nyl-2-buten-1-one showed $\lambda\lambda_{max}$ at 254 (log ϵ 4.24) and 330 nm (log ϵ 1.77). Its mass spectrum gave a M^+ at 524 plus fragments at *m/e* 506, 488, 419, 401, 299, 262, 157, 105, and 77. The 100-MHz ^{1}H-NMR spectrum evinced multiplets at δ 7.97 and 7.45 (20 H), a multiplet at δ 6.80 (4 H), and a broad singlet at δ 4.48 (4 H). The proton-decoupled ^{13}C-NMR spectrum showed lines at 40.1 and 48.5 (alicyclic C), 128.9, 129.2, 129.4, 133.1, 136.6, and 137.9 (aromatic C), 134.2 and 145.1 (olefinic C), and 190.9 and 198.1 ppm (carbonyl C).

Solid-State Photochemistry of (*E,Z*)-1,4-Dibenzoyl-1,3-butadiene (2). Irradiation of **2** was carried out in a manner similar to that for **1** (vide supra). The product was shown by TLC to consist of two compounds of nearly identical R_f. Thus far the mixture has resisted all attempts at separation.

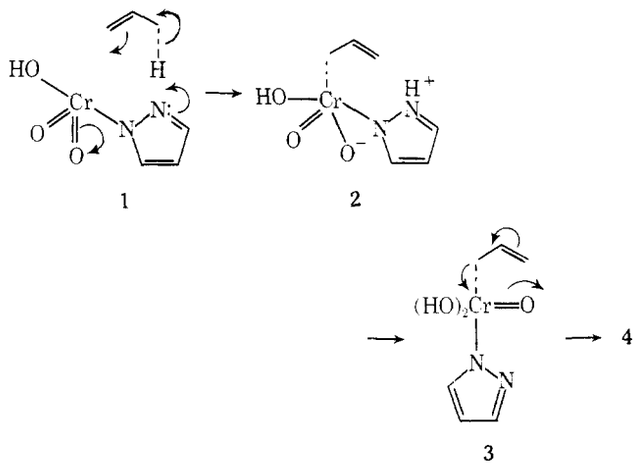
Acknowledgments. We wish to thank Drs. Michael Shapiro and Renate Coombs of Sandoz, Inc. for their help in obtaining ^{13}C-NMR and mass spectra and Mr. Robert Casani for obtaining the UV spectra.

Registry No.—**1**, 65682-02-2; **2**, 65682-03-3; **4**, 107-22-2; **5**, 859-65-4; **7**, 65682-04-4; 2-phenacyl-5-phenylfuran, 54980-24-4; 1-phenyl-2-buten-1-one, 495-41-0.

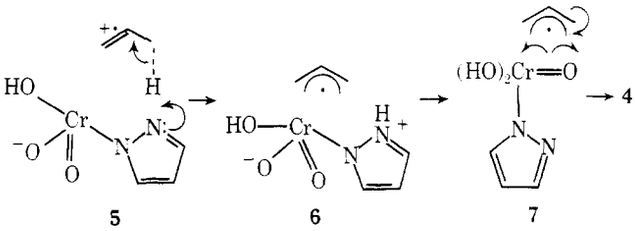
References and Notes

(1) P. S. Bailey and J. H. Ross, *J. Am. Chem. Soc.*, **71**, 2370 (1949).
(2) G. M. J. Schmidt et al., "Solid State Photochemistry", D. Ginsburg, Ed., Verlag Chemie, Weinheim, Germany, 1976, pp 93–144.
(3) P. S. Bailey, W. W. Hakki, and H. W. Bost, *J. Org. Chem.*, **20**, 1034 (1955).
(4) M. Lahav and G. M. J. Schmidt, *J. Chem. Soc. B*, 312 (1967).
(5) C. Harries and F. Temme, *Ber.*, **40**, 165 (1904).
(6) F. Ramirez and S. Dershowitz, *J. Org. Chem.* **22**, 41 (1957).

