Table I. Stereochemistry and Relative Rate Constants for Cyclization of 6-Hepten-2-yl and Related Radicals at 65° [a]

Radical	k_c/k_t [b]	cis/trans
1a	0.26	2.3
1b	0.30	2.3
1c	3.0	2.3

[a] Total yields of products were >80%; they were normalized to 100% for computational purposes. [b] Determined over a four-fold range of initial stannane concentration.

1a–c the cis mode of cyclization is favored. The observed cis:trans ratios are mutually consistent and in reasonable agreement with those obtained in some of the earlier work.[1] It thus appears that preferential cis cyclization may be a general feature[3] of radicals containing the 6-hepten-2-yl system.[11]

On simple thermodynamic grounds trans cyclization would be expected to be more favorable than cis, since the transition state, 7, for the former process is less subject to nonbonded repulsions than is that for the latter, 8.[4] However, application of orbital symmetry considerations[12] affords a contrary view.

One model for the transition state for alkyl radical addition to an olefinic bond involves interaction of the half-filled p orbital with the vacant π* orbital.[13] Hyperconjugative mixing [14,15] of the former with adjacent CH σ and σ* orbitals produces a modified delocalized orbital[15] which is of similar symmetry to the acceptor π* orbital. Thus, in the transition state, 8, leading to cis disubstituted product there is a secondary attractive interaction between the alkyl substituent and the olefinic bond (see 9) which is not available in the transition state, 7, for trans cyclization.

7   8

primary 〈   〉 secondary

9
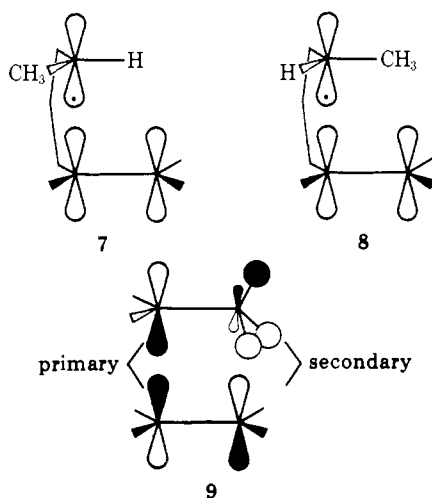
Hoffmann, Levin, and Moss[15] have pointed out that such interactions should be important only in highly exothermic reactions where the transition state occurs at large separation of the reaction partners. The re-

(11) However, preferential cis cyclization is not exhibited by 1-substituted hex-5-enyl radicals in which the free electron is delocalized onto substituents such as cyano, carbethoxy, or phenyl: M. Julia and M. Maumy, Bull. Soc. Chim. Fr., 434 (1966); C. Walling and A. Cioffari, J. Amer. Chem. Soc., 94, 6064 (1972).

(12) R. B. Woodward and R. Hoffmann, Angew. Chem., 81, 797 (1969).

(13) A. L. J. Beckwith, G. E. Gream, and D. S. Struble, Aust. J Chem., 25, 1081 (1972), and references cited therein.

(14) R. Hoffmann, Accounts Chem. Res., 4, 1 (1971).

(15) R. Hoffmann, C. C. Levin, and R. A. Moss, J. Amer. Chem. Soc., 95, 629 (1973).

actions described here, having ΔH of approximately −18 kcal/mol, appear to meet these criteria.

Finally, our results and those previously recorded strongly suggest that cyclopolymers formed from suitable 1,6-diolefins[16] probably comprise predominantly cis disubstituted five-membered cyclic units.

(16) For reviews see G. C. Cornfield, Chem. Soc. Rev., 1, 523 (1972); W. E. Gibbs and J. M. Barton in "Kinetics and Mechanism of Polymerization," Vol. I, part I, G. E. Ham, Ed., Marcel Dekker, New York, N. Y., 1967, Chapter 2.

