Table II. Nmr Spectra of Thymine Dimer and Its Hydrogenolysis Products[a]

Compd	Thymine dimer[b]	Ureido alcohol[b]	Dialcohol[b]	Bicyclic acid[c]	Cyclobutanedicarboxylic acid[c]	Lactone VII[d]
≥CMe	8.67 (s) (6 H)	8.97 8.93 (6 H)	8.97 (s) (6 H)	8.66 8.60 (6 H)	8.71 (s) (6 H)	8.85 (6 H) 8.83
≥CCH_2		6.23 (2 H)	6.57 (s) (4 H)			6.20 (d) (1 H) 5.80 (d) (1 H) AB system J = 9.5 cps
≥CH	6.24 (s) (2 H)	5.30 (d) (1 H) 5.15 (d) (1 H) J = 5.0 cps	6.17 (d) (2 H) J = 4.5 cps	6.16 (d) (1 H) 5.90 (d) (1 H) AB system J = 6.0 cps	5.90 (s) (2 H)	6.03 (d) (1 H) 5.65 (d) (1 H) AB system J = 9.0 cps
		+D_2O: 5.28 (s) (1 H) 5.15 (s) (1 H)	+D_2O: 6.11 (s) (2 H)			

[a] Spectra were measured at 60 Mc/sec on a Varian A-60 spectrometer. Values are given in τ with tetramethylsilane as internal or external standard. [b] Solvent $(CD_3)_2SO$. [c] Solvent D_2O. [d] Mixture of $(CD_3)_2SO$ and D_2O.

dimer (II) obtained by the irradiation of frozen solutions of thymine (I)[1] was reductively cleaved by sodium borohydride in aqueous solution at room temperature to the monoalcohol III, mp 260°, and the dialcohol IV, mp 208.5°, in yields depending on the duration of the reduction (Table I). The dimer II was unreactive to borohydride in pyridine,[9] a solvent which often intensifies the reductive effect. This hydrogenolysis of a heterocyclic system has its precedent in the reductive ring opening of dihydrothymine,[10] dihydrothymidine,[11] free and bound dihydrouridine,[12] glutarimides, succinimides, barbiturates, and some hydantoins.[13]

The nmr spectra of III and IV (Table II) in deuterated DMSO showed the methylene protons at τ 6.23 and 6.57, respectively, in addition to the two C–Me proton peaks and the two cyclobutane protons which exhibited a proton coupling attributable to an adjacent N–H group.

The monoalcohol III was separately reduced by sodium borohydride to the dialcohol IV. Neither the alcohol III nor the dimer II were opened up by alkali in the cold. By contrast, dihydrouracil and dihydrothymidine undergo easy alkaline ring opening to β-ureidopropionic and -isobutyric acids.[14,15]

Oxidation of III with potassium permanganate in neutral solution gave back dimer II in addition to the potassium salt of ureido acid V, mp 241°, whose nmr spectrum in D_2O showed the two cyclobutane protons at τ 6.16 and 5.90 as an AB system in addition to the two C–Me proton peaks at τ 8.66 and 8.60

Likewise, compound IV was oxidized to the novel cyclobutanedicarboxylic acid VI, which was characterized as the dicyclohexylammonium salt, mp >305°, and the γ-lactone VII, mp 207°, which was also obtained by hydrogenolysis of V with borohydride. The nmr spectrum of VII in deuterated DMSO–D_2O showed the methylene protons at τ 6.20 and 5.80 as an AB system and the cyclobutane protons at τ 6.03 and 5.65 as an AB pattern, in addition to the C–Me protons.

The formation of this γ-lactone VII conclusively proves the *cis,syn* configuration of photodimer II, in agreement with the earlier assignment.[8]

Both the bicyclic and the monocyclic acids V and VI easily reverted to dimer II on treatment with dilute hydrochloric acid.

The bicyclic acid underwent quantitative photolysis on irradiation in aqueous solutions with ultraviolet light for a few minutes. In addition to thymine (I) an unstable fragment, VIII, was formed, presumably the potassium salt of *cis*-2-methyl-3-ureidoacrylic acid. When the photolysis mixture was immediately reduced catalytically with palladium on charcoal, the stable reduction products were dihydrothymine, mp 263°, and 3-ureidoisobutyric acid, mp 117°. By contrast, the alcohol III was stable to prolonged irradiation with ultraviolet light.