Scheme I



Scheme II



Allylic Oxidation with 3,5-Dimethylpyrazole. Chromium Trioxide Complex. Steroidal Δ^5-7-Ketones

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In our work on syntheses of hydroxylated metabolites of vitamin D[1,2], we have studied various approaches to the introduction of the 5,7-diene system of the provitamins.[3] Bromination at C-7 of a Δ^5-steroid followed by dehydrobromination is a well-known procedure[4] but gives mixtures of $\Delta^{5,7}$- and $\Delta^{4,6}$-dienes, which are often difficult to separate. As an alternative, we recently described the oxidation of a 7β-phenylselenide;[2] this approach does give 5,7-diene uncontaminated by 4,6-diene, but the yield is limited by simultaneous production of a 5β-hydroxy Δ^6-steroid. The thermal decomposition of the lithium salt of a Δ^5-7-tosylhydrazone leads in excellent yield[5] to the corresponding 5,7-diene uncontaminated by 4,6-diene. Accordingly, we set out to study the conversion of Δ^5-steroids to Δ^5-7-ketones.

A number of oxidants based on chromium[6] have been reported to accomplish this transformation. In our work, we chose initially cholesteryl benzoate as a model. The allylic oxidation of cholesteryl benzoate with sodium chromate in acetic acid/acetic anhydride[7] is, in our experience, a poor reaction and our best yield of the Δ^5-7-ketone was 38%. The use of Collins reagent[8,9] produced in situ gave a 68% yield, but the volume of methylene chloride used as solvent and the amount of calcined Celite[11] used to absorb precipitated oily solids is enormous. The time required for complete reaction, in our hands, in the latter case is ca. 50 h and 3–4 days in the former. Pyridinium chlorochromate[12,13] in methylene chloride at room temperature did not bring about any allylic oxidation.

We have found that the allylic oxidation of cholesteryl benzoate with 3,5-dimethylpyrazole chromium trioxide complex[14] (DMP·CrO_3) is remarkably fast.[15] In reactions where the molar ratio of the CrO_3 to steroid is the same (ca. 20:1) as that required for complete reaction with pyridine as ligand, the reaction with DMP as ligand is complete in less than 30 min, representing a rate increase of some 100-fold. The DMP is recoverable in yields ranging from 70–90% and the yield of the Δ^5-7-ketone is routinely 70–75%.

A probable explanation for the rate enhancement of this oxidation lies partly in the much increased solubility of the chromium containing complexes but more importantly in the possibility of intramolecular acceleration due to the pyrazole nucleus. Many of the characteristics of the reaction are consistent with either of the following mechanistic schemes, proposed as reasonable heuristics. They differ only in the details of the manner in which a carbon oxygen bond is first established at C-7. In Scheme I one two-electron transfer is involved; in Scheme II two one-electron transfers take place. The salient feature of both is that the chromium complex attacks first at the double bond and not at the allylic methylene group.[16]

Both schemes assume a one-to-one addition of DMP and CrO_3 to give the complex shown[14,17] (the 3,5-methyl groups are omitted for the sake of clarity), in which one ligand site remains free on the chromium atom allowing facile attack by the π electrons of the double bond. In Scheme I, the complex attacks the 5,6-double bond by means of an "ene" reaction wherein the removal of the axial 7α-hydrogen is hastened by the appositely placed basic nitrogen of the pyrazole ligand. Such an intramolecular course of action is not possible with Py_2·CrO_3 because (a) no ligand sites are available for complexation with π electrons unless pyridine is first displaced and (b) then no basic nitrogen is available to assist in the removal of the 7α-hydrogen except by an intermolecular deprotonation by the displaced pyridine. It is for stereoelectronic reasons[18] that the Cr will attack axially at C-5 and that an axial C-H bond will be severed, since overlap of the interacting orbitals is maximum in this geometrical array.

