$\lambda_{\max}^{\mathrm{EtOH}}$ 260 mμ (ε 12,000). (Attempted recrystallization from hot water caused darkening and a less pure product.)

B. In Aqueous Acetone.—To a partial solution of 1.68 g. (10 mmoles) of methyl 6-methylcoumalate (**1f**) in 4 ml. of acetone and 4 ml. of water, 0.54 g. (1.1 mole/mole) of sodium cyanide was added over a period of 4 min. at 5–10°. The mixture became homogeneous after about 10 min., when cooling was removed; at the end of 20 min., acetone was removed *in vacuo* and the residual aqueous solution was acidified to give 1.44 g. (74%) of a slightly impure product, which after recrystallization from benzene–cyclohexane proved to be identical with the product obtained in DMF solvent.

Anal. Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.58; H, 4.69; N, 7.37.

4-Carboxy-5-cyano-2-*cis*-4-*trans*-hexadienoic Acid (3g).—The preceding half-ester **3f** (0.56 g., 2.87 mmoles) was dissolved in 1.7 ml. of 20% sodium hydroxide (3 moles/mole), and after 5 min. the solution was cooled in ice and acidified to congo red with the calculated amount of concentrated hydrochloric acid added over a period of 3–5 sec. (slow acidification in another run resulted in the precipitation of a salt, probably the monosodium salt, which was not converted readily into the diacid upon standing in the solution). The crystals, which separated rather slowly at ice temperature, were filtered off and washed with a few drops of ice-cold water, and the crude product after drying in a vacuum desiccator was recrystallized from benzene with charcoal to give 0.21 g. (40%) of **3g**, colorless needles, m.p. about 125° dec., $\lambda_{\max}^{\mathrm{EtOH}}$ 256 and 209 mμ (ε 9200 and 8500).

Anal. Calcd. for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73. Found: C, 53.16; H, 4.13; N, 8.01.

Hydrolysis of 4-Carboxy-5-cyano-3-methyl-2-*cis*-4-*trans*-hexadienoic Acid (3d).—A mixture of 3 g. of the acid and 12 ml. of concentrated hydrochloric acid was refluxed for 1.5 hr. and cooled in an ice–salt mixture, and the crystals that separated were filtered off and washed with a little ice-cold water. After drying there was obtained 0.6 g. of a material which after recrystallization from water with charcoal weighed 0.42 g. (13%) and had m.p. 214–216°, $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ (ε 9600).

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.47; H, 4.71; neut. equiv. (mol. wt./2), 107. Found: C, 50.70; H, 4.90; neut. equiv., 107.

5-*trans*-Cyano-3,4,5-triphenyl-2-*cis*-4-pentadienoic Acid (2h).[23]—To a solution of 3.36 g. (10.4 mmoles) of 4,5,6-triphenyl-2-pyrone (**1h**) in 8 ml. of DMF, 0.53 g. (1.05 moles/mole) of sodium cyanide was added and the mixture was heated with stirring for 3 hr. at 150°. After the mixture was poured into water, a little tarry material was removed with methylene chloride, and the aqueous layer was acidified to give an oil which slowly solidified. After grinding this with water and drying, **2h** was obtained as a grayish powder; recrystallization from methanol with charcoal yielded 2.93 g. (80%) of **2h**, white needles, m.p. 197–201°.

Anal. Calcd. for $C_{24}H_{17}NO_2$: C, 82.00; H, 4.88; N, 4.01. Found: C, 81.65; H, 4.64; N, 3.93.

Acknowledgment.—The author wishes to thank the National Science Foundation for generous support of this research through Grant GP-1072, and Dr. A. T. Balaban for helpful discussion and a sample of 5-cyano-3-methyl-2,4-hexadienoic acid.

[23] This configuration of the cyano group is the more likely one for steric reasons (see text), but a rigorous proof is lacking.

Bridged Polycyclic Compounds. XXVII. Addition of Thiophenol to 5-Methylenenorbornene[1]

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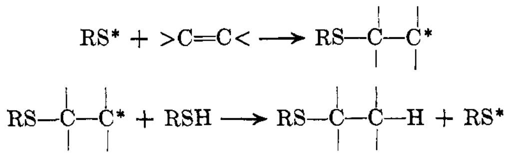
Received September 1, 1964

Free-radical addition of thiophenol to 5-methylenenorbornene (XI) gives three products, all resulting from preliminary attack of the phenylmercapto radical on the endocyclic double bond. Two of the products are formed by 1,2-addition and the third by homoconjugate addition. Dilution experiments indicate that classical radical intermediates are involved. These results are compared with those with trichloromethyl radical.

The mechanistic details of the addition of mercaptans to olefins *via* a free-radical chain mechanism have been well investigated. Kharasch, Read, and Mayo[2] have proposed the following mechanism.

