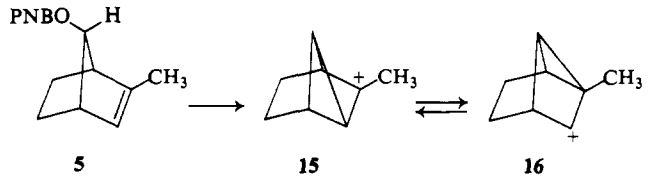
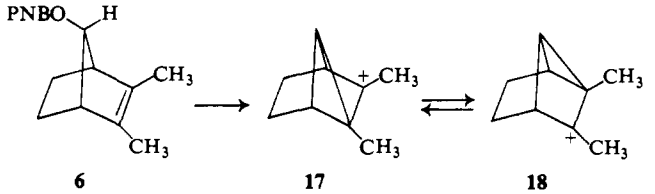


5 15 16



6 17 18

which are believed to occur through the intermediacy of symmetrical transition states.[9-12] In contrast, reactions such as the acid-catalyzed hydration of olefins, which are believed to occur *via* the formation of unsymmetrical, classical carbonium ion intermediates, do not show a cumulative effect of methyl substitution on the rate of reaction. For instance, whereas isobutylene undergoes acid-catalyzed hydration *ca.* 10^3 times faster than propene, 2-methyl-2-butene undergoes hydration slower than isobutylene and *trans*-2-butene undergoes hydration slower than propene.[9,13] It should be noted that the addition of the methyl group to the other end of the double bond *has a rate-retarding effect* in these reactions.

On the basis of the considerations discussed above we feel that our data on the solvolysis of **4**, **5**, and **6** are most consistent with the formation of a symmetrical, delocalized 7-norbornenyl cation.

Acknowledgment. The authors are indebted to the Petroleum Research Fund, administered by the American Chemical Society, for a grant which supported this investigation.

(12) See also H. Tanida and H. Ishitobi, *J. Am. Chem. Soc.*, **88**, 3663 (1966); H. Tanida, *Accounts Chem. Res.*, **1**, 238 (1968); P. von R. Schleyer and G. Van Dine, *J. Am. Chem. Soc.*, **88**, 2321 (1966).
(13) P. Riesz, R. W. Taft, Jr., and R. H. Boyd, *ibid.*, 79, 3724 (1957).
(14) Alfred P. Sloan Research Fellow, 1967–1969.
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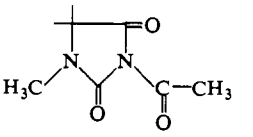
Selective Neutral Acylations

Sir:

To examine their acylating ability several new cyclic N-acylimides were prepared by standard methods and characterized by analytical and nmr data: 3-acetyl-, 3-benzoyl- and 3-*p*-tosyl-1,5,5-trimethylhydantoin; 1-acetyl-3-methyl- and 1,3-diacetyl-2,4,5-imidazolidinetrione. Acylation experiments of different types of alcohols, phenols, and amines indicated that 3-acetyl-1,5,5-trimethylhydantoin (Ac-TMH; I) is the most promising.



I

A simple procedure to prepare Ac-TMH is as follows: a solution of 1,5,5-trimethylhydantoin[1] (0.01 mol) in acetic anhydride (9 ml) is refluxed during 1.5 hr; removal of acetic acid and excess anhydride *in vacuo* followed by crystallization from ethyl acetate–hexane furnishes Ac-TMH (89% yield), mp 126–127°.[2]

A typical acetylation is: 2-naphthol (0.001 mol) in anhydrous acetonitrile (1 ml) and Ac-TMH (0.001 mol) are heated 12 hr at 80°; removal of the solvent and washing with water[3] give in quantitative yield 2-naphthyl acetate, identified by mixture melting point. Other dry solvents (benzonitrile, dioxane, chloroform, benzene, and *t*-butyl alcohol) are also suitable for this reaction.

Competition experiments provided interesting results as illustrated by the following example: 2-naphthol (0.001 mol) and 2-octanol (0.001 mol) were dissolved in benzonitrile (1 ml), Ac-TMH (0.00025 mol) was added, and the solution was heated at 80° for 12 hr; the nmr spectrum showed that the reaction was complete[4] and that practically only the phenolic acetate (δ 2.33 ppm) was formed. This and similar results suggested that Ac-TMH may be useful for the selective acetylation *under neutral conditions* of the phenolic function in the presence of the alcoholic group.

Reaction of *p*-hydroxybenzyl alcohol with an equimolecular amount of Ac-TMH in acetonitrile at 80° for 12 hr produces, according to nmr measurements, a mixture of the phenolic (91%) and alcoholic (9%) monoacetates and 1,5,5-trimethylhydantoin (100%). Under the same conditions acetic anhydride leads to the phenolic and alcoholic monoacetates and the diacetate derivative in a ratio 3:1:2 and 16% recovery of *p*-hydroxybenzyl alcohol.

