before has been prepared so stereoselectively from magnesium metal and an alkyl halide at saturated carbon,[4,5,8] we sought to determine why **3** was formed from **1**.

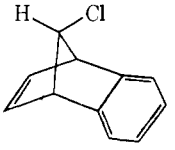
Results of preparations and deuterolyses of 7-benzonorbornadienyl Grignard reagents are in Table I.

Table I. Stereochemistry of 7-Benzonorbornadienyl Grignard Reagent Formation and Deuterolysis in THF

Reaction	% yield of **2**	Atom excess D in **2** anti	syn
C_5H_5MgBr + benzyne[a]	29	0.91	0.00
1 + Mg	86	0.48	0.05
1 + $MgCl_2$ + NaNaph[b]	93	0.35	0.28
(a) **1** + Mg, (b) NaNaph	81	0.31	0.00
1 + NaNaph	66	0.00	0.00
4 + Mg[c]	43	0.05	0.03
4 + $MgCl_2$ + NaNaph[b]	34	0.64	0.26

[a] References 1b,c. [b] Average of two runs. [c] Average of three runs.

In all cases the yield of benzonorbornadiene was determined by glpc, and the amount and location of deuterium (estimated to be ±0.05 atom excess D at each position) were determined from the relative areas of pmr signals of the Diels–Alder adduct of benzonorbornadiene and diphenylisobenzofuran.[9] By the same procedure used with **1**, treatment of *syn*-7-chlorobenzonorobornadiene (**4**)[10] with Mg turnings in THF



4

at reflux followed by deuterolysis incorporates little or no D at either position in **2**. Addition of a 15% excess of sodium naphthalenide (NaNaph) in THF to a solution of **1** or of **4** at 25° in THF which contains a 30% excess of anhyd $MgCl_2$[11] followed by deuterolysis leads to deuteration at both the syn and anti positions of **2**. Reaction of **1** with NaNaph in the absence of $MgCl_2$ followed by deuterolysis gives **2** containing no detectable D, demonstrating that organomagnesium rather than organosodium compounds are the species which react with D_2O in the NaNaph–$MgCl_2$ experiments. Excess NaNaph does not isomerize Grignard reagent **3** once it is formed, because successive preparation of **3** from **1** and Mg, addition of NaNaph, and deuterolysis place D only in the anti position of **2**.

Since Grignard solutions prepared by different methods do not incorporate D with the same stereoselectivity, once they are formed the *syn*- and *anti*-7-benzonorbornadienyl Grignard reagents must be configurationally stable for hours in THF at 25°. Tests of the stability of the Grignard solution prepared from **1**, $MgCl_2$, and NaNaph by refluxing in THF lead to no deuteration, probably because the Grignard reagents react with a carbon acid formed in side reactions of NaNaph. This complication prevents rigorous proof of the configurational stability of **3** and its syn isomer at 65°, but previous reports that 2-norbornyl[4] and 1-methyl-2,2-diphenylcyclopropyl[5] Grignard reagents are configurationally stable on a laboratory time scale in ethyl ether or THF and that several secondary alkyl Grignard reagents are configurationally stable at >100° on the nmr time scale[12,13] suggest that **3** and its syn isomer are unlikely to interconvert in refluxing THF. The syn isomer might be destroyed selectively, but there is no reason to expect that a syn/anti equilibrium mixture would be >90% anti. Therefore, the *anti*-7-benzonorbornadienyl Grignard reagent **3** apparently is formed >90% stereoselectively by two different routes.

Two disturbing features of our results are the formation of substantial undeuterated benzonorbornadiene in most experiments and the low yields of benzonorbornadiene from **4**. Experiments designed to determine the sources of these problems are in progress.

anti-7-Chlorobenzonorbornadiene forms a Grignard reagent at saturated carbon with Mg more stereoselectively than any other alkyl halide known to us.[4,5,8] This might be explained by an electron transfer–free radical surface mechanism[5,14] of Grignard reagent formation and substantial barriers to pyramidal inversion of 7-benzonorbornadienyl free radicals and carbanions, but we defer further discussion to a full paper.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(8) R. R. Sauers and R. M. Hawthorne, Jr., *J. Org. Chem.*, **29**, 1685 (1964).