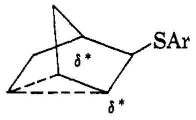


$$\mathrm{RS^* + {>}C{=}C{<} \longrightarrow RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}^*}$$

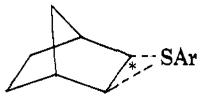
$$\mathrm{RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}^* + RSH \longrightarrow RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}H + RS^*}$$

We have been interested in the nature of the free-radical intermediate, in particular, the question of whether nonclassical structures analogous to those proposed for ionic additions need to be considered for free-radical addition reactions.

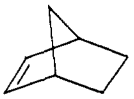
Evidence against the existence of carbon-bridged structures, such as I,[3] or sulfur-bridged structures, such as II,[4] as product-determining intermediates has already been adduced. Thus, addition of *p*-thiocresol to norbornene (III) gave only unrearranged *exo*-2-norbornyl *p*-tolyl thio ether,[3] and addition of *p*-thiocresol to a substituted norbornene (6-chloroaldrin) gave *exo–cis* addition of the thiyl radical and the hydrogen atom.[4] Addition of *p*-thiocresol to norbornadiene (IV) has also been described[5] and provided no evidence for a homoallylic nonclassical radical, V. As the ratio of the two products, *exo*-5-dehydronorbornyl *p*-tolyl thio ether and 3-nortricyclyl *p*-tolyl thio ether, varied with changes



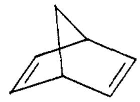
I



II



III



IV

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[1] Previous paper in series: S. J. Cristol and D. D. Tanner, *J. Am. Chem. Soc.*, **86**, 3122 (1964). The work described in this paper was presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan. 1964.

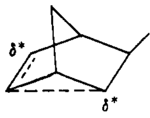
[2] M. S. Kharasch, A. T. Read, and F. R. Mayo, *Chem. Ind.* (London), 752 (1938).

[3] S. J. Cristol and G. D. Brindell, *J. Am. Chem. Soc.*, **76**, 5699 (1954).

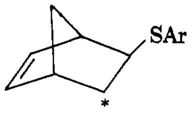
[4] S. J. Cristol and R. P. Arganbright, *ibid.*, **79**, 6039 (1957).

[5] S. J. Cristol, G. D. Brindell, and J. A. Reeder, *ibid.*, **80**, 635 (1958).

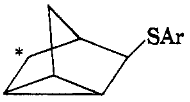
in concentration of the chain-transfer agent, *p*-thiocresol, two intermediates, presumably VI and VII, had to be the precursors of the products.



V



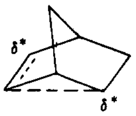
VI



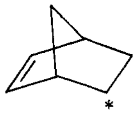
VII

Similarly, the existence of two classical radicals in the homoallylic rearrangement accompanying addition of benzenesulfonyl halides to norbornadiene was recently demonstrated.[6]

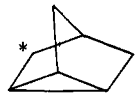
Recently, Wilt and Levin[7] studied the decarbonylation of 2-norbornene-5-carboxaldehyde. They found that a fivefold dilution of reactants had no effect on the observed ratio of products, norbornene and nortricyclene, of 4:6. They stated that this could be interpreted as evidence of either the nonclassical homoallylic radical intermediate, VIII, or perhaps more likely as a rapid equilibrium between the classical radicals, IX and X.



VIII



IX

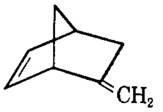


X

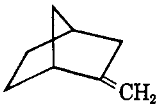
Homoconjugation of the sort indicated by V might be expected to lower the energy of the radical-addition step and thus substantially enhance the rate of addition over that of systems where such participation in the transition state is not possible.[8] To test this possibility, Trecker and Henry[9] ran a competitive reaction between equimolar amounts of norbornene and norbornadiene with the trichloromethyl radical generated from chloroform and benzoyl peroxide. They found that norbornadiene reacted 2.1 times as fast as norbornene, and cited this as evidence against anchimeric assistance involving an entity similar to V. On the other hand, norbornadiene was found[5] to be considerably more reactive than norbornene towards the *p*-thiocresoxy radical.

Huyser and Echegaray[10] reported that homoconjugation did not abnormally enhance the reactivity of 5-methylenenorbornene (XI) toward attack by the trichloromethyl radical. Rather, they found that the diolefin reacted as the sum of its isolated double bonds, a fact interpreted as evidence against the existence of a homoallylic nonclassical radical intermediate.

Huyser and Echegaray assumed that the external double bond of XI reacted about four times as fast with trichloromethyl radical as the internal double bond on the basis of a series of competitive experiments between methylenenorbornane (XII) and norbornene (III) for the trichloromethyl radical generated from carbon tetrachloride and benzoyl peroxide.



XI

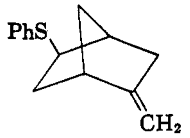


XII

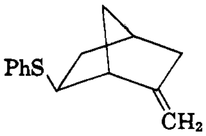
The present research was undertaken to extend the investigation of the addition of mercaptans to olefins to an unsymmetrical diolefin, 5-methylenenorbornene (XI), to look into the nature of the 1:1 addition products as involving 1,2-addition to either the endocyclic or the exocyclic double bond or 1,5-homoconjugative addition across both double bonds, and to determine whether the products related by rearrangement are derived from two isomeric free radicals or from a nonclassical mesomeric homoallylic radical for which the isomeric radicals might be considered resonance structures.