In passing from **1** to **2**, no reduction of the Cr^{VI} has taken

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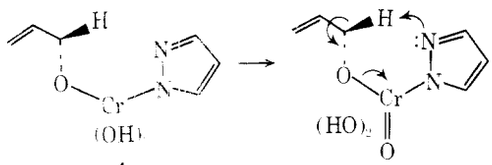
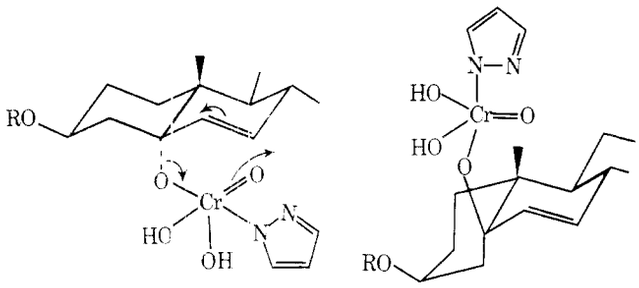
place. A proton shift from nitrogen to oxygen gives **3** (this proton shift could occur later). Although we have found no references to the isolation of Cr^{VI} alkyls, Cr^{II} and Cr^{III} alkyls have been described.[19] Complexes such as **2** or **3** containing Cr^{VI}-C σ bonds have been postulated recently by two groups.[20,21] During the 2,3-sigmatropic shift of the chromium alkyl **3** to give the intermediate **4** oxidation of the steroid takes place and reduction of Cr^{VI} to Cr^{IV} occurs.[16]

The same intermediate **4** is reached in Scheme II. In this scheme, Cr^{VI} first removes one electron from the double bond to give the radical cation[22] together with a Cr^{V} species **5**.[20] Removal of a proton from C-7 by the pyrazole ligand leads to the allyl radical **6**, which now does a further one-electron transfer[23] to give the intermediate **4**. Before further collapse



4 **8**



9 **10**

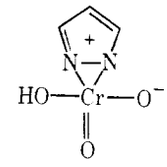
of species **4** to the Δ^5-7-ketone can occur, oxidation of Cr^{IV} to Cr^{VI}, or Cr^{V}, must take place. (Collapse of **4** directly to ketone and a Cr^{II} species is not considered likely.[24]) Again, the decomposition[25] of the resulting chromate ester **8** to the ketone is aided by an intramolecular cyclic mechanism as shown.[14]

In support of the geometrical requirements of this mechanistic scheme is the behavior of cholest-6-ene-3β,5α-diol and cholest-6-ene-3β,5β-diol, 3-benzoates,[2] with the DMP·CrO_3 reagent. At 0 °C, the 5α-hydroxy compound is oxidized very cleanly to the Δ^5-7-ketone in less than 2 min! Primary and secondary alcohols are oxidized to aldehydes and ketones at a comparable rate, indicating that the formation of the chromate ester **9** is fast and that a sigmatropic shift (albeit a 3,3 as opposed to a 2,3 in Scheme I) must ensue rapidly to give the same intermediate as **8** in the schemes above.

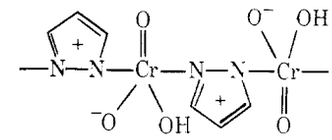
On the other hand, although oxidized in part to the Δ^5-7-ketone, the 5β-hydroxy compound reacts much more slowly and the reaction yields many by-products. The geometry of the chromate ester **10** derived from this AB-cis compound cannot accommodate a 3,3-sigmatropic shift (certainly not at least with the desirable 1,3-diaxial disposition equivalent to that in **9**). Presumably the initially formed chromate ester splits into an ion pair (or radical pair) and it is the resulting allylic carbonium ion (or radical) which is further oxidized in different ways to yield the many observed products. These, and the observations made by Dauben and Michno[13] on the oxidation of tertiary allylic alcohols with pyridinium chlorochromate, support the concerted nature of the 3,3-shift in the 5α-hydroxy case and the necessity for attack from the α face of the steroid with the geometry indicated in the schemes for the oxidation of Δ^5-steroids.

Such mechanisms rationalize some further observations. For example, no attack at C-4 is observed; the 4β-axial hydrogen and approach to the 6β position by Cr are both hindered by 1,3-diaxial interaction with the methyl group on C-10.[9,26] In addition, reaction is hastened at low temperature. This could be due in part to the large negative entropy factor that would be expected in the formation of the highly ordered transition state such as depicted in **1**, which is likely to be the rate-determining step in this sequence.