The selectivity of Ac-TMH is further illustrated by the monoacetylation of 17β-estradiol. The nmr spectrum (in $CDCl_3$) of the crude reaction product washed with water[3] shows a sharp peak of the phenolic acetate at δ 2.27 ppm; the absence of absorption in the region at δ 4.7 ppm (H α to an acetoxy group) demonstrates that the alcoholic hydroxyl is not acylated.[5] Besides, thin-layer chromatography indicates that the crude product is essentially estradiol 3-acetate containing estradiol as an impurity. Column chromatography on Florisil with benzene–acetone mixtures followed by recrystallization from ethyl acetate–hexane affords in 60% yield estradiol 3-acetate, mp 136–139° (lit.[6] mp 136.5–137.5°).

The nmr spectrum of the mixture from the reaction of

(1) O. O. Orazi, R. A. Corral, and J. D. Bonafede, *Anales Asoc. Quim. Arg.*, **45**, 139 (1957); O. O. Orazi and R. A. Corral, *Experientia*, **21**, 508 (1965).
(2) The Ac-TMH remained unchanged after several months in a desiccator.
(3) Evaporation of the aqueous extract leads to quantitative recovery of 1,5,5-trimethylhydantoin, mp and mmp 161–163°.
(4) It lacks the acetyl group signal (δ 2.65 ppm) of Ac-TMH.
(5) *Cf.* with the spectrum of estradiol diacetate: N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, Calif., 1964, p 11.
(6) K. Miescher and C. Scholz, *Helv. Chim. Acta*, **20**, 263 (1937).

p-hydroxybenzyl alcohol with N-acetylsuccinimide indicates that the latter possesses a selectivity comparable to Ac-TMH; however, N-acetylsuccinimide is a low-temperature melting solid not easily purifiable.[7] On the other hand N-acetylphthalimide[8] displays a very low reactivity; with 2-naphthol (0.001 mol) in benzonitrile (1 ml) at 80° for 8 hr, it reaches only 10% reaction, while in these conditions the consumption of Ac-TMH is complete.

Probably, the subtle selectivity of Ac-TMH is significantly dependent upon the operation of steric factors. Competition and kinetic measurements directed to study the mechanism of these reactions are in progress.

(7) All the used samples of N-acetylsuccinimide, prepared as described by J. Tafel and M. Stern, *Ber.*, **33**, 2224 (1900), contained 10–15% succinimide according to nmr spectrometry.

(8) This reagent and closely related compounds have already been used for the acylation of several types of substances: N. Rabjohn, M. Drumm, and R. Elliot, *J. Am. Chem. Soc.*, **78**, 1631 (1956); J. Bosnjak, R. I. Mamuzic, and M. L. Mihailovic, *Glasnik. Khem. Drustva Beograd*, **27**, 313 (1962) (*Chem. Abstr.*, **60**, 5391*a* (1964)), and references cited.

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Stereochemistry of Addition of Deuterium Bromide to *cis*- and *trans*-2-Butene and the Control of Interfering Olefin Isomerization[1]

Sir:

The mechanistic details of the electrophilic addition of hydrogen halides to simple olefins has not received a great deal of attention despite the synthetic importance of these reactions.[2] The stereochemistry of these additions to nonconjugated olefins has been studied only with a relatively few olefins, these being cyclic olefins. The addition of hydrogen bromide to 1,2-dimethylcyclohexene[3] and cyclohexene-1,3,3-d_3,[4] deuterium bromide to cyclohexene[5] and cyclohexene-3,3,6,6-d_4,[6] and hydrogen chloride to 1,2-dimethylcyclopentene[7] all occur predominantly *trans*. The addition of hydrogen chloride in acetic acid to cyclohexene-1,3,3-d_3 is more complicated, giving a mixture of *cis* and *trans* addition products.[8] Similar additions to norbornene occur predominantly *cis-exo* and are accompanied by rearrangements.[9]

We have investigated some of the aspects of the addition of deuterium bromide in acetic acid-O-*d* to *cis*- and *trans*-2-butene. Employing the general procedure used by previous investigators (~1 *M* DBr in DOAc with inhibitor at room temperature and subject to normal laboratory atmosphere and light), *cis*- and *trans*-2-butene produce identical mixtures of 60% *threo*- and 40% *erythro*-3-deuterio-2-bromobutane.[10,11]

Treatment of *cis*- and *trans*-2-butene with a deficient amount of hydrogen bromide in acetic acid followed by immediate recovery of the excess 2-butene revealed that olefin isomerization had occurred (*cis* ⇄ *trans* K_{eq} at 25° is 2.80). Qualitative rate measurements demonstrated that the rate of olefin isomerization is much faster than the rate of addition. The olefin isomerization is not acid catalyzed, as indicated by the incorporation of only a single deuterium atom in the 3 position[12] of the bromide and the observation that similar concentrations of hydrogen chloride and *p*-toluenesulfonic acid in acetic acid do not lead to any substantial amounts of isomerization over a period of 14 days at 42°.