When 5-methylenenorbornene (XI) was mixed with an approximately equimolar amount of thiophenol, a highly exothermic reaction occurred. The resulting product mixture was distilled under reduced pressure and comprised a mixture of isomeric 1:1 adducts produced in yields ranging from 77–94%. An n.m.r. spectrum of the reaction mixture indicated a complete absence of the resonance of the olefinic protons of norbornene and related bicyclic olefins. Present was a pair of singlets at τ 5.1 and 5.4 due to the resonances of the two terminal protons of the exocyclic double bond. Further, an integration of the spectrum indicated that only one proton gave rise to a multiplet at τ 6.71, a peak identified as arising from protons α to a sulfur atom by a comparison with the n.m.r. spectra of the thio ethers resulting from mercaptan reaction with III,[3] IV,[5] and related olefins.[4]

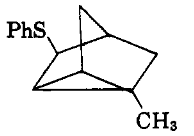
From the n.m.r. data on the reaction mixture, the products were postulated to be 5-methylene-*exo*-2-norbornyl phenyl thio ether (XIII) and 5-methylene-*exo*-3-norbornyl phenyl thio ether (XIV), both arising from 1,2-additions to the endocyclic double bond of XI, and 1-methyl-*anti*-3-nortricyclyl phenyl thio ether (XV), arising from a 1,5-homoconjugative addition of thiophenol following initial attack of the phenylmercaptyl radical at the 2-position of XI. It was possible to separate the three isomers by preparative-scale gas chromatography.



XIII



XIV



XV

When the reaction mixture was treated with mercaptoacetic acid, another exothermic reaction occurred. This reaction mixture was neutralized with base and extracted with diethyl ether. Removal of the ether left the thio ether that had not reacted with the thiol acid. This thio ether had an infrared spectrum identical with that of the first fraction from the gas chromatography of the XI-thiophenol reaction, with a peak at 11.81 μ, characteristic of 1-substituted nortricyclenes.[11]

The n.m.r. spectrum of this thio ether showed a resonance peak at τ 6.82, characteristic of protons α to

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[6] S. J. Cristol and D. I. Davies, *J. Org. Chem.*, **29**, 1282 (1964).

[7] J. W. Wilt and A. A. Levin, *ibid.*, **27**, 2319 (1962).

[8] Note similar considerations in the acetolysis of dehydronorbornyl brosylate, in which the enhancement of rate over that anticipated is interpreted by the assumption that there is electron delocalization in the intermediate carbonium ion: S. Winstein, H. M. Walborsky, and K. Schreiber, *J. Am. Chem. Soc.*, **72**, 5795 (1950).

[9] D. J. Trecker and J. P. Henry, *ibid.*, **85**, 3204 (1963).

[10] E. S. Huyser and G. Echegaray, *J. Org. Chem.*, **27**, 429 (1962).

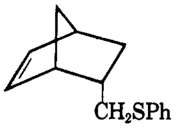
[11] H. Hart and R. A. Martin, *ibid.*, **24**, 1267 (1959); H. Hart and R. A. Martin, *J. Am. Chem. Soc.*, **82**, 6362 (1960); L. Kaplan, H. Kwart, and P. von R. Schleyer, *ibid.*, **82**, 2342 (1960).

sulfur atoms. Further, an integration of the spectrum indicated only one proton α to the sulfur atom. The n.m.r. spectrum also gave evidence of a tertiary methyl group with a singlet at τ 8.88 integrating for three equivalent protons. These data indicate that the saturated thio ether resulted from homoconjugative addition of thiophenol with initial attack of the phenylmercaptyl radical at the 2-position of XI. The n.m.r. spectrum is not consistent with that anticipated for an addition following initial attack of the phenylmercaptyl radical at the 8-position.

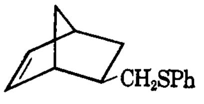
The unsaturated isomers, XIII and XIV, were prepared from the Diels–Alder adduct of cyclopentadiene and allyl bromide, dehydronorbornylcarbinyl bromide. Thiophenol was added to the double bond of this bromide (a 90:10 *endo–exo* mixture by gas chromatography) and the resulting mixture was dehydrobrominated with potassium *t*-butoxide in *t*-butyl alcohol.

The two unsaturated thio ethers, a 50:50 mixture of positional isomers by gas chromatography, were isolated by preparative-scale gas chromatography. The infrared spectra of these two isomers were identical with the infrared spectra of the last two fractions collected from the gas chromatographic separation of the 5-methylenenorbornene–thiophenol reaction mixture.

The *endo–exo* epimers, XVI and XVII, respectively, which would result from a 1,2-addition of thiophenol to the exocyclic double bond of XI, were prepared by the Diels–Alder reaction between cyclopentadiene and allyl phenyl sulfide. These were formed in an 85:15 *endo–exo* ratio. Infrared absorptions at 5.80, 7.55, 11.10, and 14.00 μ were present in this reaction mixture which were absent in the infrared spectrum of the XI–thiophenol reaction mixture.



