ 4.38).[1g] Stereochemical ratios of **1** and **6** were determined by the relative NMR integrated areas for protons H_{3x} and H_{3n}. A somewhat lower *exo*-phenyl preference is observed with α-phellandrene (**3**) as diene (63% 3-*exo*-phenyl isomer **6**) than with cyclohexa-1,3-diene (80% 3-*exo*-phenyl isomer **8**).[1g]

The mixture of **1** and **6** was reduced with lithium aluminum hydride in ether to afford a mixture of the 3-*endo*-phenylamine **9** and the 3-*exo*-phenylamine **10**. Column chromatography gave amines **9** (42%) and **10** (58%) in a ratio comparing favorably with the ratio of **1** to **6** (37/63) obtained by NMR integration. Reaction of the mixture of **9** and **10** as reported by Harter and Liisberg[3g] with methyl iodide in acetone at room temperature afforded a crystalline methiodide **11** from the major 3-*exo*-phenyl isomer **10** and a residue of the minor 3-*endo*-phenyl isomer **9** which had not been methylated. The gross structural features of the cycloadduct **6** were confirmed by pyrolyzing the hydroxide salt of quaternary ammonium salt **11** to form amine **12**. The structure of **12** was determined from its NMR spectrum; the spectral analysis did not enable a determination of the relative stereochemistry of the alkyl substituents of **12**.

Mechanistic Discussion. Several reaction sequences for formation of cycloaddition products from diene and immonium ions have been proposed.[1g] These are shown in Scheme

Scheme I. Mechanistic Alternatives for Formation of Isoquinuclidine 6



I for isoquinuclidine **6**; the mechanistic scheme for the stereoisomer **1** is the same in principle.

Path 1. A stepwise addition of the diene **3** to the carbon of the immonium ion **5** leads to the terminally methyl-substituted allylic cation **13**; intramolecular trapping of **13** leads to isoquinuclidine **6**. An anti orientation for isopropyl would result from attack of **5** at the less hindered face of the diene, but the distance of the isopropyl group from the reaction site makes it difficult to account for facial selectivity via this mechanistic pathway. The preferential 3-*exo*-phenyl stereochemistry favoring **6** over **1** results if the immonium ion **5** approaches the diene **3** with the larger phenyl substituent

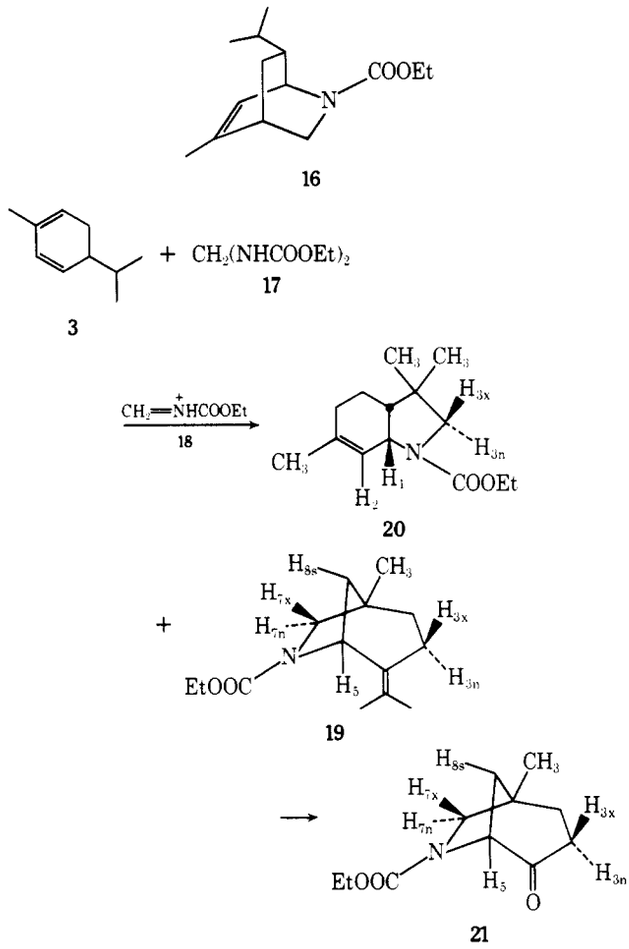
oriented predominantly over the diene and away from the hydrogens of the diene bridge to give **13.** Subsequent bond rotation to **14** and intramolecular ring closure leads to 3-*exo*-phenylisoquinuclidine (**6**).[7] Since Dreiding molecular models suggest intolerable steric interaction between phenyl and the allylic proton in a path 1 transition state going to **13** but affording the stereoisomeric 3-*endo*-phenylisoquinuclidine (**1**), we do not favor the path 1 mechanism.