However, this is probably not the only factor involved in the improved reaction at low temperature. If the complex is allowed to stand at room temperature, it rapidly loses its activity. This may be explained by the possibility of ligand reorganization as in **11**, or more likely by polymerization of



11



12

the oxidant caused by bridging via pyrazole nuclei[17] as in **12**.

Experimentally, the reaction is straightforward. It is important to prepare the oxidant at low temperature (usually −25 to −20 °C) by adding the DMP *as quickly as possible* to the CrO_3 suspended in dry methylene chloride. It is equally important that the CrO_3 be dried over P_2O_5 before use for most efficient oxidation. When the molar ratio of CrO_3 to steroid is ca. 20, the reaction is complete in ca. 30 min; when it is ca. 10, the reaction takes as long as 5 h for completion. A typical reaction is conducted thus: Chromium trioxide (6.0 g, 60.0 mmol) is suspended in dry methylene chloride (50 mL) at −20 °C and the DMP (5.76 g, 60 mmol) is added in one portion. After stirring at −20°C for 15 min, cholesteryl benzoate (2.44 g, 5 mmol) is added and the mixture is stirred for 4 h while maintaining the temperature between −10 and −20 °C. Sodium hydroxide solution (25 mL, 5 N) is then added and the mixture is stirred for 1 h at 0 °C. The phases are then separated. The organic layer is washed with dilute hydrochloric acid to remove the DMP, which can be recovered by subsequent basification of this acidic wash. The methylene chloride phase is now washed with water and saturated sodium chloride solution and evaporated to yield a residue, which is crystallized from cyclohexane to give 7-ketocholesteryl benzoate, 1.86 g, 74%.

A number of Δ^5-steroids have been converted to the Δ^5-7-ketones in a similar manner; for example, 25-hydroxycholesteryl benzoate, stigmasteryl benzoate, 1α,25-hydroxycholesterol, 1,3-diacetate, and 17α-methylandrost-5-ene-3β-17β-diol diacetate.[31]

Registry No.—DMP, 67-51-6; CrO_3, 1333-82-0; DMP·CrO_3, 53143-09-2; cholesteryl benzoate, 604-32-0; 7-ketocholesteryl benzoate, 6997-41-7; cholest-6-ene-3β,5α-diol 3-benzoate, 64746-63-0; cholest-6-ene-3β,5β-diol 3-benzoate, 64746-65-2.

References and Notes

(1) W. G. Salmond and K. D. Maisto, *Tetrahedron Lett.*, 987 (1977); W. G. Salmond, M. C. Sobala, and K. D. Maisto, *ibid.*, 1237 (1977); W. G. Salmond and M. C. Sobala, *ibid.*, 1695 (1977). For a brief review which includes some other work see W. G. Salmond, "Vitamin D, Biochemical Chemical and Clinical Aspects Related to Calcium Metabolism", Walter deGruyter, New York, N.Y., 1977, pp 61–70.

(2) W. G. Salmond, M. A. Barta, A. M. Cain, and M. C. Sobala, *Tetrahedron Lett.*, 1683 (1977).

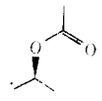
(3) For an excellent review of the vitamin D isomer system, see E. Havinga, *Experientia*, **29**, 1181 (1973).

(4) See, for example, L. F. Fieser and M. Fieser, "Steroids", Reinhold, New York, N.Y., 1959, p 158ff.

(5) L. Caglioti and P. Casselli, *Chim. Ind. (Milan)*, 559 (1963); W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *J. Am. Chem. Soc.*, **90**, 4762 (1968); W. G. Dauben and D. S. Fullerton, *J. Org. Chem.*, **36**, 3277 (1971).

(6) For a review of the more classical methods, see ref 7.