XVI

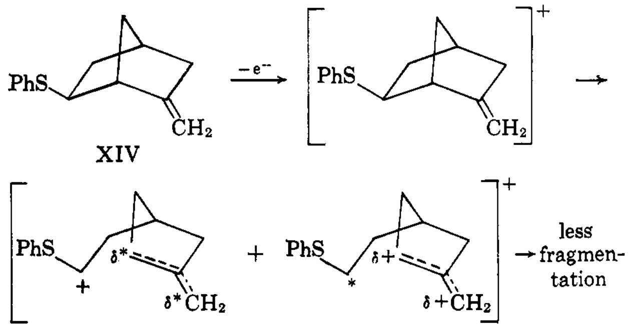


XVII

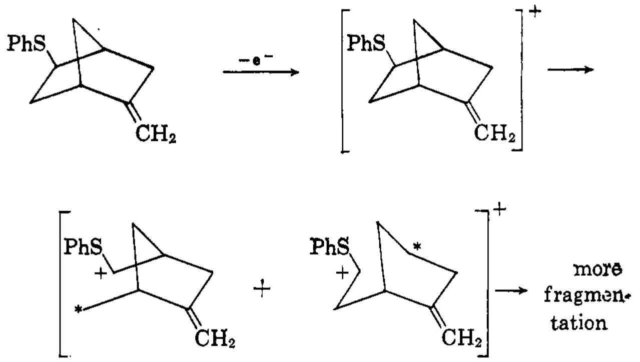
An attempt to determine the stereochemistry of the phenylmercapto group in XIII and XIV using n.m.r. spectroscopy was without success. The spectra had multiplets with identical splittings of 8, 5, and 2 c.p.s. for the proton α to the sulfur atom. The 8-c.p.s. coupling appears to be from the *cis*-proton coupling and the 2-c.p.s. coupling from the *trans*-proton coupling.[12] The 5-c.p.s. coupling can arise from either a coupling with the *anti*-7-proton[13] if the phenylmercapto group has the *exo* configuration, or from a coupling with the adjacent bridgehead proton[12] if the phenylmercapto group has the *endo* configuration. However, since it has been well established that attacks on the double bond of norbornene (III) and norbornadiene (IV) occur exclusively from the *exo* direction,[3,5,6,14,15] the *exo* configuration was empirically assigned to the phenylmercapto group. This assignment leads to an *anti* configuration for the two substituents of the nortricyclic derivative XV.

Mass-spectral fragmentation patterns were used in part to differentiate between the two unsaturated thio ethers XIII and XIV. It was predicted[16] that the molecular ion of XIV would be more stable than the molecular ion of XIII and would, therefore, contribute a higher percentage to the total spectrum.

From the postulated fragmentation scheme for the two isomers, the initial fragmentation of the molecular ion of XIV would result in the relatively stable allyl radical (XVIII) or the allyl carbonium ion (XIX).



Formation of these entities would result in less over-all fragmentation than would isomeric ions XX and XXI from the molecular ion of XIII, since the latter pair has no stabilizing feature to limit further fragmentation. Thus, by comparing the amounts that the molecular ions contribute to the total spectrum, the one which has the higher percentage of m/e = M should be the isomer XIV, while the one with the lower percentage should be the isomer XIII.



Mass spectra were run on the two unsaturated fractions collected by gas chromatography from the XI–thiophenol reaction mixture. It was found that the ratio of the unfragmented percentage for the last gas chromatographic fraction to that of the second gas chromatographic fraction was 1.75, and that this ratio was constant at either 15 e.v. or at 70 e.v. or under varied inlet temperatures.

This indicated that the first fraction off the gas chromatograph was the saturated isomer XV; the second fraction was the unrearranged isomer of XV, XIII; and the third fraction was the positional isomer XIV.

It then remained to determine the nature of the radical intermediate in the reaction. If the thiyl radical attacks XI at the 3-position, then no homoallylic rearrangement can occur, and the product is one from a 1,2-addition to the endocyclic double bond XIV.

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(12) F. A. L. Anet, *Can. J. Chem.*, **39**, 789 (1961).

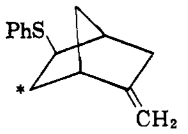
(13) J. Meinwald and Y. C. Meinwald, *J. Am. Chem. Soc.*, **85**, 2514 (1963).

(14) S. J. Cristol and J. A. Reeder, *J. Org. Chem.*, **26**, 2182 (1961).

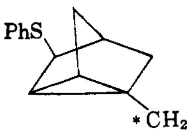
(15) E. C. Kooyman and G. C. Vegter, *Tetrahedron*, **4**, 382 (1958).

(16) We are indebted to Dr. Klaus Biemann for this prediction, and to Mr. David C. Sheesley for the mass spectral data.

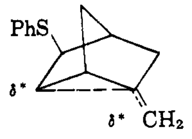
However, if the thiyl radical attacks XI at the 2-position first, then two mechanisms are possible. One involves the classical radical XXII, which may either chain transfer with mercaptan to yield XIII, or else may isomerize to XXIII and then chain transfer to yield XV. The other mechanism involves the nonclassical mesomeric homoallylic intermediate XXIV, which may chain transfer with mercaptan at either of two positions to yield the two products XIII and XV.