(9) S. J. Cristol and A. L. Noreen, *J. Amer. Chem. Soc.*, **91**, 3969 (1969).

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(12) (a) G. M. Whitesides and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 4878 (1965); **89**, 2799 (1967); (b) E. Pechhold, D. G. Adams, and G. Fraenkel, *J. Org. Chem.*, **36**, 1368 (1971).

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(14) (a) G. M. Whitesides, Lecture at the 23rd National Organic Symposium of the American Chemical Society, Tallahassee, Fla, 1973; (b) H. W. H. J. Bodewitz, C. Blomberg, and F. Bickelhaupt, *Tetrahedron*, **29**, 719 (1973).

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Received August 11, 1973

Influence of Geometry on Cyclopropyl Participation in the Thermolysis of Azo Compounds. A Photoelectron Spectroscopic Rationalization[1]

Sir:

Recent work[2,3] has shown that the reactivity of thermal decomposition grows substantially for the azo compounds (**1–4**) with increasing dihedral angle between the plane of the cyclopropane ring and the rest of the structure. Below we present a rationalization of this phenomenon by means of the photoelectron (pe) spectra of **1** and **2**.

(1) Part 41 of "Theory and Application of Photoelectron Spectroscopy;" part 40: W. Schäfer, A. Schweig, F. Bickelhaupt, and H. Vermeer, submitted for publication.

(2) E. L. Allred and A. L. Johnson, *J. Amer. Chem. Soc.*, **93**, 1300 (1971).

(3) B. M. Trost and R. M. Cory, *J. Amer. Chem. Soc.*, **93**, 5573 (1971).

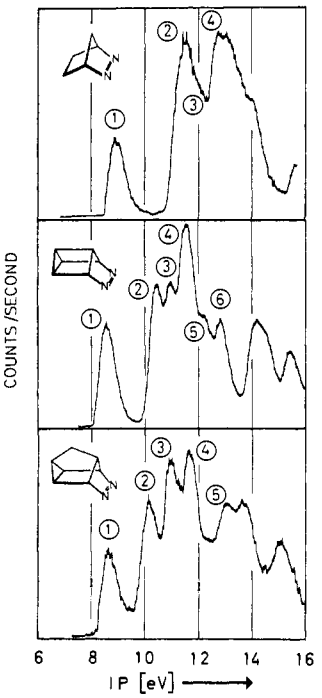


Figure 1. Sections of the photoelectron spectra of the azo compounds **1**, **2**, and **5**. For the measured vertical ionization potentials and the assignment of bands, see Figure 2. The He-I (584 Å) photoelectron spectra were recorded on a PS-18 spectrometer from Perkin-Elmer, Beaconsfield (England).

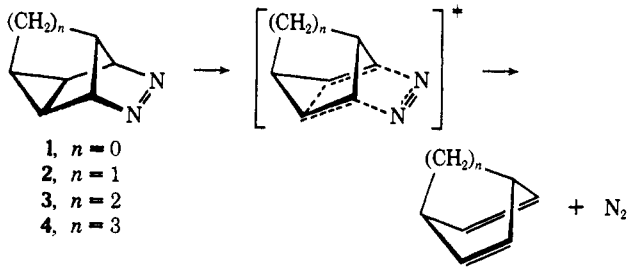
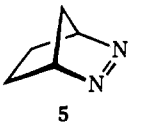


Figure 1 shows sections of the pe spectra of **1**, **2**, and, for comparison, of **5** and Figure 2 displays the correla-



5

tion diagram of the highest occupied MO's of **1**, **2**, **5**, and cyclopropane. Band 1 in all the spectra must be assigned to the antibonding (n_-) nitrogen lone pair combination. The assignment of the following bands in the spectra of **1** and **2** is made possible by comparison with the spectrum of **5**. Band 2 in this spectrum exhibits vibrational structure with a spacing of 1050 cm^{-1} (corresponding vibrational frequency in the molecular ground state = 1508 cm^{-1} [4] corresponding frequency in *trans*-Me—N=N—Me = 1562 cm^{-1}).[5] Accordingly this band must be assigned to the π (N=N) MO

(4) S. G. Cohen and R. Zand, *J. Amer. Chem. Soc.*, **84**, 586 (1962).