This novel hydrogenolysis of thymine dimers is now being carried out with sodium borotritide[16] for the localization and quantitation of the photolesion in irradiated polynucleotides and nucleic acids.

(9) S. Yamada, Y. Kikugawa, and S. Ikegami, *Chem. Pharm. Bull.* (Tokyo), **13**, 394 (1965).
(10) G. Ballé, P. Cerutti, and B. Witkop, *J. Am. Chem. Soc.*, **88**, 3946 (1966).
(11) Y. Kondo and B. Witkop, XXIIth IUPAC Congress, Prague, Sept 4–10, 1967, Abstracts, in press.
(12) P. Cerutti, K. Ikeda, and B. Witkop, *J. Am. Chem. Soc.*, **87**, 2505 (1965).
(13) Y. Kondo and B. Witkop, in preparation.
(14) R. D. Batt, J. K. Martin, J. McT. Ploeser, and J. Murray, *ibid.*, **76**, 3663 (1954).
(15) W. E. Cohn and D. G. Doherty, *ibid.*, **78**, 2863 (1956).
(16) *Cf.* P. Cerutti and N. Miller, *J. Mol. Biol.*, **26**, 55 (1967).
(17) Fellow in the Visiting Program, U. S. Public Health Service, 1967–present.

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On the Mechanism of Benzylic Substituent Hydrogenolysis

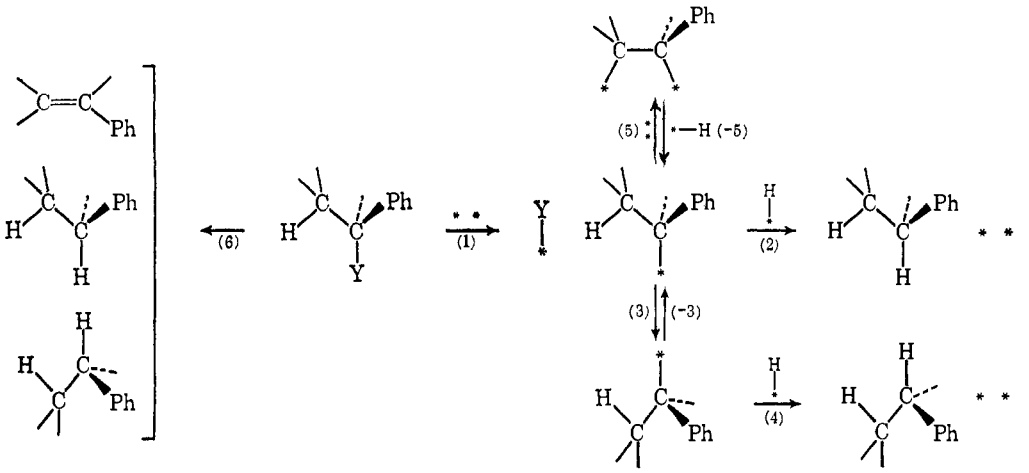
Sir:

The heterogeneous catalytic hydrogenolyses of benzylic substituents, whereas formally straightforward, probably are accomplished by a variety of complex and fundamentally different surface processes.[1]

We wish to present here for consideration a qualitative and general hydrogenolysis mechanism. The mechanism to which we will refer is formulated in Scheme I. With the exception of step 6 it largely paral-

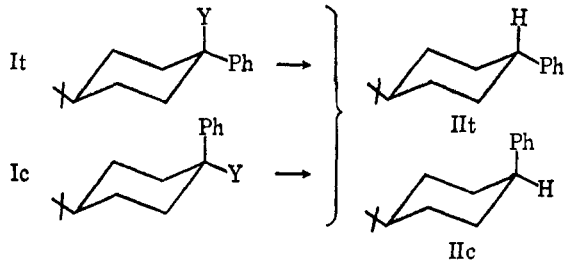
(1) S. Mitsui and Y. Kundo, *Chem. Ind.* (London), 381 (1965), and references cited therein; W. A. Bonner and J. A. Zderic, *J. Am. Chem. Soc.*, **78**, 3218 (1956), and references cited therein; A. M. Khan, F. J. McQuillin, and I. Jardine, *J. Chem. Soc., Sect. C*, 136 (1967).

