

mass spectrum (150 °C), m/z (relative intensity) 354 (M^+ , 100), ^1H NMR ($\text{Me}_2\text{SO}-d_6$) δ 6.12 (1 H, s, NH); 3.50 (1 H, dd, $J = 6.6$, 2.4 Hz, H-2); ^{13}C NMR ($\text{Me}_2\text{SO}-d_6$) 62.8 and 62.3 (C-2, C-3), 41.2 (C-7).

(2*S*,7*R*)-2,3,4,5,6,7-Hexahydroalstonine (4b): 79% yield; ^1H NMR ($\text{Me}_2\text{SO}-d_6$) 7.48 (1 H, s, H-17), 5.42 (1 H, m, NH), 4.38 (1 H, dq, $J = 6.5$, 12.0 Hz, H-19), 3.62 (3 H, s, CO_2CH_3), 3.42 (1 H, dd, $J = 6.6$, 2.4 Hz, H-2), 1.29 (3 H, d, $J = 6.5$ Hz, H-18).

(2*R*,7*S*)-2,7-Dihydroisoajmalicine (4c): 54% yield; ^1H NMR ($\text{Me}_2\text{SO}-d_6$) δ 5.46 (1 H, br s, NH), 3.45 (1 H, dd, $J = 6.8$, 2.7 Hz, H-2); ^{13}C NMR ($\text{Me}_2\text{SO}-d_6$) 62.1 (C-2), 53.3 (C-3), 41.2 (C-7).

(2*R*,7*S*)-2,7-Dihydroakuammigine (4d): 59% yield; IR (CHCl_3) 3380, 2830, 2775, 1695, 1615 cm^{-1} ; ^1H NMR ($\text{Me}_2\text{SO}-d_6$) δ 5.65 (1 H, br s, NH), 3.32 (1 H, dd, $J = 7.0$, 2.9 Hz, H-2); ^{13}C NMR (CDCl_3) 63.4 (C-2), 57.6 (C-3), 40.3 (C-7).

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Registry No. 1a, 483-04-5; 1b, 6474-90-4; 1c, 483-03-4; 1d, 642-17-1; 2a, 36104-59-3; 2b, 86940-56-9; 2c, 86940-57-0; 2d, 86940-58-1; 3a, 73232-42-5; 3b, 86940-59-2; 3d, 86940-60-5; 4a, 86940-61-6; 4b, 86940-62-7; 4c, 86940-63-8; 4d, 86940-64-9.

Further Characterization of the 1,1-Diphenyl-2,2-dimethylpropyl Radical

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Introduction

Recently¹ we have had occasion to examine in some detail the mechanism of that abnormal version of the Finkelstein reaction that leads to coupled products rather than the expected alkyl iodides. These reactions go via carbocation intermediates that are either reduced directly by iodide to free radicals or form transient covalent iodides. Thus, triphenylmethyl chloride reacts with sodium iodide in acetone to give a complex mixture that clearly displays the proton NMR of the triphenylmethyl dimer. In contrast, 1,1-diphenyl-2,2-dimethylpropyl chloride reacts under similar conditions to form 1,1-diphenyl-2,2-dimethylpropane and 2,3-diphenyl-3-methyl-1-butene in equal amounts. Both products arise through the intermediate 1,1-diphenyl-2,2-dimethylpropyl cation.

Anticipating the formation of the 1,1-diphenyl-2,2-dimethylpropyl free radical in the above reaction, we felt that an examination of this radical and its dimer products would be worthwhile. First reported by Schlenk and Racky,² the radical was initially reported to form a dimer that did not dissociate like that of triphenylmethyl. Subsequently, Conant and Bigelow³ suggested that this observation was erroneous. They prepared the radical by the method of Ziegler by first generating the corresponding anion from the chloride and sodium amalgam. Oxidation of the anion to the radical was achieved with the tetramethylethylene dibromide (TMEDB). The radical di-