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Structurally Isomeric and Diastereoisomeric Adducts from the Nitration of 1,2,4-Trimethylbenzene. The Orientation and Mechanism of Side-Chain Substitution of Arenes

Sir:

Several nitronium acetate (acetyl nitrate) cis and trans adducts which contain the 4-nitro-1,4-dihydrophenyl moiety have been isolated from nitration of methylbenzenes and substituted methylbenzenes in acetic anhydride.[1–4] We wish to report the first example of the formation of structurally isomeric adducts. Our results also show that 1,4 adducts are intermediates in side-chain substitution of arenes under electrophilic conditions[5,6] and unambiguously reveal the orientation of such substitution.

Nitration of pseudocumene (1,2,4-trimethylbenzene) at −45° gave a mixture[7] which contained 50% dienes. The acetoxynitrodienes 1a, 1b, 2a, and 2b were isolated by low-temperature chromatography. The general arguments for the assignment of the 1,4-adduct structure have been given elsewhere.[3,8,9] Nmr shift reagent studies using Eu([²H₉]fod)₃ made possible the crucial assignment of the 1 and 2 structures. The reagent complexes preferentially at the acetate group,[10] and thus the structure 1 was assigned to that pair of isomers in which, on the addition of the reagent, the methyl doublet moved less rapidly and the lone vinyl proton moved more rapidly downfield than in the other pair.

The reactions of 1 and 2 parallel those of the p-xylene adducts[2,11] depicted in Scheme I. Both 1 and 2 under-

(1) D. J. Blackstock, A. Fischer, K. E. Richards, J. Vaughan, and G. J. Wright, Chem. Commun., 641 (1970).

(2) D. J. Blackstock, J. Cretney, A. Fischer, M. P. Hartshorn, K. E. Richards J. Vaughan, and G. J. Wright, Tetrahedron Lett., 2793 (1970).

(3) A. Fischer and J. N. Ramsay, J. Chem. Soc., Perkin Trans. 2, 237 (1973).

(4) A. Fischer and C. C. Greig, J. Chem. Soc., Chem. Commun., 396 (1973).

(5) H. Suzuki, K. Nakamura, and M. Takeshima, Bull. Chem. Soc. Jap., 44, 2248 (1971), and other papers in this series.

(6) G. Illuminati, L. Mandolini, A. Patara, and E. Baciocchi, Tetrahedron Lett., 4161 (1972), and previous papers in the series.

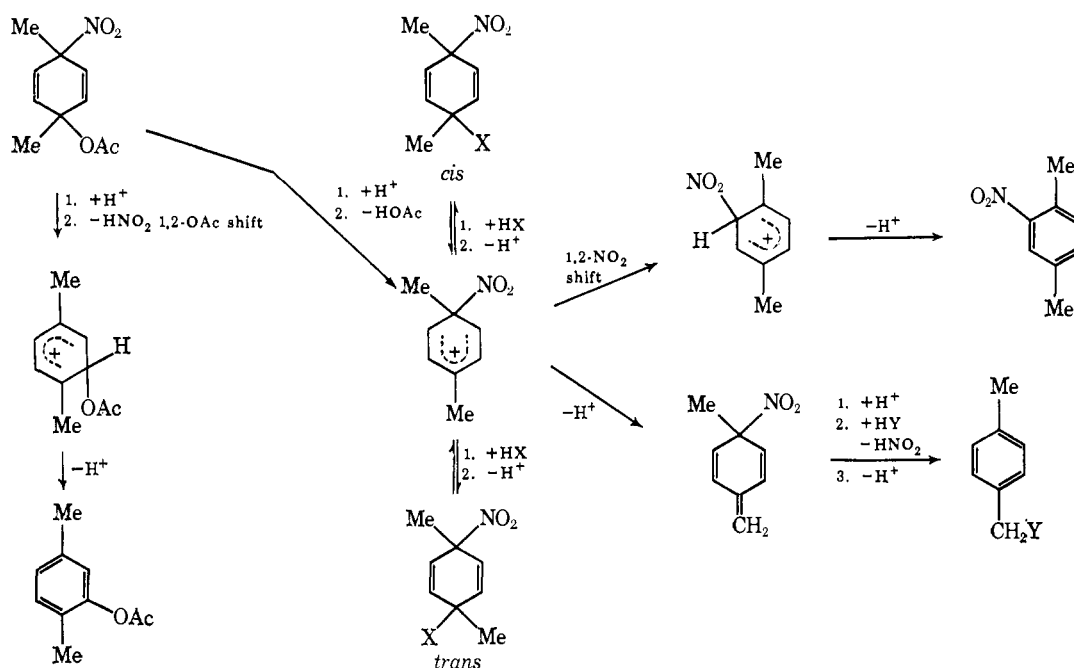(7) Individual members of a pair of diastereoisomeric adducts are designated a and b.