Scheme I



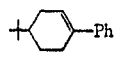
lels the classical Horiuti–Polanyi mechanism which has been applied successfully in qualitatively understanding the surface processes encountered during the hydrogenation[2a] and isotopic-exchange reactions.[2b] Step 6 represents some surface reaction which leads *directly* to desorbed alkene and/or hydrogenolysis product with inversion and/or retention of configuration. The following data are given from which some reasonable conclusions can be drawn regarding the operation of processes outlined in Scheme I.

Hydrogenolyses of 1-Y-*cis*- and -*trans*-4-*t*-butyl-1-phenylcyclohexanes (Ic and It), respectively, were conducted at 25° employing 10% Pd–C and Pt catalysts in acetic acid solvent at 3 atm of hydrogen and Ni(R) (Raney nickel W-2) in ethanol under atmospheric conditions. The composition of product, IIc and IIt, was determined by glpc.[3] Both Ic and It (Y = OH)[3] were converted readily to products with Y = OAc and OMe. Stereochemical assignment to the sulfur-containing derivatives will not be detailed here as the C–S bonds hydrogenolyzed stereoconvergently. The results, which cover the three stereochemical extremes, are summarized in Table I. They indicate that three fundamentally different surface processes may be involved.



The stereoconvergent hydrogenolyses (expt 1, 2, 8–12) all lead to 83 ± 7% of IIc. The percentage of IIc at thermodynamic equilibrium (25°) is about 0.7.[3] These hydrogenolyses (a) proceed through a common intermediate or (b) those of Ic and It proceed with about 83% retention and 83% inversion of configuration, respectively. It is unlikely that alternative b is operating. This alternative is experimentally rejected by deuteriogenolyses (in DOAc) of Ic and It (Y = OH) over Pd–C under conditions otherwise identical with those of expt 2 in Table I. Here, Ic gave IIc + IIt containing 81% D_1, 12% D_2, and 2% D_3, whereas It gave IIc + IIt containing 77% D_1, 17% D_2, and 3% D_3.[4] If Ic is reacting with 80% retention and It with 90% inversion of configuration, the two surface processes must differ fundamentally and the resulting deuterium distributions would be expected to differ appreciably. Alternative a must be operating for these hydrogenolyses. Desorbed alkene, 1-phenyl-4-*t*-butylcyclohexene, is excluded as a possible common intermediate by expt 13–15 where the hydrogenation stereochemistry under hydrogenolysis conditions does not approach that observed for hydrogenolysis. We conclude that the common intermediate is the monoadsorbed substrate that results directly from step 1 of the formulated mechanism and which reaches configurational equilibrium by steps 3, −3 prior to steps 2

Table I. Stereochemistry of Hydrogenolyses

Expt	Catalyst[a]	Y	% IIc from Ic[b]	% IIc from It[b]	Reaction stereochemistry
1	Pt[c]	OH[d]	76	74	Stereoconvergent
2	Pd–C[e]	OH	80	90	Stereoconvergent
3	Ni(R)[f]	OH	93	6	Stereospecific retention
4	Pt[c]	OAc[d]	26	80	Stereospecific inversion
5	Pd–C[e]	OAc	7	96	Stereospecific inversion
6	Ni(R)[f]	OAc	2	95	Stereospecific inversion
7	Ni(R)[f]	OMe	86	20	Stereospecific retention
8	Ni(R)[f]	SPh	88	85	Stereoconvergent
9	Pd–C[e]	SOPh	80	77	Stereoconvergent
10	Ni(R)[f]	SOPh	85	88	Stereoconvergent
11	Pd–C[e]	SO_2Ph	79	82	Stereoconvergent
12	Ni(R)[f]	SO_2Ph	88	89	Stereoconvergent
13	Pt	Hydrogenation of 	47		
14	Pd–C[e]		53		
15	Ni(R)[f]		41		