(7) C. W. Marshall, R. E. Ray, I. Laos, and B. Riegel, *J. Am. Chem. Soc.*, **79**, 6308 (1957).
(8) J. C. Collins, W. W. Hess, and F. J. Frank, Tetrahedron Lett., 3363 (1968).
(9) W. G. Dauben, M. Lorber, and D. S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969).
(10) R. Ratcliffe and R. Rodehurst, *J. Org. Chem.*, **35**, 4000 (1970).
(11) The workup of the reaction is facilitated considerably if dry Celite is added to the reaction mixture.
(12) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(13) W. G. Dauben and D. M. Michno, *J. Org. Chem.*, **42**, 682 (1977).
(14) E. J. Corey and G. W. J. Fleet, *Tetrahedron Lett.*, 4499 (1973).
(15) For an example of benzylic oxidation effected by this reagent, see E. McDonald and A. Suksamrarn, *Tetrahedron Lett.*, 4425 (1975).
(16) It has been suggested that the acid-catalyzed allylic oxidation of olefins by chromic acid in aqueous acetic acid involves direct abstraction of a hydrogen atom by Cr^{IV}: P. Müller and J. Rocek, *J. Am. Chem. Soc.*, **96**, 2836 (1974). See also P. Müller and T. T. Khoi, *Tetrahedron Lett.*, 1939 (1977). It is not at all clear that such a mechanism is relevant in nonaqueous systems involving Cr^{VI} coordinated with basic heterocyclic ligands.
(17) S. Trofimenko, *Chem. Rev.*, **72**, 497 (1972).
(18) E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.*, **78**, 6269 (1956).
(19) For a leading reference see J. K. Kochi and J. W. Powers, *J. Am. Chem. Soc.*, **92**, 137 (1970). The 2,3-sigmatropic shift of a Cr^{VI} alkyl such as **3** would be expected to be very fast.
(20) Persuasive arguments that the oxidation of allylic alcohols proceeds via Cr^{VI}–olefin π complex → Cr^{VI}–C σ complex have been made: P. Sundararaman and W. Herz, *J. Org. Chem.*, **42**, 813 (1977). These workers also argue against the involvement of charged species such as **5** in Scheme II. However, since the question is still not resolved, Scheme II is included here for completeness.
(21) Oxidation of olefins with CrO_2Cl_2 has also been argued to proceed via the initial formation of a CrO_2Cl_2 olefin π complex, followed by rearrangement to a σ complex: K. B. Sharpless, A. Y. Teranishi, and J-E. Bäckvall, *J. Am. Chem. Soc.*, **99**, 3120 (1977).
(22) The formation of such a radical cation could rationalize the abundant formation of 5β,6β-epoxide with those reagents such as Na_2CrO_4/AcOH/Ac_2O which are accompanied by nuclephilic species. Axial attack[18] by acetate at the 6β position of the radical cation **5** leads to the radical **13**, further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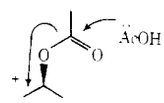

14

oxidized by electron transfer to the tertiary carbonium ion **14**, which cyclizes to the oxide with the formation of acetic anhydride. In aqueous systems, of course, water would be the nucleophile.
(23) As in Scheme I the formal proton transfer from N to O designated in **6** → **7** could occur after this second electron transfer.
(24) See, for example, G. Dyrkacz and J. Rocek, *J. Am. Chem. Soc.*, **95**, 4756 (1973); E. J. Corey and L. S. Melvin, *Tetrahedron Lett.*, 929 (1975).
(25) F. Holloway, M. Cohen, and F. H. Westheimer, *J. Am. Chem. Soc.*, **73**, 65 (1951); J. Rocek F. H. Westheimer, A. Eschenmoser, L. Moldovanyi, and J. Schreiber, *Helv. Chim. Acta*, **45**, 2554 (1962).
(26) It has been clearly established that other eneophiles such as singlet oxygen[27] and diazodimethyl dicarboxylate[28] attack Δ^5-, Δ^6-, and $\Delta^{5,7}$-steroids exclusively from the α face. It is curious that the Sharpless[29] mechanism for allylic oxidation with SeO_2 requires that the initial ene reaction take place from the β side since the SeO_2 oxidation of Δ^5-steroids gives mixtures of 4β-hydroxy-Δ^5-, and 6β-hydroxy-Δ^4-steroids.[30] (Only the former is explicable by the Sharpless mechanism.) Work is in progress in our laboratory toward explaining this dichotomy.
(27) See, for example, G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957); A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961).
(28) A. van der Gen, J. Lakeman, M. A. M. P. Gras, and H. O. Huisman, *Tetrahedron* **20**, 2521 (1964).
(29) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **94**, 7154 (1972); D. Arigoni, A. Vasella, K. B. Sharpless, and H. P. Jensen, *ibid.*, **95**, 7917 (1973).
(30) For example, see O. Rosenheim and W. W. Starling, *J. Chem. Soc.*, 377 (1937); A. Butenandt and E. Hausmann, *Ber. Dtsch. Chem. Ges.*, **70**, 1154 (1937); and C. A. Kind and W. Bergmann, *J. Org. Chem.*, **7**, 341 (1942).
(31) For other examples, see W. G. Salmond, U.S. Patent 4 006 172 (February 1, 1977).