Path 2. Cyclic stepwise or concerted [$_{\pi}4 + _{\pi}2$] transition states might be involved. The observed regiochemistry in forming **6** from intermediate **14** or transition state **15** is that expected from consideration of allylic carbonium ion stabilities. A concerted cycloaddition of a charged immonium ion **5** to diene **3** via **15** might be expected to have a transition state polarization paralleling in stability the ground state allylic cation **14.** An anti orientation for the isopropyl group can be suggested on the basis of the rule of steric approach control[8] in cycloaddition reactions as has been done for other α-phellandrene cycloadducts.[9] The preferential formation of 3-*exo*-phenylisoquinuclidine (**6**) in a kinetically controlled cycloaddition[10] would result if carbethoxyl has a greater endo preference than phenyl and if the immonium ion **5** has the more stable[1b] *E* configuration.[11] Substituent preferences determined in the Diels–Alder reaction of cyclopentadiene with *trans*-cinnamic acid methyl ester show 44% *exo*-phenyl isomer and 2-phenylmethylacrylic acid affords 60% *exo*-phenyl isomer.[8] These results indicate that phenyl and carbethoxyl have similar endo substituent preferences in the Diels–Alder reaction and they are consistent with the observed 63/37 ratio of **6**/**1** in a cyclic transition state. It is nevertheless possible that the *exo*-phenyl preference may be due to other factors associated with a longer lived carbonium ion species formed by a stepwise, but cyclic, reaction. Selectivity in trapping of intermediate **14** by external urethane nucleophile may affect the observed stereochemical preference.[1g]

Reaction of α-Phellandrene with Methylenebisurethane. In an attempt to synthesize the isoquinuclidine ring system **16** by a [4 + 2] cycloaddition α-phellandrene (**3**) and methylenebisurethane **17** were reacted in benzene or chloroform using boron trifluoride etherate and copper bromide catalysts. Two major products were isolated; neither adduct corresponds to the expected cycloaddition product **16!** The major products, assigned structures **19** and **20,** arise not by 1,4-cycloaddition, but by novel 1,3-cycloadditions of iminourethane to *p*-menthadiene isomers of α-phellandrene.

The structures of **19** and **20** were assigned with the aid of NMR spectral parameters. Of special interest to the present study was the NMR ($CDCl_3$) resonance for the major product *N*-carbethoxy-1-methyl-4-isopropenyl-6-azabicyclo[3.2.1]-octane (**19**) at δ 1.60 (s) for the two isopropylidene methyl groups and the absence of peaks in the vinyl region. Proton H_5 at δ 4.84 (d, $J_{5,8s}$ = 6 Hz) is allylic and next to nitrogen. The proton H_{7x} at δ 3.26 (d, J = 10 Hz) is coupled only to H_{7n} at δ 3.02 (d)[12] confirming the bridgehead position for the singlet methyl at δ 1.05. One of the allylic protons H_3 appears at δ 2.48 (dd, J = 15.5, 5.7 Hz); the other H_3 proton is part of a broad envelope from δ 0.8 to 2.0. Ozonolysis of **19** afforded 1-methyl-6-azabicyclo[3.2.1]oct-4-one (**21**). The NMR spectrum of **21** showed a single methyl peak at δ 0.78 (s) confirming cleavage of the isopropylidene double bond and loss of the allylic methyl groups.

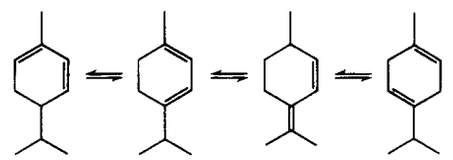
The NMR spectrum of the minor product *N*-carbethoxy-3,7,7-trimethyl-9-azabicyclo[4.3.0]non-2-ene (**20**) showed peaks for the protons H_{8x} and H_{8n} next to nitrogen at δ 3.32 and 3.10 only mutually coupled with J = 11 Hz; geminal methyls appear as singlets at δ 1.02 and 0.98. Olefinic proton H_2 at δ 5.94 is broad, but narrows to a broadened doublet, J = 3 Hz (long-range coupling), upon irradiation of H_1 at δ 4.20 (broad). The allylic methyl appears as a singlet at δ 1.72. The



difficulty in resolving H_1 precluded determination of the stereochemistry of ring fusion using spin decoupling techniques;[13c] however, the broadening of H_1 suggests the more flexible cis configuration for **20** in agreement with mechanistic considerations (vide infra).

Mechanism. Equilibration studies[14] of *p*-menthadienes in sulfuric acid (Scheme II) show that α-phellandrene (**3**), the

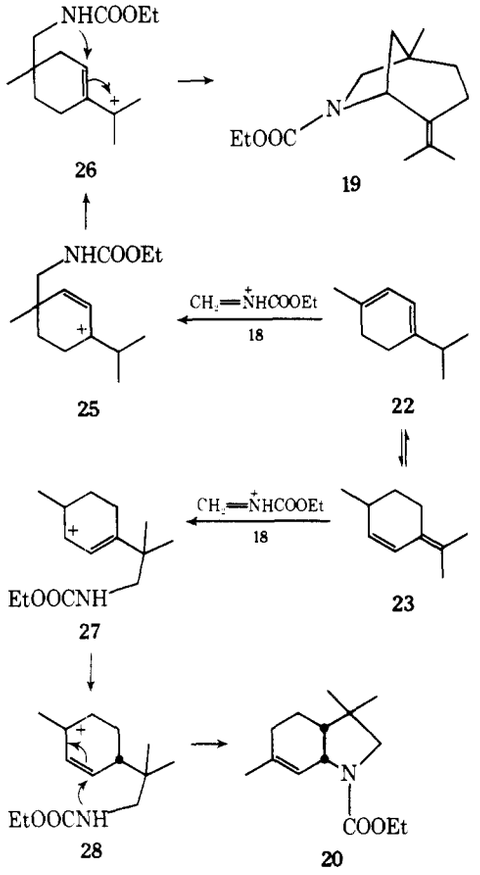
Scheme II. Equilibrium Concentrations of *p*-Menthadienes in Acid[14]