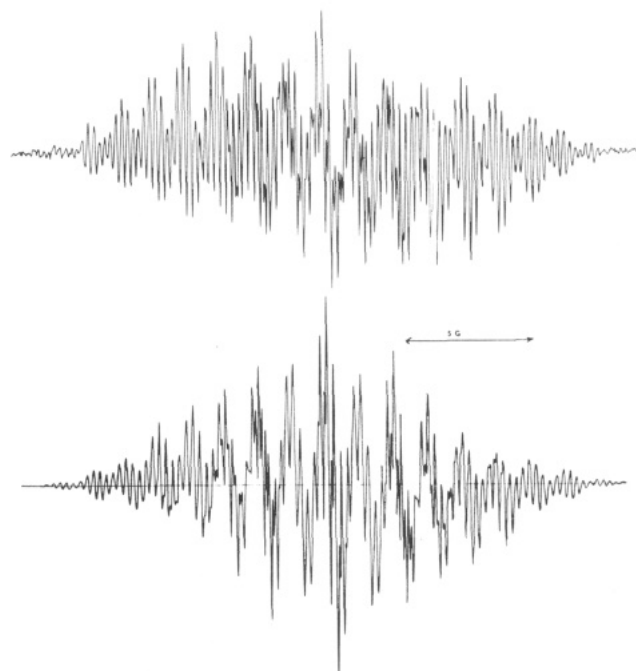


Figure 1. The ESR spectrum of the 1,1-diphenyl-2,2-dimethylpropyl radical (upper) and the computer simulation of same (lower).

merized reversibly and reacted with oxygen in contrast to the report of Schlenk and Racky. More recently, Lorand and Wallace⁴ published the electron spin resonance (ESR) spectrum of the radical generated by the thermal decomposition of *tert*-butyl 2,2-diphenyl-3,3-dimethylperbutanoate. No detailed analysis was made beyond the assignment of the hyperfine couplings to the methyl protons as 0.24 G.

Results and Discussion

The 1,1-diphenyl-2,2-dimethylpropyl radical was generated under nitrogen directly in the ESR tube by the addition of an ether solution of the corresponding anion to TMEDB. The spectrum is shown in Figure 1 as is the computer-simulated spectrum. Since the spectrum can theoretically contain up to 750 lines, the fitting is not a trivial matter. Working with information derived from the wings of the spectrum and judgments from related structures, the best set of hyperfine coupling constants was found to be $a_{\text{H}^\circ} = 2.6$, $a_{\text{H}^{\text{m}}} = 1.3$, $a_{\text{H}^{\text{p}}} = 2.7$, and $a_{\text{H}^{\text{Me}}} = 0.24$ G, respectively. Only the absolute magnitude of the meta coupling can be derived from the experimental spectrum though it may be presumed to be negative in sign as in other benzyl-like systems. Changes in these by as little as +0.05 G produced marked changes in the central portion of the spectrum where many overlapping lines occur. The ring couplings are estimated to be good to ± 0.1 G and the couplings to the methyl protons to ± 0.02 G.

The ESR parameters of diphenylmethyl and fluorenyl radicals have been determined and compared previously.^{5,6} The α -hydrogen coupling constants (14.7 and 13.9 G, respectively) have been interpreted as indicating a high degree of planarity and electron delocalization in the diphenylmethyl system. A similar conclusion can be drawn from

(1) W. B. Smith and G. D. Branum, *Tetrahedron Lett.*, 2055 (1981).

(2) W. Schlenk and G. Racky, *Justus Liebigs Ann. Chem.*, **394**, 201 (1912).

(3) J. B. Conant and N. M. Bigelow, *J. Am. Chem. Soc.*, **50**, 2041 (1928).

(4) J. P. Lorand and R. W. Wallace, *J. Am. Chem. Soc.*, **96**, 1402 (1974).

(5) A. R. Bassindale, A. J. Bowles, A. Hudson, and R. A. Jackson, *Tetrahedron Lett.*, 3185 (1973).

(6) A. Atto, A. Hudson, R. A. Jackson, and N. P. C. Simmons, *Chem. Phys. Lett.*, **33**, 477 (1975).

the couplings at the ortho and para positions and their analogous positions in fluorenyl (for instance, 3.7 and 3.98 G for the ortho hydrogen and the 3-position in diphenylmethyl and fluorenyl, respectively). In contrast, the well-established "propeller" conformation of the phenyls in triphenylmethyl necessitates less delocalization of the electron with a resultant lowering of the ortho coupling constant to 2.6 G.⁷ An intermediate case is represented by the 1,1,2,2-tetraphenylethyl radical⁸ where the adjacent benzhydryl structure introduces enough steric hindrance to twist the two conjugated phenyls from their desired planar configuration ($a_{H^{\circ}} = 3.0$ G). It is apparent from the values given above that the couplings for the 1,1-diphenyl-2,2-dimethylpropyl radical compare favorably with those for triphenylmethyl, suggesting that the steric effect of the *tert*-butyl on the two phenyls is very comparable to a third phenyl group.