(5) E. Haselbach and E. Heilbronner, *Helv. Chim. Acta*, **53**, 684 (1970). This assignment agrees with independent investigations (R. S. Boyd, J. C. Bünzli, J. P. Snyder, and M. L. Heyman, *J. Amer. Chem. Soc.*, **95**, 6478 (1973); F. Brogli, W. Eberbach, E. Haselbach, E. Heilbronner, V. Hornung, and D. M. Lemal, *Helv. Chim. Acta*, **56**, 1933 (1973)).

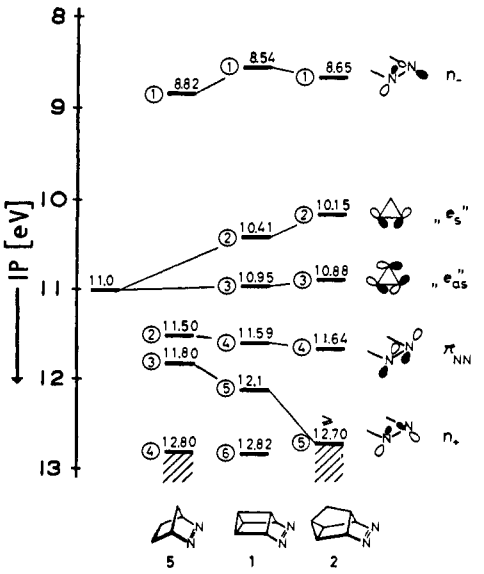


Figure 2. Correlation diagram of the highest occupied MO's of **1**, **2**, **5** and cyclopropane. The numbers shown above the levels are vertical ionization potentials [eV].

(found in *trans*-Me—N=N—Me at 11.84 eV).[5] Finally shoulder 3 must be assigned to the bonding (n_+) lone pair combination (observed in *trans*-Me—N=N—Me at 12.3 ev).[5]

Additionally in **1** and **2** there is a cyclopropane unit. The highest occupied MO's in cyclopropane are the degenerate outer σ MO's (e_s and e_{as}) centered at 11.0 eV. By symmetry, the e_s MO can mix with the π (N=N) and/or n_+ MO's. If this mixing is effective the e_s MO should be destabilized and the π (N=N) and/or n_+ MO's stabilized. On the contrary, the e_{as} MO can be expected to remain at nearly the same energy in **1** and **2**. The pe spectra of **1** and **2** are in full accordance with these expectations. In both spectra two new bands 2 and 3 arise due to ionizations from the "e_s" and "e_{as}" MO's, respectively, while the π (N=N) band 4 and n_+ band 5 are stabilized. The ordering of these latter two levels is derived from INDO calculations and by comparison to the pe spectrum of tricyclo[3.2.1.-$0^{2,4}$]oct-6-ene.[6] The subsequent discussion, however, is independent of their exact ordering.

The point of interest with these results (*cf.* Figure 2) is the increasing destabilization of the cyclopropane e_s MO and simultaneously the increasing stabilization of the π (N=N) and n_+ MO's in going from **1** to **2**. This result directly reflects the growing overlap between the interacting MO's with increasing dihedral angle.

With respect to the reactivity differences observed, two conclusions can be drawn. (i) One of the cyclopropane bonds is partially broken in the transition state. Thus, the fact that the "e_s" MO lies at higher energy for **2** than for **1** indicates that it would take less energy to break this bond. (ii) The N≡N triple bond is partially formed in the transition state. Consequently, the fact that the π (N=N) and n_+ lie at lower energy for **2** than for **1** indicates that it would be easier to form this bond. Moreover, as increasing bond

(6) H. Basch, M. B. Robin, N. A. Kuebler, C. Baker, and D. W. Turner, *J. Chem. Phys.*, **51**, 52 (1969). Also see P. Bischof, E. Heilbronner, H. Prinzbach, and H. D. Martin, *Helv. Chim. Acta*, **54**, 1072 (1971).

strength[7] is usually reflected in decreasing bond length, the C—C bond will be longer and the N=N bond shorter in **2** than in **1**; this makes **2** geometrically closer to the transition state (principle of least motion)[8] and consequently more reactive.

It is already known that copper complexes of the azo compounds as well as the *N*-oxides of the azo compounds are thermally much more stable.[9] Such would be predicted for the reasons given above.