(8) A. Fischer and D. R. A. Leonard, Can. J. Chem., 50, 3367 (1972).

(9) A. Fischer and C. C. Greig, Can. J. Chem., in press.

(10) J. K. M. Sanders and D. H. Williams, J. Amer. Chem. Soc., 93, 641 (1971).

(11) J. N. Ramsay, Ph.D. Thesis, University of Victoria, 1973.

Scheme I

went exchange reactions of acetate for other nucleophiles when treated with the appropriate mildly acidic reagents, and adducts 3 (X = OH, OMe), from 1a or 1b, and 4, from 2a and 2b, were formed. The rearomatization products which accompanied the exchange products or which, under most conditions, were formed exclusively were benzyl and aryl derivatives.[12] From 1a and 1b the side-chain products were *exclusively* 3,4-dimethylbenzyl derivatives, $3,4\text{-}Me_2C_6H_3CH_2Y$, where Y = OAc, NO_2, $OCOCF_3$, ONO_2, or OMe. Each compound in the sequence was obtained as the predominant benzyl product when 1a and 1b were treated with acetic anhydride, nitrous acid, trifluoroacetic acid, nitric acid, or acidified methanol, respectively. Minor amounts of 3,4-dimethylbenzyl acetate and 3,4-dimethylphenylnitromethane were formed in competition with the other side-chain products. With the exception of the reaction in methanol, which gave some 6-methoxypseudocumene, no aryl substitution products were detected in any of the reactions of 1a or 1b under anhydrous conditions. It is noteworthy that no nitroarenes were detected as rearomatization products[13,14] of 1a or 1b. The 1,2 shift of the nitro group in phenonium ion 5 would be endothermic, since the product phenonium ion 6 would be less stable[15] than 5. Hence all of 5 is converted into the exocyclic methylene derivative 7 and eventually to 3,4-dimethylbenzyl products. These results clearly indicate that the pathway for the formation of side-chain substitution products when arenes are subjected to electrophilic reagents involves initial attack by an electrophile at a nuclear site *ipso* to a methyl group and eventual incorporation of a nucleophile at a methyl group *para* to this site (Scheme I). In this connection it is significant that side-chain products are not obtained from adducts which do not have a methyl group at the

site of the acetate.[3,9,16] When 1a in inert solvents (tetrahydrofuran or methylene chloride) was treated with aqueous acid only 3- (minor) and 5-acetoxypseudocumene were obtained. This result confirms the postulated[2] intramolecular 1,2 shift of acetate.

When adducts 2a and 2b were subjected to the same reagents which led to exclusive formation of side-chain products from 1a and 1b, nuclear-substituted products were obtained predominantly, with only minor amounts of the side-chain derivatives. However, it is significant that the side-chain products were (with an exception dealt with below) 2,4-dimethylbenzyl derivatives, $2,4\text{-}Me_2C_6H_3CH_2Y$, where Y = OAc or NO_2. This result confirms again that the substituted methyl group is *para* to the nuclear site of initial *ipso* attack by the electrophile. The nuclear products were 5-nitropseudocumene, 6-acetoxypseudocumene, and minor amounts of 3- and 5-acetoxypseudocumene. 5-Nitropseudocumene was the dominant product when 2a and 2b were treated with strong acids (trifluoroacetic acid, nitric acid in methylene chloride, and sulfuric acid in chloroform). The phenonium ion 8 is formed and preferentially rearranges to the more stable phenonium ion 9, the precursor of 5-nitropseudocumene. Deprotonation of the phenonium ion 8 competes inefficiently with the 1,2-nitro shift because the resulting exocyclic methylene derivative 10 exhibits a severe steric interaction between the methyl group and adjacent vinyl proton. 6-Acetoxypseudocumene is the product expected from a 1,2-acetate shift in 2 (*cf.* Scheme I). Other acetate shift processes must also occur since small amounts of the 3- and 5-isomers were also formed.