XXII



XXIII



XXIV

The method of Seubold[17] was used to distinguish between these two mechanisms. If the nonclassical radical XXIV is the reaction intermediate, than a dilution of the chain-transfer agent, thiophenol, will have no effect on the ratio of products XIII and XV that are derived from it. However, if the classical radical XXII is the first-formed intermediate, then a dilution of the chain-transfer agent would result in slower chain transfer to produce XIII, and thus favor isomerization to XXIII, which would then chain transfer to yield the rearranged, saturated product XV.[18]

We therefore allowed 5-methylenenorbornene to react with thiophenol at various dilutions and under various temperatures, estimating the percentages of the three products by gas chromatography. The results of these experiments are summarized in Table I. The method of presentation of the tabulated results is as follows. No per cent yield is calculated, the percentages of the three isomers are determined assuming a 100% yield for the reaction products, XIII, XIV, and XV. Little diadduct may be expected since an excess of diolefin was used. The gas chromatograms indicated that the reactions were essentially complete at the time of the analyses. Analytical samples were taken from the reaction flask and injected into the chromatograph.

Experiments 1, 2, and 3 represent conditions of decreasing concentration of mercaptan; one observes that as predicted, the ratio of nortricyclic product XV to olefin XIII increases markedly with decrease in concentration of mercaptan.

TABLE I

REACTION CONDITIONS AND PRODUCT COMPOSITIONS IN THE ADDITION OF THIOPHENOL TO 5-METHYLENENORBORNENE

Expt.[a]	XIII, %	XIV, %	XV, %	XV:XIII
1[b]	40 ± 1	23 ± 1	37 ± 1	0.9 ± 0.1
2[c]	33 ± 1	23 ± 1	46 ± 1	1.4 ± 0.1
3[d]	31 ± 1	19 ± 2	50 ± 1	1.6 ± 0.1
4[e]	41 ± 1	23 ± 1	36 ± 1	0.9 ± 0.1
5[f]	30 ± 1	25 ± 2	42 ± 2	1.4 ± 0.2

[a] All experiments were run with a 1.05:1.00 molar ratio of diolefin to mercaptan. All experiments except 5 were run at room temperature with no external coolant. [b] Mercaptan added instantaneously to diolefin, no solvent. [c] Mercaptan solution added instantaneously to diolefin solution; both reactants diluted with 10 vol. of chlorobenzene. [d] Same as experiment 2, except mercaptan solution added dropwise to diolefin solution. [e] Same as expt. 1, but with 20 vol. of water to act as heat absorber. [f] Same as expt. 2, but heated to 100° before addition.

Since the addition reaction is extremely exothermic (the reaction mixture reaches a maximum temperature of 82° within 20 sec. after mixing 0.5 g. of each of the reactants at room temperature), it seemed possible that the increase in rearranged product might reflect a temperature effect rather than a concentration effect. This is shown not to be the case by a comparison of expt. 2 and 5, the former run at room temperature and the latter at 100°, and by a comparison of expt. 1 and 4, the latter run with an internal coolant and the former without a coolant.

Thus, the experimental results clearly demonstrate that the nonclassical radical intermediate XXIV cannot be the sole common precursor of XIII and XV, but that there must be two separate radical species involved.

This conclusion is not only consistent with other results in this laboratory,[3-6] but also with the results of other workers on free-radical additions to norbornadiene and related bicyclic olefins,[9,10,19-21] where no evidence could be found favoring nonclassical radical intermediates.

The gas chromatographic data from the dilution experiments verify the assignments of structure from the mass-spectral fragmentation patterns. Only the intermediate radical XXII, which is the precursor of XIII, the second fraction in the chromatography of the XI–thiophenol reaction product, can rearrange to XXIII and yield the saturated product XV. The third fraction in the chromatography remained essentially constant in the dilution experiments and can only be XIV, since its precursor radical cannot rearrange, but can only chain transfer to yield XIV.

The conclusion of Huyser and Echegaray[10] which suggested that the trichloromethyl radical would react principally with the exocyclic double bond of XI was somewhat surprising to us since we had expected the more strained, internal double bond of XI to be the inherently more reactive one. Alder and Windemuth[22] had reported that the internal double bond reacted preferentially with phenyl azide and with hydrogen under catalytic conditions.

We found that XI reacted with 1 equiv. of hydrogen within 30 min. when a palladium-on-charcoal catalyst was used, and reacted with a second equivalent of hydrogen over a period of several hours with the same catalyst. We also found that XI reacted immediately with 2 equiv. of hydrogen when platinum oxide was used as the catalyst. The n.m.r. spectrum of the monohydrogenated product using palladium on charcoal verified Alder's assumption[22] that the product was essentially methylenenorbornane (XII) and that there was little 5-methylnorbornene in the hydrogenation mixture.