Since the NMR studies of Lankamp et al.,⁹ the dimer structure of triphenylmethyl has been settled as 4-(triphenylmethyl)-1-(diphenylmethylene)-2,5-cyclohexadiene. The subtle interplay of steric factors involved in triaryl-methyl dimerization is brought home by the fact that 9-phenylfluorenyl dimerizes to the ethane.¹⁰ Similarly the 2-*tert*-butyl and 2,6-dimethyl derivatives of diphenylmethyl each dimerize to their methylenecyclohexadiene analogues,⁹ while benzhydryl bromide when shaken overnight with mercury in chloroform is 50% converted to 1,1,2,2-tetraphenylethane.

Conant and Bigelow understandably assumed the dimerization of 1,1-diphenyl-2,2-dimethylpropyl to form the ethane.³ Counterindications can be read into their report in that when the chloride was reacted with a deficiency of sodium-potassium amalgam a stable dimer was isolated to which they assigned a structure analogous to the Chichibabin hydrocarbon (*p*-benzhydryltetraphenylmethane). No structure proof was given.

When an ether solution of radical, generated as above, was examined by proton NMR, a rather symmetrical multiplet resembling an AA'BB' system was observed at 6.1 and 6.3 ppm. The spectrum was complicated by a number of absorptions in the region. This multiplet, however, is just within the span shown by the cyclohexadiene protons of an ether solution of the triphenylmethyl dimer. There was also a weak absorption at the position expected for the H-4 proton on the cyclohexadiene ring. Attempts to relate this absorption to those of the presumed cyclohexadiene protons by spin decoupling did not succeed.

The formation of anions by treating an alkyl halide with sodium amalgam results in a complex system. Bent and co-workers¹¹ studied a number of systems where radicals, anions, and sodium amalgam were all in equilibrium. Indeed, observation of the red anion solutions produced here gave proton NMR spectra much like those observed above after treatment with TMEDB. Furthermore, ESR signals were readily observed in the red anion solutions. Only when a large excess of sodium amalgam was used could these ESR signals be suppressed, and the signals in the proton NMR attributed to the cyclohexadiene dimer disappeared from such solutions also.

Hydrolysis by water of an anion solution generated from 1,1-diphenyl-2,2-dimethylpropyl chloride and excess sodium amalgam in ether gave 1,1-diphenyl-2,2-dimethylpropane. Treatment of a portion of this same anion solution with TMEDB and workup with water gave a stable hydrocarbon whose structure was readily assigned by ¹³C NMR as 4-(2,2-dimethyl-1,1-diphenylpropyl)-1-(2,2-dimethyl-]-phenylpropyl)benzene, the analogue to the Chichibabin hydrocarbon. This observation, when coupled with the more tenuous proton NMR observations above, supports the methylenecyclohexadiene structure for the dimer of the radical in this study.

Experimental Section

Proton NMR spectra were obtained on a Varian EM-390 spectrometer, while carbon-13 spectra were acquired on a JEOL FX-60 spectrometer. Proton spectra were determined in deuteriochloroform for stable compounds as were the carbon-13 spectra. Proton NMR spectra of the anion solution and radical dimer were determined in ether with the instrument unlocked, using the ether quartet to standardize the chemical shifts. ESR spectra were determined on a Varian Model E 102A instrument with a 9.5-GHz microwave bridge and with use of the 100-MHz modulation frequency.

Anion and Radical Solutions. The method of Ramart-Lucas¹² was used to prepare 1,1-diphenyl-2,2-dimethylpropyl chloride. The anion solutions in ether were prepared following the recipe of Conant and Bigelow,³ i.e., 15 g of the chloride in 100 mL of anhydrous ether was shaken in a round-bottomed flask with freshly prepared sodium amalgam (23 g of sodium in 35 g of mercury). The flask was purged with nitrogen before shaking, and the pressure was vented several times after starting. After 6-8 h the flask was inverted, and the various salts and mercury were allowed to settle. These were then drawn off through the stopcock. All procedures were carried out in a glovebag under prepurified nitrogen or argon.

A 25-mL aliquot of the anion solution from the above preparation was poured into 100 mL of 1 N hydrochloric acid, and the ether layer was separated, washed with water, and dried over anhydrous magnesium sulfate. Rotary evaporation of the ether solution gave ca. 1 g of crude 1,1-diphenyl-2,2-dimethylpropane, mp 52-53 °C (lit.¹³ mp 55-56 °C). This material appeared to be pure both by proton and carbon-13 NMR: ¹H NMR δ 1.35 (9 H, CH₃), 7.1-7.6 (m, 10 H, aromatic); ¹³C NMR δ 38.8 (CH₃), 40.4 (s), 88.3 (s, C_α), 126.7 (C₃ and C₄), 130.5 (C₂), 144.9 (C₁). These assignments follow from the results of single-frequency off-resonance decoupling (sford) and previously established polyphenylated structures.¹⁴

Small samples of the anion solution were utilized for NMR or ESR examination. In the ESR studies of the radical, the anion solution was added to enough TMEDB to destroy the red color (50-100 mg) in a quartz ESR tube. This was then capped, and the spectrum was determined.