Acknowledgments. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the National Science Foundation. We wish to thank Professor S. F. Nelsen for a generous gift of some azo compounds.

(7) The increased bond strength of the N=N bond in **2** compared to **1** is also reflected in the corresponding vibrational stretching frequency, *i.e.*, for **2** = 1502 cm^{-1} (R. C. Cookson, S. S. H. Gilani, and I. D. R. Stevens, *J. Chem. Soc. C*, 1905 (1967)) and for **1** = 1493 cm^{-1} (B. M. Trost and R. M. Cory, *J. Amer. Chem. Soc.*, **93**, 5572 (1971)).

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Received September 13, 1973

Photosensitized Oxygenation of Tryptophan Methyl Ester and N_b-Methyltryptamine. Isolation and Identification of 3a-Hydroxypyrroloindole and 4a-Hydroxy-1,2-oxazinoindole

Sir:

Oxidation mechanisms of aromatic substrates catalyzed by oxygenases have received much attention in recent years.[1] Not long ago we reported[2] a model reaction for the oxidation of tryptophan by monooxygenases, *viz.*, the conversion of N_a,N_b-dimethyltryptamine to 3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrroloindole (**1**) by photolysis with pyridine 1-oxide (path A).

In the metabolic transformation of tryptophan to kynurenine by tryptophan 2,3-dioxygenase[3] the hydroperoxyindolenine (**3**) has been suggested as a primary intermediate.[4] The photosensitized oxygenation of tryptophan to *N*-formylkynurenine (**5**) provides a model reaction for the enzymatic oxidation which is believed to proceed *via* a dioxetane intermediate[5] derived from **3**. In a third pathway (C) the ethylamino side chain[4] in **3** participates with the formation of 3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrroloindoles (**4**), possessing the novel ring system of the sporidesmins[6] and brevianamide E.[7]

We now report one-step syntheses of 3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrroloindole (**4b**) and 4a-hydroxy-1,2,3,3a,8,8a-hexahydrooxazinoindole (**9**) which are probably formed (path C) *via* 3a-hydroperoxytetrahydropyrroloindole (**7**) when tryptophan methyl ester (**2b**) and N_b-methyltryptamine (**6**), respectively, were photooxygenated. A 4.4 m*M* solution of **2b** in benzene (250 ml) was irradiated (300-W flood lamp) for 15 hr in the presence of Rose Bengal (50 mg in 5 ml of MeOH) while oxygen was bubbled through the reaction vessel. Column chromatography followed by preparative tlc of the crude photolysate gave 3.7% **4b**, mp 166–167°:[8] λ_{max}^{EtOH} nm (ϵ) 244 (7900), 302 (2300); $\lambda_{max}^{EtOH\text{-}HCl}$ nm (ϵ) 236.5 (7400), 295 (2300);[9] *m/e* 234 (M^+); ν_{max}^{KBr} cm^{-1} 3417, 3395, 3272, 3240 (OH, NH); δ ($CDCl_3$) 2.30–2.60 (m, 2, CH_2), 3.07 (broad s, 3, NH, OH), 3.73 (s, 3, CH_3), 3.60–3.90 (m, 1, C_2H), 5.02 (s, 1, NCHN).

Previously, photosensitized oxidations of tryptophan have been conducted in either water or organic acids such as HCOOH or CH_3CO_2H,[10] where participation of the ethylamino side chain is unfavorable and the reaction consequently proceeds *via* path B. When photooxygenation of **6** was carried out under similar reaction conditions (200-W Halogen lamp) for 7 hr, crystalline 4a-hydroxy-2-methyl-2,3,4,4a,9,9a-hexahydro-1,2-oxazino[6,5-*b*]indole (**9**) (25–30%) was isolated:[11] mp 197–198°, *m/e* 206 (M^+); λ_{max}^{EtOH} nm (ϵ) 242 (7460), 297 (2300); $\lambda_{max}^{EtOH\text{-}HCl}$ nm (ϵ) 236 (7590), 293 (2050); δ (C_5D_5N) 2.50 (s, N_b-Me), 2.20–2.90 (m, CH_2CH_2), 4.70 (broad s, OH, NH), 5.37 (s, NCHO), ν_{max}^{KBr} cm^{-1} 3300, 3150 (OH, NH), 990 (N–O). The formation of **9** may result from the intramolecular oxidation of the intermediate 3a-hydroperoxyindolenine (**7**) to the *N*-oxide (**8**),[12] which then spontaneously rearranges to **9**.