With the direction of addition of thiophenol to XI known, it is evident that an anomaly is present either in this addition or in that of the trichloromethyl radical. Thus, we have found that the endocyclic double bond of XI is much more reactive than the exocyclic double bond towards phenylmercapto radical, while Huyser

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[17] F. H. Seubold, *J. Am. Chem. Soc.*, **75**, 2532 (1953).

[18] For a mathematical derivation of the predictions, see ref. 5.

[19] M. M. Martin and D. C. DeJongh, *J. Am. Chem. Soc.*, **84**, 3526 (1962).

[20] J. A. Berson and C. J. Olsen, *ibid.*, **84**, 3178 (1962).

[21] J. A. Berson, C. J. Olsen, and J. S. Walia, *ibid.*, **84**, 3337 (1962).

[22] K. Alder and E. Windemuth, *Ber.*, **71**, 1939 (1938).

and Echegaray[10] reported that the exocyclic double bond of XI should be about four times as reactive as the endocyclic double bond towards the trichloromethyl radical.

We propose that it is the addition of the trichloromethyl radical that is anomalous; that, due to its extreme bulk, it cannot easily attain the close proximity to the endocyclic double bond necessary for reaction, because of steric interference with the hydrogens on the methylene bridge and on the bridgehead. Thus, in the case of 5-methylenenorbornene, the trichloromethyl radical reacts with the less hindered exocyclic double bond, rather than with the inherently more reactive endocyclic one.

Experimental

Reagents.—5-Methylenenorbornene, supplied by the Dow Chemical Company, was redistilled, but not immediately prior to use. Thiophenol was Eastman White Label. Dehydronorbornylcarbinyl bromide was prepared by the method of Alder.[22]

Preparation of 5-Methylenenorbornene.—To 24.2 g. (0.2 mole) of refluxing collidine (Eastman White Label) was added 18.1 g. (0.1 mole) of dehydronorbornylcarbinyl bromide. After 24 hr. at reflux, a red-brown solid, presumably collidine hydrobromide, was on the bottom of the reaction flask. The reaction mixture was dissolved in diethyl ether and extracted with three 250-ml. portions of 8% aqueous hydrochloric acid. After distillation of the ether, the product was distilled at 100–103° (630 mm.). 5-Methylenenorbornene (14.5 g., 80%) was obtained and 3.6 g. of unchanged bromide was left in the distillation flask. The diolefin obtained gave identical infrared and n.m.r. spectra with those of a sample of XI obtained from Dr. E. S. Huyser.[10] The n.m.r. spectrum showed a triplet at τ 4.1 for the endocyclic olefinic protons and two singlets at 5.1 and 5.4 for the exocyclic olefinic protons.

Addition of Thiophenol to 5-Methylenenorbornene.—Thiophenol was added in one portion to a flask of 5-methylenenorbornene with stirring. In all additions, the diolefin was present in a 5–10 mole % excess in order to minimize diaddition. The reaction temperature immediately rose to 105° following mixing of the reactants and 5-methylenenorbornene was condensed in a reflux condenser. After 2 to 3 min., the temperature began to drop.

Distillation of the reaction mixture resulted in the collection of two fractions. Unchanged diolefin distilled at room temperature at 1 mm., the adduct distilled at 130–140° (1 mm.), and a dark residue remained in the flask. The adduct was obtained in yields ranging from 77–94% and was pale yellow in color. The residue accounted for the remainder. A redistilled sample of adduct was analyzed.

Anal. Calcd. for $C_{14}H_{16}S$: C, 77.72; H, 7.46; S, 14.82. Found: C, 78.12; H, 7.61; S, 14.12.

The three isomers were separated and collected from preparative-scale gas chromatography on column A.

Thiophenol was also added in a dropwise manner. The first addition comprised about 10% of the total amount of thiophenol added and the rest was added dropwise from a dropping funnel at a rate of 2 drops a minute. Flow was begun from the funnel as soon as the reaction was initiated. This dropwise procedure resulted in the higher yields of the dark residue, presumably telomeric in nature.

Preparation of 1-Methyl-3-nortricyclyl Phenyl Sulfone.—To 3.0 g. (14 mmoles) of the XI–thiophenol adduct was added 1.0 g. (12 mmoles) of mercaptoacetic acid. After 24 hr., the reaction mixture was dissolved in 0.2 *N* sodium hydroxide and extracted with diethyl ether. Evaporation of the ether yielded 1.2 g. (5.6 mmoles) of the saturated thio ether XV.

The saturated thio ether was dissolved in 5 ml. of glacial acetic acid and added to a solution of 1.6 g. (10 mmoles) of potassium permanganate in 10 ml. of glacial acetic acid. The reaction mixture immediately turned brown. The reaction mixture was neutralized with potassium carbonate solution and extracted with diethyl ether. Evaporation of the ether left a colorless residue, which, after two recrystallizations from pentane, gave 1.3 g. (93%) of colorless crystals, m.p. 36–37°.

Anal. Calcd. for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49; S, 12.91. Found: C, 67.72; H, 6.71; S, 13.01.