The balance of the anion solution was treated with a solution of TMEDB in ether until the red color was discharged. The solution was then poured into water, and the ether layer was separated and dried over anhydrous magnesium sulfate, and the ether was evaporated under vacuum. The crude residue (ca. 5 g) gave proton and carbon-13 NMR spectra of a single relatively pure compound, mp 136.5-138 °C. Conant and Bigelow report a melting point of 138-141 °C for the dimer formed by reaction of TMEDB on the anion and mp 145 °C for the dimer formed with a deficiency of sodium-potassium alloy. Anal. Calcd for C₃₃H₃₈: C, 91.42; H, 8.58. Found; C, 91.08; H, 8.85.

The proton NMR of the above material was relatively uninformative, i.e., β 0.95 (s, 9 H, CH₃), 1.25 (s, 9 H, CH₃), 3.55 (s, 1 H, α -proton), 6.8-7.2 (phenyl "Christmas tree", 19 H). The carbon-13 spectrum displayed 18 lines appropriate to the structure for 4-(1,1-diphenyl-2,2-dimethylpropyl)-1-(1-phenyl-2,2-di-

(7) A. H. Maki, R. D. Allendoerfer, J. C. Danner, and R. T. Keys, *J. Am. Chem. Soc.*, **90**, 4225 (1968).

(8) F. A. Neugebauer and W. R. Grok, *Tetrahedron Lett.*, 1005 (1973).

(9) H. Lankamp, W. Th. Nauta, and C. MacLean, *Tetrahedron Lett.*, 249 (1968).

(10) H. A. Staab, K. S. Rao, and H. Brunne, *Chem. Ber.*, **104**, 2634 (1971).

(11) H. E. Bent and M. Dorfman, *J. Am. Chem. Soc.*, **57**, 1452 (1935), and references therein.

(12) M. Ramart-Lucas, *C. R. Hebd. Seances Acad. Sci.*, **154**, 1088 (1912).

(13) E. J. Skerret and D. Woodcock, *J. Chem. Soc.*, 2804 (1952).

(14) T. W. Proulx and W. B. Smith, *J. Magn. Reson.*, **23**, 477 (1976).

methylpropyl)benzene. By a combination of peak intensities, sford, previously related assignments,¹⁴ and the data for the 1,1-diphenyl-2,2-dimethylpropane above it was possible to assign each line in this spectrum as follows: (1) For the 1,1-diphenyl-2,2-dimethylpropyl group, 64.8 (C-1), 39.6 (C-2), 32.5 (CH₃), phenyl 147.2 (C-1), 126.9 (C-2,6), 131.4 (C-3,5), and 125.7 (C-4); (2) For the 1-phenyl-2,2-dimethylpropyl group, 63.8 (C-1), 35.1 (C-2), 29.2 (CH₃), phenyl 143.2 (C-1), 129.9 (C-2,6), 127.8 (C-3,5), and 126.0 (C-4); and finally for the benzene moiety, 140.4 (C-1), 128.4 (C-2,6), 130.9 (C-3,5), and 144.5 ppm (C-4).

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Registry No. 1,1-Diphenyl-2,2-dimethylpropyl radical, 51974-45-9; 1,1-diphenyl-2,2-dimethylpropane, 38842-11-4; 1,1-diphenyl-2,2-dimethylpropyl dimer, 86943-05-7; 4-(1,1-diphenyl-2,2-dimethylpropyl)-1-(1-phenyl-2,2-dimethylpropyl)-benzene, 86943-06-8.

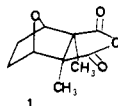
High Pressure [4 + 2] Cycloaddition of Dichloromaleic Anhydride and Furan

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The total synthesis of cantharidine (1) has long been an



intriguing pursuit, owing to its simple structure as well as its physiological properties. The obvious [4 + 2] Diels-Alder cycloaddition reaction between dimethylmaleic anhydride and furan was investigated as early as the 1920's;^{1,2} however, such a direct synthetic approach failed, even at pressures as high as 42 000 atm.^{3,4}

It was suggested that the failure of the [4 + 2] cycloaddition of dimethylmaleic anhydride to furan was a result of both electronic and steric factors. The electron-donating methyl groups of the dimethylmaleic anhydride decrease its dienophilicity and create a sterically hindered environment in the transition state. Efforts to utilize very high pressure in order to react furan and 2,5-dihydrothiophene-3,4-dicarboxylic anhydride led to the quantitative production of the cycloaddition adduct.⁴ This work demonstrated for the first time that a single Diels-Alder reaction can generate the vicinally tetrasubstituted 7-oxabicyclo[2.2.1]heptenyl system.