Various experiments indicate that the olefin isomerization reaction requires the presence of hydrogen bromide and oxygen or light.[13] These observations suggest a bromine atom catalyzed isomerization, the bromine atoms being produced in either of the following reactions.[15]

$$O_2 + HBr \rightleftarrows HOO\cdot + Br\cdot$$

$$HBr \overset{h\nu}{\rightleftarrows} H\cdot + Br\cdot$$

In our hands the presence of relatively large quantities of typical radical inhibitors used by previous investigators (hydroquinone, alkylphenols, etc.) has *no* effect on the olefin isomerization reaction.[16] Interestingly, the reaction of a mixture of 1-butene and an excess of *cis*-3-hexene with hydrogen bromide in acetic acid leads to isomerization of the *cis*-3-hexene (*cis* ⇄ *trans* K_{eq} at 25° of 10.0) but produces *none* of the radical addition product 1-bromobutane. Only when oxygen is bubbled through

(1) Research partially supported by the National Science Foundation, Grant GP-4497, and the Alfred P. Sloan Foundation.

(2) For a recent review of electrophilic addition reactions see: R. C. Fahey in "Topics in Stereochemistry," Vol. 3, E. L. Eliel and N. L. Allinger, Ed., Interscience Publishers, New York, N. Y., 1968, pp 237–342.

(3) G. S. Hammond and T. D. Nevitt, *J. Amer. Chem. Soc.*, **76**, 4121 (1954).

(4) R. C. Fahey and R. A. Smith, *ibid.*, **86**, 5035 (1964).

(5) I. V. Smirnov-Zamkov and G. A. Piskovitina, *Ukr. Khim. Zh.*, **28**, 531 (1962).

(6) See p 248, ref 2.

(7) G. S. Hammond and C. H. Collins, *J. Amer. Chem. Soc.*, **82**, 4323 (1960).

(8) R. C. Fahey and M. Monahan, *Chem. Commun.*, 936 (1967); see also p 248 of ref 2.

(9) J. K. Stille, F. M. Sonnenberg, and T. H. Kinstle, *J. Amer. Chem. Soc.*, **88**, 4922 (1966); H. Kwart and J. L. Nyce, *ibid.*, **86**, 2601 (1964); H. C. Brown and K. T. Liu, *ibid.*, **89**, 3900 (1967).

(10) The *threo*- and *erythro*-3-deuterio-2-bromobutanes were previously prepared (P. S. Skell and R. G. Allen, *ibid.*, **81**, 5383 (1959)) by the radical addition of DBr to *cis*- and *trans*-2-butene at −70°.

(11) The bromide mixtures derived from *cis*- and *trans*-2-butene contained 0.97 and 0.99 deuterium atom, respectively. The hydrogen magnetic resonance spectra of the two samples were identical in all respects and unambiguously demonstrated that all of the deuterium was at the 3 position. The stereochemical composition of the samples was determined by infrared analysis of the corresponding benzoates, prepared by conversion of the bromides to the acetates with silver acetate in acetic acid, reduction by lithium aluminum hydride to the alcohol, and esterification with benzoyl chloride, with known mixtures of authentic samples of *erythro*- and *threo*-3-deuterio-2-butyl benzoates (D. J. Pasto, C. C. Cumbo, and J. Hickman, *ibid.*, **88**, 2201 (1966)).

(12) The acid-catalyzed isomerization of the 2-butenes in deuterium bromide–acetic acid-O-*d* would require the formation of the 3-deuterio-2-butyl cation, which on regeneration of olefin would be expected to loose preferentially a proton to produce 2-deuterio-2-butene. Thus the product bromide would contain more than one atom of deuterium.

(13) Kharasch and coworkers[14] have reported that *cis*-stilbene does not isomerize in the presence of hydrogen bromide in air, but that isomerization does occur in the presence of peroxidic substances. Light was also implicated as catalyzing the isomerization in the presence of hydrogen bromide. The isomerization is completely stopped in the presence of hydroquinone or ethyl mercaptan.

(14) M. S. Kharasch, J. V. Mansfield, and F. R. Mayo, *J. Amer. Chem. Soc.*, **59**, 1155 (1937).

(15) A similar suggestion has been made by Y. Urushibara and O. Simamura (*Bull. Chem. Soc. Japan*, **14**, 323 (1939)) to account for the isomerization of various olefins with hydrogen bromide in the presence of peroxidic substances and oxygen.

(16) See footnote 13.