Catalytic hydrogenation (PtO_2) of **9** in MeOH in the presence of a catalytic amount of HCl gave **10**: mp 151°; *m/e* 190 (M^+); λ_{max}^{EtOH} nm (ϵ) 243 (8740), 302 (2470); $\lambda_{max}^{EtOH\text{-}HCl}$ nm (ϵ) 236.5 (7980), 294.5 (2280); δ ($CDCl_3$) 2.10–2.90 (m, CH_2CH_2), 2.35 (s, N_b-Me), 3.45 (broad s, OH or NH), 4.10 (broad s, OH or NH), 4.38 (s, NCHN); δ (C_5D_5N) 2.46 (s, N_b-Me), 4.88 (s, NCHN); ν_{max}^{KBr} cm^{-1} 3300, 3080 (OH, NH).

Furthermore, instead of **8**, we obtained **9** upon oxidation of **10** with *m*-chloroperbenzoic acid,[13] indicative

(1) J. W. Daly, D. M. Jerina, and B. Witkop, *Arch. Biochem. Biophys.*, **128**, 517 (1968); D. M. Jerina, J. W. Daly, B. Witkop, P. Zaltzman-Nireberg, and S. Udenfriend, *J. Amer. Chem. Soc.*, **90**, 6525 (1968); O. Hayaishi, *Annu. Rev. Biochem.*, **38**, 21 (1969).

(2) M. Nakagawa, T. Kancko, and H. Yamaguchi, *J. Chem. Soc., Chem. Commun.*, 604 (1972).

(3) O. Hayaishi, "Oxygenases," O. Hayaishi, Ed., Academic Press, New York, N. Y., 1962, p 1; O. Hayaishi and M. Nozaki, *Science*, **164**, 398 (1969); F. Hirata and O. Hayaishi, *Biochem. Biophys. Res. Commun.*, **47**, 1112 (1972).

(4) A. Ek, H. Kissman, J. B. Patrick, and B. Witkop, *Experientia*, **8**, 36 (1952).

(5) B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, **73**, 2196 (1951); N. A. Evans, *Aust. J. Chem.*, **24**, 1971 (1971); I. Saito, M. Imuta, and T. Matsuura, *Chem. Lett.*, 1173, 1197 (1972); see also ref 10.

(6) J. W. Ronaldson, A. Taylor, E. P. White, and R. J. Abraham, *J. Chem. Soc.*, 3172 (1963).

(7) A. J. Birch and J. J. Wright, *Chem. Commun.*, 644 (1969).

(8) All new compounds gave satisfactory microanalytical data. The stereochemistry of the hydroxyl group and the carbomethoxy group in **4b** has not yet been determined. The other isomer of **4b** has not been isolated.

(9) H. F. Hodson and G. F. Smith, *J. Chem. Soc.*, 1877 (1957).

(10) W. E. Savige, *Aust. J. Chem.*, **24**, 1285 (1971), and references cited therein; general reviews for singlet oxygen, *cf.* C. S. Foote, *Science*, **162**, 963 (1968).

(11) The compound **9** was not obtained when **10** was treated under the reaction condition. When the reaction was carried out in MeOH under similar reaction conditions, only 6% yield of **9** was obtained. The stereochemistry of **9** has not yet been determined. Both **4b** and **9** were not produced when the reactions were carried out in absence of Rose Bengal, respectively.

(12) 3-Hydroperoxy-3-methyl-2-phenylindolenine oxidized Et_3N to triethylamine oxide in high yield (unpublished data): M. Nakagawa, H. Yamaguchi, and T. Hino, *Tetrahedron Lett.*, 4035 (1970); M. Nakagawa, T. Suzuki, T. Kawashima, and T. Hino, *Chem. Pharm. Bull.*, **20**, 2413 (1972).

(13) J. C. Craig and K. K. Purushothaman, *J. Org. Chem.*, **35**, 1721 (1970).