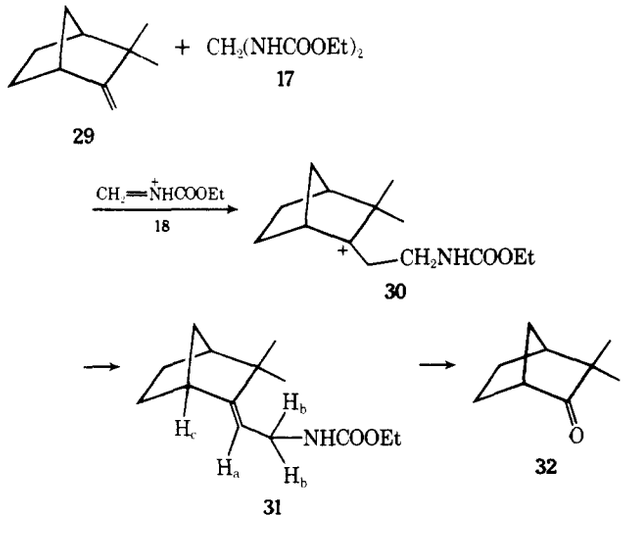
3 (0%) **22** (53%) **23** (30%) **24** (14%)

starting material in the formation of **19** and **20,** is nearly totally converted to a mixture of α-terpinene (**22**), isoterpinolene (**23**), γ-terpinene (**24**), and other minor components. Upon consideration of the data of Scheme II a postulated mechanism for formation of **19** and **20** from *p*-menthadienes in acidic medium can be shown in Scheme III. Addition of an acid complexed iminourethane **18** to the less hindered end of the major conjugated diene **22** in an equilibrating mixture of *p*-menthadienes will afford cation **25.** Proton loss and reprotonation will give a new allylic cation **26,** which upon internal trapping by the proximate nucleophilic urethane nitrogen gives **19.** Similarly, addition of protonated iminourethane **18** to the exocyclic terminus of **23** will afford allylic cation **27.** Deprotonation of **27** and reprotonation to give **28** will lead to **20** upon intramolecular cyclization by urethane nitrogen. Consideration of models of a planar allylic cation **28** indicates that ring closure will lead to a cis ring fusion in **20**[13] because of conformational rigidity of the intermediate.

Scheme III. Proposed Mechanisms for Formation of 19 and 20



Consistent with the proposed mechanism of Scheme III was the reaction of α-terpinene (22) with methylenebisurethane 17 to give 19 and 20 in a 60/40 ratio. The greater percentage of 20 in this reaction possibly indicates a greater percentage of 23 in a preequilibrium mixture of p-menthadienes than found during the reaction with α-phellandrene (3). Although the p-menthadiene equilibrium has been reached from α-pinene,[15] attempted reactions with α- and β-pinene, Δ-carene, or limonene did not lead to a clean formation of 19 and 20, but to mixtures of numerous components. This is reasonable, since during acid-catalyzed terpene equilibration the numerous olefinic species can be trapped by protonated iminourethanes or by protons and urethane before the equilibrium mixture of p-menthadienes rich in 22 and 23 can be reached. Camphene (29) did not equilibrate to p-menthadienes during reaction with methylenebisurethane 17, but afforded cleanly



the amidoalkylation product 31. The structural assignment to 31 was based upon ruthenium tetroxide cleavage of 31 to camphenilone (32) and the NMR spectrum ($CDCl_3$) of 31, δ 4.95 (t, J = 7 Hz, H_a), 3.73 (t, J = 7 Hz, H_b), 4.74 (NH). Adduct 31 can be formed by attack of 29 on immonium ion 18 to afford carbonium ion 30; loss of a proton from 30 yields 31.

Conclusion

The reaction of benzalbisurethane 4 with α-terpinene (22) afforded a mixture of numerous components; however, TLC comparison showed no evidence for formation of 1 and 2. Thus, primary formation of 1 and 2 in the reaction of benzalbisurethane 4 with α-phellandrene (3) rather than with later formed isomeric p-menthadienes (Scheme II) is consistent with a greater reactivity of benzaliminourethane 5 than methyleneurethane 18 with α-phellandrene under conditions of boron trifluoride etherate catalysis. This contrasts with a reported much lower reactivity of 4 than 18 with norbornadiene;[2c] it is possible that steric effects in the transition state for reaction of the phenyl substituted imine 5 with norbornadiene present too high a barrier to reaction.

The present conversion of α-phellandrene to 19 represents one of the simplest synthetic routes to this azabicyclic ring system.[16] The indication that product formation can be dependent on the timing of introduction of the alkylidenebisurethane to a dienic system capable of acid-catalyzed isomerization is under further investigation in order to extend the synthetic utility of these reactions.