The side-chain substituted rearomatization product from methanolysis of both 2a and 2b was methyl 3,4-dimethylbenzyl ether. This is the single example of the substitution of the methyl group which is *ipso* to the nitro group. Both 2a and 2b are converted into 4 prior to the formation of the methoxy-substituted aromatic
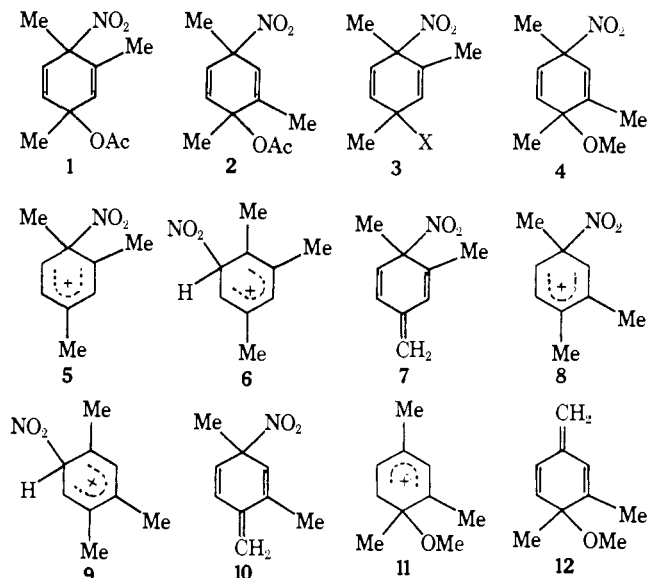
(12) Rearomatization products were identified by comparison (nmr and glpc) with authentic samples prepared by standard methods.

(13) P. C. Myhre, *J. Amer. Chem. Soc.*, **94**, 7921 (1972).

(14) R. C. Hahn and M. B. Groen, *J. Amer. Chem. Soc.*, **95**, 6128 (1973).

(15) A. Fischer and G. J. Wright, *Aust. J. Chem.*, in press.

(16) A. Fischer and C. C. Greig, *J. Chem. Soc., Chem. Commun.*, in press.

products. Methanol is a poorer leaving group than acetic acid and it is possible that in **4** the nitro group leaves to generate the more stable phenonium ion **11** in preference to the departure of the methoxy group which would give the less stable **8**. Deprotonation of **11** to **12**, followed by SN2′ substitution, would afford the observed product.

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An Unusual Fungal Metabolite, LL-N313ζ

Sir:

In the course of screening for antifungal agents from soil microorganisms, we examined extracts from *Sporormia affinis* Sacc., Bomm and Rouss [Lederle culture N313], from which several novel polyketide derived compounds were obtained.[1] More recent fermentations of the fungus have provided yet another novel metabolite, LL-N313ζ, to which we assign the absolute stereostructure **I**. To our knowledge, this carbon

I
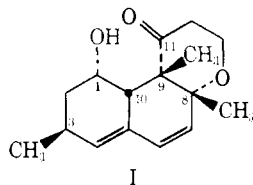
skeleton has not previously been observed in fungi.[2]

The *Sporormia* culture was fermented, harvested, and worked-up with carbon as previously described.[1] Chromatography of a concentrate over silica gel yielded, in addition to the other metabolites, the crystalline LL-N313ζ.