[a] Grams of catalyst/gram of substrate 40–80 for Ni(R) and 0.5–1.0 for Pt and Pd–C. [b] ±1%. [c] Product analyses conducted on mixtures of IIc and IIt and *cis*- and *trans*-1-cyclohexyl-4-*t*-butylcyclohexanes. Under the hydrogenolysis conditions, platinum-catalyzed hydrogenation of the phenyl group of IIc and IIt is completed without any detectable epimerization. [d] Hydrogenolysis largely precedes phenyl reduction. [e] 10% palladium on charcoal. [f] W-2.

(2) (a) S. Siegel, *Advan. Catalysis*, **16**, 123 (1966); (b) K. Schrage and R. L. Burwell, Jr., *J. Am. Chem. Soc.*, **88**, 4555 (1966).

(3) E. W. Garbisch, Jr. and D. B. Patterson, *ibid.*, **85**, 3228 (1963).

(4) The rate of isotopic exchange on the hydrocarbon hydrogenolysis product is negligible compared with the rate of hydrogenolysis on palladium–charcoal.

and 4. The equilibrium favors the *cis*-monoadsorbed substrate (catalyst surface bonded equatorially), as expected, considering that the effective size of the catalyst probably is greater than that of phenyl. Desulfurizations of similar stereochemistry have been noted.[5] Equilibrium 3, −3 conceivably could take place at a step on the surface or by a rollover mechanism connecting the monoadsorbed species between adjacent surface sites.[2b] The low percentages of greater than D_1 product in the above-described deuteriogenolyses indicate that steps 5, −5 are not intervening seriously.

If the above interpretations are basically correct, we are required to conclude that the hydrogenolyses of acetate on Pt and Pd–C catalysts (expt 4 and 5), which occur stereospecifically with inversion of configuration, do not pass through the monoadsorbed state resulting from step 1. The monoadsorbed species from Ic and It equilibrate configurationally on these catalysts and proceed to stereoconvergent product. Consequently, these hydrogenolyses happen by some *direct substitution process* (step 6) A similar mechanism probably occurs on Ni(R) catalyst (expt 6).

The Ni(R)-catalyzed hydroxyl and methoxyl hydrogenolyses (expt 3 and 7) occur stereospecifically with retention of configuration. Hydrogenolysis of It-2,2,6,6-d_4 containing 83% D_4 gave IIt containing 65% D_4 under reaction conditions which led to 6% loss of D_4 in IIt initially containing 66% D_4 This indicates that these reactions may proceed *via* steps 1 + 2 with minor divergence through step 5 and negligible equilibration (3, −3). The Ni(R) desulfurizations (expt 8, 10, and 12) differ in that local poisoning of the catalyst upon step 1 leads to local hydrogen desorption, retarding steps 2 and 4 and allowing equilibrium (3, −3) to be reached. The observation that deuterium exchange of the benzylic hydrogen of (+)-2-phenylbutane occurs[6] with retention of configuration using deuterated Ni(R) and about 12.5 times as fast as the over-all isotopic exchange is compatible with the hydroxyl hydrogenolysis mechanism proposed above. During the isotopic exchange, excursions through steps 5, −5 and 3, −3 do not compete seriously with steps 1 + 2.

Acknowledgment. Support of this work from the Petroleum Research Fund (Grant No. 1536) of the American Chemical Society is gratefully acknowledged.

(5) E. L. Eliel and S. Krishnamurthy, *J. Org. Chem.*, **30**, 848 (1965).
(6) W. A. Bonner and T. W. Greenlee, *J. Am. Chem. Soc.*, **81**, 3336 (1959).
(7) A. P. Sloan Foundation Research Fellow.