The basic solution from XI–thiophenol–mercaptoacetic acid reaction was acidified with hydrochloric acid and extracted with diethyl ether. Distillation of the ether and the unchanged mercaptoacetic acid yielded colorless crystals upon cooling. The crystals decolorized dilute potassium permanganate in acetone but not bromine in carbon tetrachloride and liberated a gas when treated with sodium carbonate solution. A recrystallization from diethyl ether yielded the acid mixture as crystals, m.p 94–106°. This mixture was not further resolved.

Anal. Calcd. for $C_{16}H_{22}O_2S_2$: C, 62.30; H, 6.54; S, 20.79. Found: C, 62.55; H, 6.75; S, 20.59.

Preparation of *exo*-2- and *exo*-3-(5-Methylene)norbornyl Phenyl Thio Ethers.—To 18.7 g. (0.1 mole) of dehydronorbornylcarbinyl bromide was added 11.0 g. (0.1 mole) of thiophenol. After 12 hr., the reaction mixture was dissolved in 100 ml. of *t*-butyl alcohol. This solution was added dropwise to a solution of potassium *t*-butoxide prepared by dissolving 12 g. (0.3 mole) of potassium in 500 ml. of *t*-butyl alcohol. The resulting solution was heated at reflux for 1 day. The reaction mixture was then flooded with water and extracted with diethyl ether. The ethereal solution was dried over calcium chloride and the ether was evaporated. A yellow liquid resulted which weighed 18.1 g. (84%).

This liquid decolorized bromine in carbon tetrachloride and dilute potassium permanganate in acetone. This liquid gave rise to a pair of singlets in the n.m.r. spectrum at τ 5.1 and 5.4 characteristic of the resonances of the exocyclic olefinic protons and no resonance at 4.1 for the endocyclic olefinic protons. An integration of the spectrum indicated only one hydrogen α to the sulfur atom, with a resonance at τ 6.7.

The isomers were separated by preparative-scale gas chromatography on column A. Infrared spectra showed that the first fraction was identical with the second fraction from the XI–thiophenol separation, and that the second fraction was the same as the third fraction from the XI–thiophenol separation. The two isomers were present in a 50:50 mixture.

Preparation of Dehydronorbornylcarbinyl Phenyl Thio Ether.—Cyclopentadiene, 1.98 g. (30 mmoles), and allyl phenyl sulfide, 5.31 g. (35.4 mmoles), were sealed in a Pyrex tube and heated to 160–170° for 8 hr. The resulting yellow liquid was distilled at 115–120° (0.25 mm.) yielding 5.96 g. (82%) of a colorless liquid. By gas chromatography on column B, the liquid was an 85:15 *endo-exo* mixture. The n.m.r. gave a symmetrical octet at τ 3.9 for the olefinic protons.

Anal. Calcd. for $C_{14}H_{16}S$: C, 77.72; H, 7.46; S, 14.82. Found: C, 77.73; H, 7.67; S, 14.82.

Dilution Experiments with the Addition of Thiophenol to 5-Methylenenorbornene. First Experiment.—To 0.5 g. (5.0 mmoles) of XI, 0.55 g. (5.0 mmoles) of thiophenol was added in one portion at room temperature (27°). The temperature immediately rose to a maximum of 82° within 20 sec. and began to drop slowly. A sample was taken for analysis after 15 min.

Second Experiment.—A solution of 1.0 g. (9.4 mmoles) of XI in 9.0 ml. of chlorobenzene was mixed with a solution of 1.0 g. (9.1 mmoles) of thiophenol in 9.0 ml. of chlorobenzene at 27°. The reaction temperature rose to 30° after 2 min. A sample was taken for analysis after 4 hr.

Third Experiment.—A solution of 1.0 g. (9.1 mmoles) of thiophenol in 9.0 ml. of chlorobenzene was added in a dropwise manner to a solution of 1.0 g. (9.4 mmoles) of XI in 9.0 ml. of chlorobenzene at 29°. No rise in temperature was observed. A sample was taken for analysis after 3 hr.

Fourth Experiment.—5-Methylenenorbornene, 1.0 g. (9.4 mmoles), was placed in a flask along with 200 ml. of distilled water at 28°. Stirring was begun and 1.0 g. (9.1 mmoles) of thiophenol was added in one portion. After 4 hr., the heterogeneous mixture was extracted with *n*-pentane. The pentane solution was dried over calcium chloride before a sample was taken for analysis.

Fifth Experiment.—A solution of 1.0 g. (9.4 mmoles) of XI in 9.0 ml. of chlorobenzene was heated to 100° in an oil bath. A solution of 1.0 g. (9.1 mmoles) of thiophenol in 9.0 ml. of chlorobenzene was heated to 100° in the same oil bath and then added in one portion to the diolefin solution. The temperature rose to 135° within 15 sec. before beginning to drop. A sample was taken for analysis after 2 hr. at 100°.