I is a crystalline material which melts at 172–173°,

(1) The elaboration of three dihydroisocoumarins and three antifungal cyclopentenone antibiotics by the same culture has previously been reported: W. J. McGahren and L. A. Mitscher, *J. Org. Chem.*, **33**, 1577 (1968); W. J. McGahren, J. H. van den Hende, and L. A. Mitscher, *J. Amer. Chem. Soc.*, **91**, 157 (1969)

(2) W. B. Turner, "Fungal Metabolites," Academic Press, New York, N. Y., 1971.

has $[\alpha]^{25}D$ −113° (MeOH) and the molecular formula $C_{16}H_{22}O_3$.[3] The ir spectrum of I shows hydroxyl absorption at 3440 cm⁻¹ and a carbonyl band at 1680 cm⁻¹. The acetate of I, mp 114–115°, has acetyl carbonyl absorption at 1735 cm⁻¹ with the ketonic band shifted to 1703 cm⁻¹ indicating chelation of the hydroxyl and carbonyl groups in I. When the carbonyl of I is reduced using sodium borohydride, the resultant product, mp 130–131°, still has strong uv absorption at 239 nm (ϵ 20,000). Since I has a maximum at 242 nm (ϵ 19,900) clearly the carbonyl is not involved in the uv chromophore. This chromophore is destroyed by catalytic reduction with the uptake of either 1 or 2 mol of hydrogen; consequently, a conjugated diene is indicated.

The presence of the decalin system in I was demonstrated by heating the reduced product mp 130–131° mentioned above with 30% Pd/C to 280° in a nitrogen atmosphere to get 1,2,6-trimethylnaphthalene.

The pmr spectrum of I shows 3-proton singlets at δ 1.08 and 1.23 for tertiary methyls and a doublet at δ 1.02 for a secondary methyl group. An exchangeable signal at δ 1.96 indicates a hydroxyl proton. The remaining 12 protons of the molecule are labeled H_a through H_l according to decreasing chemical shift values. In the olefinic region H_a is a doublet at δ 6.20, H_b a singlet at δ 5.72, and H_c is another doublet at δ 5.47. H_a and H_c constitute a classic cis vinylic AB pair ($J_{ac} = 9.5$ Hz).

All the signals mentioned so far were readily discernible upon examination of the original spectrum. The lines of the remaining protons were revealed only upon extensive spin decoupling work. H_d, H_f, H_h, and H_j located at δ 4.10, 3.92, 2.86, and 2.11, respectively, form a closed system not coupled to the remainder of the molecule. The coupling constants for this system have the following values (Hz): $J_{hj} = 14.6$, $J_{df} = 11.5$, $J_{jf} = 3.5$, $J_{jd} = 1.2$, $J_{hf} = 11.2$, and $J_{hd} = 9.0$. Clearly these protons form an ABXY system with AB and XY being geminal pairs. The chemical shift values indicate one pair, H_d and H_f, to be on a carbon bearing an oxygen and the other pair, H_h and H_j, to be adjacent to a carbonyl group.

H_c is a broad signal at δ 3.95, hence on an oxygen-bearing carbon. In the spectrum of I, H_e is completely hidden by the H_d and H_f signals but in the spectrum of the acetate of I it is shifted to δ 5.03 and spin decoupling work on this derivative showed $J_{eg} = 4.0$ Hz. In the spectrum of I, H_g is a quartet at δ 3.42 with $J_{gb} = 3.0$ Hz. H_i gives a broad signal at δ 2.50 and is coupled to the secondary methyl group with $J_{i,CH_3} = 7.0$ Hz. The other coupling constants associated with H_i are $J_{il} = 11.5$ and $J_{ik} = 5.0$ Hz. H_k is located at δ 2.0 and with H_l which is mostly hidden under the tertiary methyl signal at δ 1.23 forms a geminal pair with $J_{kl} = 13.0$ Hz.

Using this information we were able to write the gross structure below. Confirmation of this structure was provided by the proton noise decoupled 22.6-MHz PFT–cmr spectrum of I taken in $CDCl_3$. Multiplicities were obtained by off-resonance decoupling studies