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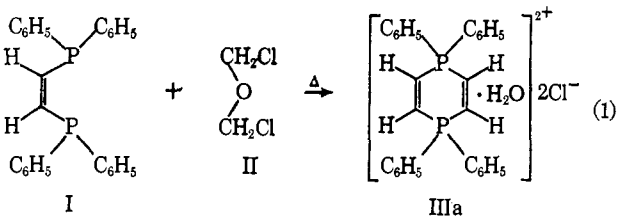
Two Syntheses of the Four-π-Electron 1,4-Diphosphoniacyclohexadiene-2,5 System

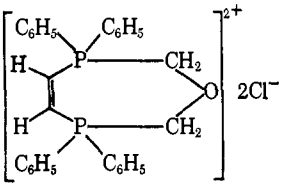
Sir:

We wish to report the formation of 1,1,4,4-tetraphenyl-1,4-diphosphoniacyclohexadiene-2,5 dichloride (IIIa) by reaction of *cis*-vinylenebis(diphenylphosphine)[1] (I) with bis(chloromethyl) ether (II) (eq 1).



I + II → IIIa (1)

Compound IIIa, mp 251–253° (from ethyl acetate–methanol) (*Anal.* Calcd for $C_{28}H_{24}Cl_2P_2 \cdot H_2O$: C, 65.75; H, 5.09; Cl, 13.89; P, 12.13. Found: C, 64.56; H, 5.11; Cl, 14.53; P, 11.96) gave an infrared spectrum exhibiting bands at 1430 and 1105 cm^{-1}, typical of a phenylphosphonium salt. The absence of a band between 1120 and 1250 cm^{-1} verified that no phosphoryl group was present. Both the water solubility and positive aqueous silver nitrate test supported the phosphonium salt structure. Treatment of IIIa with aqueous sodium picrate gave an immediate precipitate of the dipicrate IIIb, mp 235–237° (from acetonitrile) (*Anal.* Calcd for $C_{40}H_{28}N_6O_{14}P_2$: C, 54.67; H, 3.19; N, 9.57; Cl, 0.00. Found: C, 54.59; H, 3.39; N, 9.65; Cl, 0.00), showing that all of the halogen in IIIa as ionic. Although the calculated analysis for IIIa is identical with that of the expected product 3,3,6,6-tetraphenyl-1-oxa-3,6-diphosphoniacycloheptene-4 dichloride (IV), the absence of a carbon–oxygen single bond stretching band in the infrared spectrum makes assignment of this structure to III untenable.



IV

Furthermore, solutions of IIIa in methanol-d_4 gave 60-MHz proton nmr spectra showing only a phenyl complex centered at τ 2.1 and three peaks at τ 0.53, 0.97, and 1.42. Cyclic and acyclic *cis*-vinylenebis(diphenylphosphonium) salts have been observed to exhibit a "pseudo-triplet" downfield from the phenyl protons.[2,3] In the previous examples, however, the center peak was much broader and shallower than in the case of IIIa in which the ratio is 1:2:1. The ratio of phenyl protons to this "triplet" was exactly 5:1 in IIIa. Increase of temperature did not change this ratio. Use of trifluoroacetic acid as the solvent led to essentially the same nmr spectrum, showing that neither exchange with methanol-d_4 nor protonation by trifluoroacetic acid occurs. If IIIa actually had structure IV, the nmr spectrum would show a signal at τ ~4.0 for the methylene protons.[4]

The novelty of this synthetic path made it desirable to produce IIIa by a more unequivocal route. Recent production of the 2,5-diphenyl derivative of III by treatment of diphenyl(phenylethynyl)phosphine with HBr in glacial acetic acid[3] suggested extension of this method to diphenylethynylphosphine[5] (V) (eq 2). A

(1) A. M. Aguiar and D. Daigle, *J. Am. Chem. Soc.*, **86**, 2299 (1964).
(2) A. M. Aguiar and H. Aguiar, *ibid.*, **88**, 4090 (1966).
(3) A. M. Aguiar, K. C. Hansen, and G. S. Reddy, *ibid.*, **89**, 3067 (1967).
(4) A. M. Aguiar, K. C. Hansen, and J. T. Mague, *J. Org. Chem.*, **32**, 2383 (1967).
(5) C. Charrier, M. P. Simonnin, W. Chodkiewwicz, and P. Cadiot, *Compt. Rend.*, **258**, 1537 (1964).