It was suggested that another reason for the failure of the cycloaddition reaction between dimethylmaleic anhydride and furan was due to the aromaticity of furan (poor Diels-Alder diene). The cycloaddition products derived from furan are generally susceptible to thermal cycloreversion so as to prevent the use of high reaction temperatures.

Recently two groups have successfully shown that more reactive furan derivatives, isobenzofuran⁵ and 3,4-di-

methoxyfuran,⁶ reacted quantitatively with dimethylmaleic anhydride to form mostly the exo-cycloaddition products. These furan derivatives possess excellent Diels-Alder reactivity owing to their favorable resonance stability. They are therefore able to overcome the steric effect during the course of the cycloaddition. These investigators^{5,6} showed that suitable modifications, both in maleic anhydride and furan, overcome the electronic and/or steric problems, and the [4 + 2] cycloaddition will proceed to yield tetrasubstituted 7-oxabicyclo[2.2.1]heptenyl compounds.

In order to examine further this possibility, we investigated the reaction between dichloromaleic anhydride and furan.

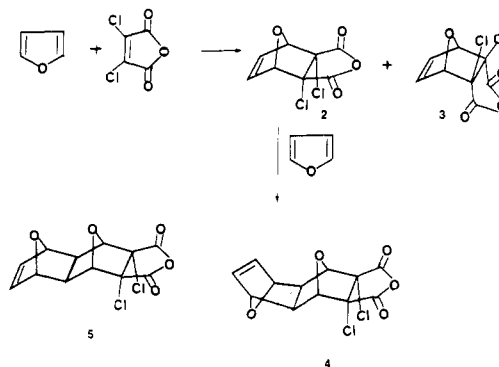
Results and Discussion

Dichloromaleic anhydride dissolved in excess furan was placed in a sealed tube and allowed to stand at room temperature. The solution gradually turned red and after 2 weeks became black. However, mostly unreacted dichloromaleic anhydride was recovered. When the same solution was heated at 80–90 °C, a black solid and hydrogen chloride were produced. After 3 days the dichloromaleic anhydride was converted quantitatively to the black material that did not dissolve in common organic solvents and did not melt, even at 350 °C.

The dichloromaleic anhydride-furan solution was pressurized to 5000 atm and heated at 50 °C for 15 h. A white solid product was isolated and purified (mp 224 °C). The analytical data for the compound showed that it corresponded to the endo, exo 1:2 adduct 4.

The tetrahydrofuran solution of dichloromaleic anhydride and furan in a 1:1 mole ratio was pressurized to 5000 atm and heated at 50 °C. The same 1:2 adduct was obtained in 22.4% yield and no detectable quantity of monoadduct was isolated.

These results suggest that the electron-withdrawing chloro groups of dichloromaleic anhydride increased its dienophilicity, and the application of high pressure overcame the steric hindrance. Thus, the reaction gave first the [4 + 2] cycloaddition product. Jurczak and co-workers⁶ reported that the Diels-Alder reaction of 3,4-dimethoxyfuran and dimethylmaleic anhydride under high pressure yielded the exo-cycloaddition product and that no endo product was detected. Similarly, the reaction of dichloromaleic anhydride and furan may first form the exo 1:1 adduct 2, which may then be more reactive toward furan to produce the endo, exo 1:2 adduct 4. Another



reason for the inaccessibility of the exo 1:1 adduct 2 may be due to the instability of this adduct at atmospheric pressure. Reaction of furan and dichloromaleic anhydride first proceeded to yield 2 under high pressure. However,

(1) Von Bruchhausen, F.; Borsch, H. W. *Arch. Pharm. Ber. Dtsch. Pharm. Ges.* **1928**, *266*, 697.

(2) Diels, O.; Alder, K. *Chem. Ber.* **1929**, *62*, 554.

(3) Gladysz, J. A. *CHEMTECH* **1979**, 372.

(4) Dauben, W. G.; Kessel, C. R.; Takemura, K. H. *J. Am. Chem. Soc.* **1980**, *102*, 6893.

(5) McCormick, J. P.; Shimmyozu, T. *J. Org. Chem.*, in press.

(6) Jurczak, J.; Kozluk, T.; Filipek, S.; Eugster, C. H. *Helv. Chim. Acta* **1982**, *65*, 1021.