Experimental Section

NMR spectra were determined on a Varian Associates XL-100-15 spectrometer using Me_4Si as internal standard. Solutions of 5–10% solute in $CDCl_3$, acetone-d_6, or benzene-d_6 were used for NMR measurements. Chemical shifts were where necessary obtained with the aid of decoupling experiments. NMR spectra were simplified by observation at elevated temperatures (77–88 °C) in order to rapidly average urethane conformations. At ambient temperatures superimposed spectra of conformers often complicate the observed patterns for the protons directly adjacent to nitrogen.

General Procedure for Reaction of Terpenes. A solution of diene (13.6 g, 0.1 mol) in 100 mL of dry benzene or chloroform was added dropwise over 30 min to a stirred refluxing solution of alkylidenebisurethane (0.1 mol) and 5 mL of boron trifluoride etherate in 200 mL of dry benzene or chloroform. In some cases copper bromide (1–2 g) was initially added. After refluxing for 3–15 h the reaction mixture was cooled, washed with water, aqueous sodium carbonate, 10% hydrochloric acid, and water, and then dried over magnesium sulfate. Solvent was removed in vacuo and the residue was extracted with petroleum ether. After evaporation of solvent the product was isolated by distillation, column chromatography, or VPC. The α-phellandrene (3) (MCB) was 83% pure by VPC; 17% had aromatized.[24] Wallach's[25] procedure was used to convert terpineol to α-terpinene (22), which was purified by spinning band distillation. Camphene (29) was obtained from MCB.

3-*endo*- and -*exo*-Phenyl-5-methyl-7-isopropylisoquinuclidines (1 and 6). Reaction of α-phellandrene (3) with benzalbisurethane 4 in benzene with boron trifluoride catalysis according to the Harter procedure[3g] afforded a liquid mixture of the previously reported, inadequately characterized, and incorrectly identified 1 and 6: bp 141–153 °C (0.125 mm) [lit.[3g] bp 170 °C (2 mm)]; NMR (acetone-d_6, 70 °C) of the mixture of 1 and 6, δ 0.78 (3 H, t, J = 6 Hz), 0.86–1.86 (10 H, m), 1.86, 1.88 (3 H, two s), 2.50 (H_4, m), 3.95 (2 H, q), 4.36 (H_{3n}, m, $J_{3n,4}$ = 4.75, $J_{3n,8a}$ = 2 Hz, 63% of a proton integral), 4.60 (H_{3x}, d, $J_{3x,4}$ = 4 Hz, 37% of a proton integral), 4.90 (H_1, m), 6.00 (H_6, m), 7.20 (5 H, m). The 63/37 ratio of 6/1 was determined from the relative integrals for H_{3n} and H_{3x} of 6 and 1.

***N*-Methyl-3-*endo*- and -*exo*-phenyl-5-methyl-7-isopropylisoquinuclidines (9 and 10).** Reduction of 1.1 g of the mixture of 1 and 6 with lithium aluminum hydride according to the procedure of Harter[3g] afforded an endo/exo mixture of amines 9 and 10, bp 101–110 °C (0.15 mm) [lit.[3g] bp 110 °C (0.5 mm)]. The amines could be separated by dry column chromatography (Analtech, silica gel GF, 1000 μm, 10 hexane:1 ethyl acetate) to give 9, 410 mg (42%), and 10, 570 mg (58%). NMR ($CDCl_3$) of 9 showed δ 0.64–1.84 (10 H, m), 1.94 (3 , s), 2.20 (3 H, s), 2.24 (1 H, m), 2.94 (H_{3x}, broad s), 3.34 (H_1, dd, J = 2, 5

Hz), 5.88 (1 H, d, J = 5 Hz, some small coupling), 7.30 (5 H, m). NMR ($CDCl_3$) of **10** showed δ 0.80–1.90 (10 H, m), 1.48 (3 H, s), 2.26 (H_4, m), 2.34 (3 H, s), 3.06 (H_{3n}, broad singlet), 3.30 (H_1, dd, J = 5, 1 Hz), 6.14 (H_6, m, $J_{1,6}$ = 5 Hz), 7.20 (5 H, m).

Hofmann Degradation of Amine 10. Treatment of the amine mixture **9** and **10** according to Harter[3g] with methyl iodide in acetone at room temperature afforded the crystalline methiodide **11** of the major 3-*exo*-phenyl isomer **10**: mp 194–195 °C (acetone) (lit.[3g] mp 193–194 °C); NMR ($CDCl_3$) δ 0.92 (3 H, d, J = 6 Hz), 1.04 (3 H, d, J = 6 Hz), 0.90–1.30 (3 H, br), 2.20 (3 H, s), 2.64 (3 H, s), 2.86–2.70 (2 H, br), 3.66 (3 H, s), 4.86 (H_1, d, J = 6 Hz), 5.16 (H_{3n}, br), 6.26 (H_6, d), 7.42 (5 H, s). The minor 3-*endo*-phenyl isomer **9** failed to quaternize and remained in the mother liquor.