Estimation of Isomer Ratios.—Isomer ratios of the three products from XI–thiophenol dilution experiments were determined by gas chromatography on column A. Samples were taken directly from the reaction flask and injected into the gas chromatograph. The resulting chromatograms were then analyzed by measuring the peak areas by triangulation. Checks of the triangulation method were performed by cutting the peaks from the chromatogram and weighing the peaks. It was found that the two methods of analysis agreed to within 1%. Percentages were rounded off to the nearest per cent since the molar responses of the three isomers were not determined but were assumed to be equal. The ranges were determined from reanalyses and from analyses of duplicate experiments.

Hydrogenation of 5-Methylenenorbornene.—Palladium-on-charcoal catalyst (100 mg., 10%) was weighed into a hydrogenation flask and 15 ml. of 95% ethanol was added. The flask was shaken on the hydrogenator for 10–15 min. With 25 ml. of ethanol, 0.108 g. (1.02 mmoles) of XI was added to the hydrogenation flask. The calculated hydrogen uptake for one double bond at 25.5° and 635 mm. was 29.9 ml.; it was found to be 26.0 ml. after 30 min.

The palladium-on-charcoal catalyst was removed by filtration and then the ethanol was removed by distillation. The n.m.r. spectrum of the resulting colorless liquid indicated complete reaction of the endocyclic double bond as no resonance at τ 4.1, characteristic of the norbornene olefinic protons, was present. Also, the two singlets at τ 5.1 and 5.4, due to the exocyclic double bond protons of XI, were still present in the hydrogenated adduct.

When the n.m.r. sample was added to 25 ml. of ethanol containing 50 mg. of platinum oxide and subjected to hydrogenation, 32 ml. of hydrogen was taken up within 15 min. The n.m.r. spectrum of this sample showed no resonances due to olefinic protons.

Analytical.—All gas chromatographic analyses were performed on one of two columns. Column A was a 3-m., $^3/_8$-in. copper column packed with 20M Carbowax (25%) on Chromosorb P, 35/80 mesh. Column temperature was approximately 170° and helium flow rate was about 80 ml./min. Column B was a 1-m., $^1/_4$-in. copper column packed with PDEAS (25%) on Chromosorb P, 35/80 mesh. Column temperature was approximately 180° and helium flow rate was about 50 ml./min. Infrared spectra were obtained from a Beckman IR-5 recording spectrometer. Nuclear magnetic resonance spectra were obtained using a Varian Associates Model A-60 spectrometer. Mass spectra samples were collected from gas chromatography and the spectra were obtained on a Consolidated Electrodynamics Corp. Model 21-103C spectrometer.

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The Synthesis, Properties, and Some Reactions of Steroidal D-Homo α-Amino Ketones

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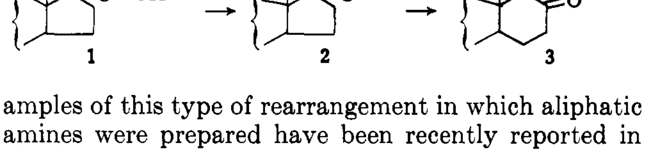
Several steroidal D-ring tertiary α-ketols were heated with methylamine and with ammonia, affording rearranged D-homo α-amino ketones. The products were shown to be derivatives of 17aβ-methyl-17aα-amino- (or methylamino-) D-homoandrostan-17-one, 17aα-methyl-17aβ-amino- (or methylamino-) D-homoandrostan-17-one, and 17β-methyl-17α-methylamino-D-homoandrostan-17a-one, depending upon the starting ketol employed. Some of the chemical transformations of these compounds are discussed and their physical and spectral properties are tabulated. It is shown that the sign of the Cotton effect of an α-axial aminocyclohexanone is not necessarily the same as that of the corresponding α-axial hydroxycyclohexanone. The mechanism of the rearrangement reaction leading to these α-amino ketones is discussed.

It has been shown that substituents on the D-ring of steroid hormones can markedly affect their physiological properties. In particular, groups attached to the 17α-position have been shown to influence anabolic, progestational, glucocorticoid, and electrolyte-regulating activities.[1] There have been few reported examples of the introduction of an amino group adjacent to a carbonyl function on the D-ring of a steroid,[2] and the pharmacological activity of steroids substituted in this manner has not been investigated. The synthesis of such a series of D-homo steroidal α-amino ketones is the subject of this paper.[3]

The aniline–mercuric chloride catalyzed hydration of a 17α-ethinyl-17β-hydroxy steroid (**1**) has been shown to give, in addition to the expected 17β-hydroxy-17α-pregnan-20-one, a nitrogenous by-product.[4] The structure of this compound was postulated by Shoppee and Prins to be a 17aξ-anilino-17aξ-methyl-17-keto-D-homo steroid (**3**).[4c,d] The formation of this anilino steroid presumably involved a 1,2-migration of the C-13 tertiary alkyl group of the intermediate α-hydroxy anil (**2**) from C-17 to C-20.[4c,d] Additional examples of this type of rearrangement in which aliphatic amines were prepared have been recently reported in simpler systems.[5] The driving force for this type of rearrangement is presumably the 35 kcal./mole of free energy released in the formation of the thermodynamically more stable amino ketone system from the less



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