Electrocatalytic Hydrogenation of Aromatic Compounds

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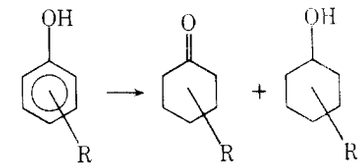
We are currently interested in exploring electrocatalytic organic reactions and report here some initial results which survey electrohydrogenations of aromatic compounds. This particular aspect of electrocatalysis seems to have obtained only limited attention. The possibility of hydrogenation at the very mild conditions normally employed in electrosynthesis, room temperature, and atmospheric pressure is, however, attractive. Furthermore, the electrochemical production of hydrogen directly at the surface of the catalyst would circumvent the compression, transportation, and storage of hydrogen.

Electrocatalytic hydrogenation of olefins has been the subject of numerous investigations employing both precious metal catalyst electrodes,[1-3] like palladium, platinum, and rhodium, as well as "spongy" nickel. The latter is capable of hydrogenating activated double and triple bonds in very good yields.[4,5]

The reduction of aromatic compounds was discovered long ago. Early workers[6,7] hydrogenated phenol in dilute H_2SO_4 at a platinized platinum (Pt|Pt) cathode to cyclohexanol in fair material yield, but with low current efficiency. Under similar conditions[8] the three isomeric cresols have been hydrogenated, yielding in each case an unseparated mixture of alcohols and ketone. The electrocatalytic hydrogenations of cinnamic acid, phenylacetic acid, and benzoic acid at a Pt|Pt cathode in a pressurized cell have also been reported.[9]

The most widely used electrode in electrocatalytic hydrogenation has been a platinum electrode covered with different kinds of metal "blacks".[2,3] To reduce cost we investigated the use of carbon rods as the conductive base for the catalyst, an approach recently successfully applied in other fields of electrocatalysis.[10] These electrodes were used to hydrogenate several aromatic compounds. As shown in Tables I and II we were able to hydrogenate different phenols, anisole, aniline, benzoic acid, cumene, and *tert*-butylbenzene to the corresponding cyclohexyl compounds in fair to excellent yields. Special attention was given to phenol reduction, in part because we wished to evaluate the competition between hydrogenation and hydrogenolysis of the hydroxy group. The hydrogenation of phenol in dilute H_2SO_4 was initially shown to be much more efficient on a Pt|C electrode than on Pt|Pt. After passage of the theoretical amount of electricity (6 F/mol) at a Pt|C electrode, the isolated mixture contains cyclohexanone (**2**, R = H) and cyclohexanol (**3**, R = H) together with phenol (**1**, R = H).



1 2 3

If a larger amount (12 F/mol) of current is passed the only isolated product is cyclohexanol. The material yield though is still low, suggesting a high degree of hydrogenolysis to benzene and cyclohexane. Cyclohexane could, indeed, be detected by gas chromatography in the catholyte before workup of the reaction mixture.

On a Rh|C electrode the material yield was much higher producing 92% cyclohexanol, with a current efficiency as high as 79%. This is the highest yield reported and it is a quite satisfactory method for the synthesis of cyclohexanols. The observed difference between platinum and rhodium is very similar to the results obtained in normal catalytic hydrogenation where platinum is known to give considerable hydrogenolysis of phenols and phenyl ethers as compared to a rhodium catalyst.[11,12]

It is also clear from the results in Table I that the activity of the catalyst metals follows at least qualitatively the se-

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