The methiodide **11** (375 mg) was placed with silver oxide (226 mg) in 1:1 methanol–water (5 mL) and stirred for 2 h at 25 °C. The mixture was filtered, the residue was washed with methanol–water (5 mL), and the filtrate was concentrated in vacuo at 100 °C. The residue (248 mg) was distilled at 140–145 °C (0.3 mm) to afford amine **12** (77 mg): NMR ($CDCl_3$) δ 2.20 (s, NMe_2), 5.00, 5.06 (H_a, H_b, s, s), 5.74 (H_c, d, $J_{c,d}$ = 10 Hz), 6.28 (H_d, dd, $J_{d,f}$ = 3 Hz), 3.12 (H_e, td, $J_{e,g}$ = 11.5, $J_{e,hh'}$ = 4 Hz), 1.90 (H_f, m), 3.66 (H_g, d), 1.28–1.64, (H_h, $H_{h'}$, H_i, m, $J_{f,hh'}$ = 8 Hz), 0.76 (CH_3, d, J = 6 Hz), 7.10–7.50 (Ph, m).

Anal. Calcd for $C_{19}H_{27}N$: C, 84.70; H, 10.10; N, 5.20. Found: C, 84.59; H, 9.80; N, 5.09.

***N*-Carbethoxy-1-methyl-4-isopropenyl-6-azabicyclo[3.2.1]-octane (19) and *N*-Carbethoxy-3,7,7-trimethyl-9-azabicyclo[4.3.0]non-2-ene (20).** Reaction of α-phellandrene (**3**, 8.2 g, 0.06 mol) in $CHCl_3$ with methylenebisurethane **17** (11.6 g, 0.06 mol) according to the general procedure afforded upon distillation (0.16 mm) mainly **19**, 3.1 g (22%), bp 100–110 °C, and a 60/40 mixture of **19** and **20**, 1.5 g (11%), bp 110–120 °C; the mixture was separated by VPC (6 ft × 0.25 in. SF-96 on Chromosorb W, 140 °C). Further distillation afforded a mixture of minor components. Use of benzene as solvent resulted in slightly lower yields (20–25%) but the **19/20** ratio of 84/16 changed little. Longer reflux times (20 h) resulted in disappearance of **19** and **20** as shown by GC monitoring of the reaction. At 30 °C adducts **19** and **20** were not formed. The NMR spectrum of **19** ($CDCl_3$, 80 °C) showed δ 0.8–2.0 (broad envelope), 4.84 (H_5, d, $J_{5,8s}$ = 6 Hz), 3.26 (H_{7x}, d, J = 10 Hz), 3.02 (H_{7n}, d), 2.48 ($H_{3x(3n)}$, dd, J = 15, 6 Hz), 1.76 (H_{8s}), 1.05 (CH_3), 1.60 (CH_3C=), 1.61, 1.71 (in acetone-d_6).

Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.89; H, 9.70; N, 5.91. Found: C, 70.78; H, 9.85; N, 5.72.

The NMR spectrum ($CDCl_3$, 80 °C) of **20** showed δ 1.1–2.0 (broad), 4.20 (H_1, buried under CH_2 of ethyl ester), 5.94 (H_2, broad, narrows to a broadened doublet, J = 3 Hz, upon irradiation of H_1), 3.32, 3.10 ($H_{8x,8n}$, d, J = 11 Hz), 1.02, 0.98 (CH_3, singlets), 1.72 (CH_3C=, s).

Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.89; H, 9.70; N, 5.91. Found: C, 70.82; H, 9.41; N, 5.84.

***N*-Carbethoxy-1-methyl-6-azabicyclo[3.2.1]octan-4-one (21).** Ozone[26] was bubbled through a methylene chloride (5 mL) solution of **19** (234 mg, 1 mmol) at −78 °C for 2 h. The blue color was discharged by bubbling nitrogen through the solution and dimethyl sulfide (2 mL) in methylene chloride (2 mL) was added dropwise. Methylene chloride (10 mL) was added, the solution was extracted with water (6 × 5 mL) and dried over magnesium sulfate, and solvent was removed in vacuo to afford 190 mg (91%) of oil, bp 100–110 °C (0.05 mm) (molecular distillation). VPC (5 ft × 0.25 in. 6% XF 1150 Chromosorb W, 180 °C, t_R 20 min) gave pure **21**: NMR (benzene-d_6, 80–85 °C) δ 1.0–1.8 (complex), 1.1 (3 H, t, J = 7 Hz), 4.02 (2 H, q, J = 7 Hz), 4.14 (H_5, d, $J_{5,8s}$ = 5.8 Hz), 3.36 (H_{7x}, d, J = 10.3 Hz), 3.08 (H_{7n}, dd, J = 10.3, 1.5 Hz), 1.8–2.50 ($H_{3x(3n)}$, broad multiplet), 0.78 (CH_3, s).

Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.56; H, 8.06; N, 6.64. Found: C, 62.80; H, 8.26; N, 6.64.

Reaction of Methylenebisurethane 18 with α-Terpinene (22). Reaction of α-terpinene (**22**, 2.05 g, 0.015 mol) in chloroform for 5 h according to the general procedure afforded **19** and **20** in a 60/40 ratio by VPC, 1.04 g (25%).

Reaction of Methylenebisurethane 18 with Camphene (29). Reaction of camphene (**29**, 2.75 g, 0.02 mol) according to the general procedure afforded upon distillation at 120–130 °C (0.01 mm) 3.3 g (69%) of **31**: IR (neat) 3350, 1710 cm^{-1}; NMR ($CDCl_3$) δ 4.95 (H_a, t, J = 7 Hz), 4.74 (NH), 4.08 (OCH_2, q), 3.73 (H_b, t, J = 7 Hz), 2.95 (H_c, m), 0.98 (s, 3 H), 1.0–1.9 (m, 10 H).

Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.76; N, 5.90. Found: C, 70.64; H, 9.67; N, 5.96.

Oxidation of 31 to Camphenilone (32). A solution of ruthenium tetroxide in carbon tetrachloride (25 mL) was prepared from ruthenium dioxide tetrahydrate (200 mg, soluble form).[27] Adduct **31** (200 mg) in carbon tetrachloride (5 mL) was added to the solution and stirred at 25 °C for 24 h. Filtration, removal of solvent, and molecular distillation (80 °C, 0.2 mm) afforded an oil which was further purified by GC to give camphenilone (**32**); IR, NMR, and VPC retention time were identical with those of a known purified sample (Chemical Samples). Ozonolysis of **31** was less effective in cleaving the olefinic bond; only trace amounts of camphenilone (**32**) were formed.

Acknowledgment. We acknowledge support of this research by the National Institutes of Health CA-12020. We thank C. Pyun, K. Cleaver, D. Weir, J. Reilly, and A. Mancuso for technical assistance.

Registry No.—**1**, 62227-97-8; **3**, 99-83-2; **4**, 3693-54-7; **6**, 62278-86-8; **9**, 62278-87-9; **10**, 62278-88-0; **11**, 62227-99-0; **12**, 62228-00-6; **17**, 3693-53-6; **18**, 62227-98-9; **19**, 61654-90-8; **20**, 61654-91-9; **21**, 61654-92-0; **22**, 99-86-5; **29**, 79-92-5; **31**, 62228-01-7.

References and Notes

(1) For the previous papers in this series: (a) G. R. Krow, R. Rodebaugh, U. K. Nadir, and A. Gaspari, *Tetrahedron Lett.*, 2943 (1976); (b) G. R. Krow, C. Pyun, C. Leitz, J. Marakowski, and K. Ramey, *J. Org. Chem.*, **39**, 2449 (1974); (c) G. R. Krow, C. Pyun, R. Rodebaugh, and J. Marakowski, *Tetrahedron*, **30**, 2977 (1974); (d) G. Krow, R. Rodebaugh, J. Marakowski, and K. C. Ramey, *Tetrahedron Lett.*, 1899 (1973); (e) G. Krow and R. Rodebaugh, *Org. Magn. Reson.*, **5**, 73 (1973); (f) G. Krow, R. Rodebaugh, M. Grippi, G. DeVicaris, C. Hyndman, and J. Marakowski, *J. Org. Chem.*, **38**, 3094 (1973); (g) G. Krow, R. Rodebaugh, R. Carmosin, W. Figures, H. Pannella, G. DeVicaris, and M. Grippi, *J. Am. Chem. Soc.*, **95**, 5273 (1973).

(2) (a) H. E. Zaug, *Synthesis*, 2, 49 (1970), has reviewed reactions of *N*-ethoxycarbonylimines; (b) T. Imagawa, K. Sisido, and M. Kawanisi, *Bull. Chem. Soc. Jpn.*, **46**, 2922 (1973); (c) T. Sasaki, S. Eguchi, M. Sugimoto, and F. Hibi, *J. Org. Chem.*, **37**, 2317 (1972); (d) J. Biehler and J. Fleury, *J. Heterocycl. Chem.*, **8**, 431 (1971); (e) D. Ben-Ishai and E. Goldstein, *Tetrahedron*, **27**, 3119 (1971); (f) A. B. Evnin, A. Lam, and J. Blyskal, *J. Org. Chem.*, **35**, 3097 (1970); (g) E. Goldstein and D. Ben-Ishai, *Tetrahedron Lett.*, 2631 (1969); (h) J. D. Hobson and W. D. Riddell, *Chem. Commun.*, 1180 (1968); (i) M. Cava, C. Wilkins, D. Dalton, and K. Bessho, *J. Org. Chem.*, **30**, 3772 (1965); (j) M. P. Quan, T. Karns, and L. Quin, *Chem. Ind. (London)*, 1553 (1964); (k) M. P. Cava and C. Wilkins, *ibid.*, 1422 (1964).

(3) (a) P. Rijsenbrij, R. Loven, J. Wijnberg, W. Speckamp, and H. Huisman, *Tetrahedron Lett.*, 1425 (1972); (b) R. P. Loven, W. Zunnebeld, and W. N. Speckamp, *Tetrahedron*, **31**, 1723 (1975); (c) W. Zunnebeld and W. N. Speckamp, *ibid.*, **31**, 1717 (1975); (d) R. Albrecht and G. Kresze, *Chem. Ber.*, **98**, 1431 (1965); (e) G. Kresze and R. Albrecht, *ibid.*, **97**, 490 (1964); (f) D. vor der Brück, R. Bühler, and H. Plieninger, *Tetrahedron*, **28**, 791 (1972); (g) C. Harter and S. Liisberg, *Acta Chem. Scand.*, **22**, 2685 (1968); (h) J. M. Biehler and J. P. Fleury, *Tetrahedron*, **27**, 3171 (1971).

(4) G. R. Krow, R. Rodebaugh, C. Hyndman, R. Carmosin, and G. DeVicaris, *Tetrahedron Lett.*, 2175 (1973).

(5) Ibogamine: K. Nakanishi, T. Goto, S. Ito, S. Natori, and S. Nozoe, Ed., "Natural Products Chemistry", Vol. 2, Academic Press, New York, N.Y., 1975, pp 406–415. See also dioscorine: W. A. McDavies, I. G. Morris, and A. Pinder, *Chem. Ind. (London)*, **35**, 1410 (1961).

(6) Securine: T. Nakano, T. H. Yang, and S. Terao, *Tetrahedron*, **19**, 609 (1963); *J. Org. Chem.*, **28**, 2619 (1963).

(7) An intermediate such as **13** or **14** is present in the reaction medium, since previous studies of additions of cyclic conjugated dienes[1f,g] to immonium ion **5** have identified side products derived from carbonium ion intermediates.

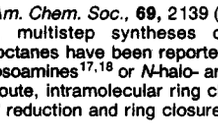
(8) J. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961); see also ref 1g, Table IV.

(9) A. S. Onishchenko, "Diene Synthesis", Jerusalem, Israel Program for Scientific Translations, 1964, p 53.

(10) Although the **1/6** ratio is essentially unchanged over reaction times from 5 to 15 h, there may be reversible steps before product formation and stereochemical preferences may be affected.

(11) Cyclopentadiene and cyclohexa-1,3-diene react with *Z* immonium ions to afford 3-endo-substituted adducts.[1c]

(12) Proton H_{7x} is assigned the downfield resonance on the basis of the shifts in *N*-carbethoxy-7-azabicyclo[3.2.1]oct-2-ene (i).[4]



i

(13) The parent hexahydroindole ring system of **20** has been prepared: (a) W. Oppolzer and W. Fröstl, *Helv. Chim. Acta*, **58**, 590 (1975). (b) B. M. Trost and J. P. Genet, *J. Am. Chem. Soc.*, **98**, 8516 (1976). (c) M. Modotoff and R. F. Sprecher, *Tetrahedron*, **30**, 2623 (1974). (d) Mesembrine alkaloids incorporate the hexahydroindole ring system of **20**: P. Coggon, D. S. Farrier, P. W. Jeffs, and A. T. McPhail, *J. Chem. Soc. B*, 1267 (1970).

(14) R. B. Bates, E. S. Caldwell, and H. P. Klein, *J. Org. Chem.*, **34**, 2615 (1969).

(15) W. A. Mosher, *J. Am. Chem. Soc.*, **69**, 2139 (1947).

(16) For comparison, multistep syntheses of 4(2)-substituted 6(7)-azabicyclo[3.2.1]octanes have been reported involving ring closure of *N*-halo- and *N*-nitrosoamines[17,18] or *N*-halo- and *N*-nitrosoamides[19] by an intramolecular π-route, intramolecular ring closure by internal nitrogen nucleophiles,[13b,20] reduction and ring closure of substituted pyrroles,[21]

ring opening of tricyclic aziridinium ions,[22] and molecular rearrangement of other bycyclic systems.[4,23]
(17) (a) P. Gassman and J. Dygos, *Tetrahedron Lett.*, 4745 (1970); (b) J. M. Surzur, L. Stella, and R. Nouguier, *ibid.*, 903 (1971); (c) G. Esposito, R. Furstoss, and B. Waegell, *ibid.*, 899 (1971).
(18) Y. L. Chow, R. A. Perry, and B. C. Menon, *Tetrahedron Lett.*, 1549 (1971).
(19) (a) E. Flesia, A. Croatto, P. Tordo, and J. M. Surzur, *Tetrahedron Lett.*, 535 (1972); (b) Y. L. Chow and R. A. Perry, *ibid.*, 531 (1972).
(20) Z. I. Horii, T. Imanishi, M. Hanaoka, and C. Iwata, *Chem. Pharm. Bull.*, **20**, 1774 (1972).
(21) W. Davies, A. Pinder, and I. Morris, *Tetrahedron*, **18**, 405 (1962).
(22) W. Nagata, S. Hirai, K. Kawata, and T. Aoki, *J. Am. Chem. Soc.*, **89**, 5045 (1967).
(23) (a) J. Huffman, T. Kamiya, and C. Rao, *J. Org. Chem.*, **32**, 700 (1967); (b) L. A. Paquette and J. F. Kelly, *ibid.*, **36**, 442 (1971); (c) R. O. Hutchins and L. Rua, *ibid.*, **40**, 2567 (1975); (d) G. Buchi, D. Coffen, K. Kocsis, P. Sonnet, and F. Ziegler, *J. Am. Chem. Soc.*, **87**, 2073 (1965); **88**, 3099 (1966).
(24) Some commercial samples of α-phellandrene (Eastman) have appreciable (one-third) alcohol impurity according to David Todd, Worcester Polytechnic Institute.
(25) O. Wallach, *Justus Liebigs Ann. Chem.*, **275**, 105 (1893).
(26) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966).
(27) (a) H. Nabata, *Tetrahedron*, **19**, 1959 (1963); (b) L. M. Berkowitz and P. N. Rylander, *J. Am. Chem. Soc.*, **80**, 6682 (1958).

Thermal Decomposition of Bis(diphenylmethyl) Diselenide

Joseph Y. C. Chu* and Jerry W. Lewicki

Xerox Corporation, Webster Research Center, Rochester, New York 14644

Received January 26, 1977

The thermal decomposition of bis(diphenylmethyl) diselenide (1) has been investigated in the melt and in chlorobenzene solution. In the melt, 1 decomposes readily at 210 °C under reduced pressure with quantitative formation of 1,1,2,2-tetraphenylethane (3) and elemental selenium. The decomposition products at 140 °C are 3 (87%), Se (86.4%), bis(diphenylmethyl) selenide (6.5%), and 6.5% of starting material. In chlorobenzene solution, the decomposition follows first-order kinetics over the temperature range 100–120 °C and polyselenides are produced as additional products. The results are consistent with a radical mechanism involving C–Se and Se–Se bond scissions.

The thermal instability of organic diselenides has often been cited in the literature, but little is known about the kinetics and mechanisms of these thermal decomposition reactions. Morgan and Burstall[1-3] reported that cyclic diselenides, e.g., 1,2-diselenacyclohexane, 1,2-diselenacycloheptane, and 1,2-diselenacyclooctane, lose one selenium atom with concomitant ring contraction when they were heated. Similarly, bis(chloromethyl) diselenide thermally decomposed to give elemental selenium and bis(chloromethyl) selenide.[4] Recently, Lardon[5] has shown that benzyl diselenide undergoes rapid thermal decomposition in the melt or in solution at 150–170 °C to produce a complex mixture of products, including dibenzyl selenide, selenium, and several dibenzyl polyselenides. Substantial quantities of toluene and some 1,2-diphenylethane were formed after heating the melt to 225 °C for about 1 h.

Apart from these studies little else has appeared in the literature. Previously, the thermal instability of bis(diphenylmethyl) diselenide (1) was noted,[6] but its thermal chemistry has not been reported. As part of our continuing studies on the chemistry of organochalcogens,[7-9] we initiated a detailed study of thermal chemistry of this diselenide **1**. In the present work, we have investigated the thermal decomposition of 1 in the melt and in solution over the temperature range 100–210 °C. The decomposition products were identified. The kinetics of decomposition were determined and the reaction mechanism is discussed.

Results and Discussion

Diselenide 1 was conveniently prepared in 78% yield by the reaction of sodium diselenide[10] with benzhydryl chloride in ethanol. Bis(diphenylmethyl) selenide (2) was synthesized by treating benzhydryl chloride with an ethanolic solution of sodium hydrogen selenide[9] and sodium ethoxide.

Thermolysis of 1 neat under reduced pressure at 210 °C was completed within 20 min and yielded 1,1,2,2-tetraphenylethane (3) and elemental selenium as the only products (eq 1). In contrast to benzyl diselenide,[5] formation of monoselenide and polyselenides was not observed. It appears that 1 is much less stable than benzyl diselenide and the former has weaker C–Se bonds. At 140 °C, heating 1 for 23 h resulted in a decreased yield of 3 (87%) and selenium (86.4%) with formation now of monoselenide 2 (6.5%) and recovery of 1 in 6.5% yield. Monoselenide 2, when heated at 140 °C for 23 h, converted to diselenide 1 (15.8%), selenium (16%), 3 (55.2%), and polyselenides 4 (13.8%), with some 2 (15.2%) remaining. This suggests that 2 is one of the major initial products in the thermolysis of 1 at lower temperatures (140 °C) and that it further decomposes under prolonged conditions.

$$\underset{\mathbf{1}}{Ph_2CHSeSeCHPh_2} \xrightarrow{\Delta} \underset{\mathbf{3}\ (99.4\%)}{Ph_2CHCHPh_2} + \underset{(99.8\%)}{Se} \qquad (1)$$

The kinetics of decomposition of 1 were studied in purified and degassed chlorobenzene at temperatures of 100–120 °C. The rate of disappearance of 1 was determined spectrometrically by following the decrease in peak area of the methine proton with a chemical shift of δ 4.95 in the NMR spectrum. In all cases, the decomposition reactions obeyed a first-order rate law. Figure 1 shows typical first-order plots. The rate constants determined from the slopes of the first-order plots for the thermal decomposition of 1 in chlorobenzene in the temperature range 100–120 °C are listed in Table I. The lack of rate constant change with variation in initial concentration of 1 listed in Table I further supports a first-order kinetic scheme for this decomposition reaction. Nonlinear first-order plots were obtained at reaction temperatures exceeding 120 °C. The control reactions showed that monoselenide 2, one of the initial decomposition products, is not stable at temperatures above 120 °C and further decomposed to re-form diselenide 1 along with other products. The deviation from the first-order kinetics is apparently due to the secondary