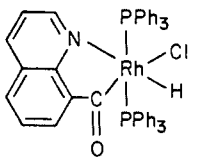
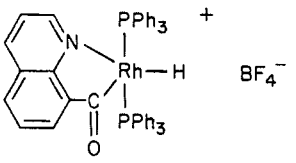
ceptionally stable complexes containing a carbon–metal σ bond can be isolated. We expected that an aldehyde containing a coordinating group could form an isolable complex corresponding to **1** since the extra ligand would give a coordinatively saturated, 18-electron complex, retarding acyl to alkyl rearrangement. Chelation would also disfavor reductive elimination to return the starting aldehyde.[7]

A readily available aldehyde able to form a chelate is 8-quinolinecarboxaldehyde (**3**).[8] Addition of **3** to a saturated solution of $RhCl(PPh_3)_3$ in CH_2Cl_2 gave a yellow precipitate after 10 min. One recrystallization from CH_2Cl_2–ether gave the acylrhodium(III) hydride **4** in 95% yield.[9] The low value



4



5

of the Rh–Cl stretching frequency (230 cm^{-1}) implies that the chlorine is trans to the acyl group,[10] leading to the stereochemistry shown. The acyl hydride **4** is the first stable intermediate to be isolated from a $RhCl(PPh_3)_3$ promoted aldehyde decarbonylation reaction and provides support for the mechanism given above. Differential thermal analysis of **4** showed it to be stable up to its melting point of 175–176 °C. Heating **4** in benzene at reflux for several hours caused no decomposition. Only after 4 h in xylene at reflux was reductive elimination completed, giving quantitative yields of quinoline and *trans*-$RhCl(CO)(PPh_3)_2$. Addition of excess triphenylphosphine slowed this decomposition.

Treatment of **4** with $AgBF_4$ in toluene–CH_2Cl_2 at 0 °C gave rise to the coordinatively unsaturated **5** (as the CH_2Cl_2 solvate), isolated in quantitative yield as hygroscopic yellow needles after one recrystallization from CH_2Cl_2–ether.[11] This salt is stable indefinitely at room temperature, even though a vacant (solvent occupied) site is available in **5** to facilitate the acyl to alkyl rearrangement.[12] Decarbonylation at room temperature does not occur, presumably because the intermediate alkyl would be part of a strained, four-membered-ring chelate. As with **4** decarbonylation occurs at elevated temperatures.

Earlier work has suggested acylrhodium(III) hydrides react with olefins, in effect adding an aldehyde C–H bond across an olefin to form a ketone.[13] For example, the reaction of 4-pentenal with $RhCl(PPh_3)_3$ gave cyclopentanone. This process, by analogy to the hydroformylation reaction, has been termed hydroacylation.[14] With the isolation of **5** we can confirm the suggestion that acylrhodium(III) hydrides are reagents for the hydroacylation of terminal olefins. Treatment of a THF suspension of **5** with excess 1-octene and 8-quinolinecarboxaldehyde at 50 °C gave, after 30 min, a 55% yield (based on **5**) of 8-quinolinyl *n*-octyl ketone. Reaction with the coordinatively saturated **4** gave no hydroacylation product under these conditions. None of the branched-chain ketone was detected. The unreacted hydrocarbon consisted of a mixture of octenes, in which the 3- and 4-octenes predominated. The nature of the rhodium species remaining is under investigation. No Rh–H bonds remain, as determined by IR spectroscopy.

Further work is in progress on the stabilization of other acylrhodium(III) hydrides and the development of systems for catalytic hydroacylation.

Acknowledgment is made to D. J. Freed, M. L. Kaplan, B. K. Teo, and especially M. L. Schilling for valuable assistance in the collection of spectral data.

References and Notes

(1) J. Tsuji and K. Ohno, *Synthesis*, **1**, 157 (1967); B. M. Trost and M. Preckel, *J. Am. Chem. Soc.*, **95**, 7862 (1973); P. D. Hobbs and P. D. Magnus, *J. Chem. Soc., Chem. Commun.*, 856 (1974); D. J. Dawson and R. E. Ireland, *Tetrahedron Lett.*, 1899 (1968).
(2) M. C. Baird, C. J. Nyman, and G. Wilkinson, *J. Chem. Soc. A*, 348 (1968); H. M. Walborsky and L. E. Allen, *J. Am. Chem. Soc.*, **92**, 5465 (1971); J. Tsuji in "Organic Synthesis via Metal Carbonyls", Vol. 2, I. Wender and P. Pino, Ed., Wiley, New York, N.Y., 1977, pp 595–654.
(3) J. K. Stille and M. T. Regan, *J. Am. Chem. Soc.*, **98**, 1508 (1974); J. K. Stille and R. W. Fries, *ibid.*, **96**, 1518 (1974); D. L. Egglestone, M. C. Baird, C. J. Lock, and G. Turner, *J. Chem. Soc., Dalton Trans.*, 1576 (1977).
(4) A. M. Abeysekera, R. Grigg, J. Trocha-Grimshaw, and V. Viswanatha, *J. Chem. Soc., Perkin Trans. 1*, 1395 (1977), recently reported the first acylrhodium(III) complexes isolated from the reaction of a rhodium(I) complex with aldehydes.
(5) C. Masters, *J. Chem. Soc., Chem. Commun.*, 1258 (1972); R. J. Hodges, D. E. Webster and P. B. Wells, *Chem. Commun.*, 462 (1971).
(6) M. I. Bruce, *Angew. Chem., Int. Ed. Engl.*, **16**, 73 (1977); G. W. Parshall, *Acc. Chem. Res.*, **8**, 113 (1975).
(7) We propose the term chelate trapping to describe this strategy of attaching a coordinating group to the organic substrate near the site at which reaction occurs to stabilize by chelation an otherwise labile transition metal complex.
(8) V. M. Rodionov and M. A. Berkengeim, *J. Gen. Chem. USSR*, **14**, 330 (1944); *Chem. Abstr.*, **39**, 4076 (1945).
(9) Anal. Calcd for $C_{46}H_{37}ClNOP_2Rh$: C, 67.37; H, 4.54; N, 1.71. Found: C, 67.03; H, 4.65; N, 1.65. IR (CH_2Cl_2): 2020, 1660 cm^{-1}. ^1H NMR (90 MHz) ($CDCl_3$): δ 8.85 (1 H, d, J = 5 Hz, α – H on quinoline ring), −11.93 (1 H, overlapping d of t, J_{P-H} = 6, J_{Rh-H} = 15 Hz).
(10) J. W. Dart, M. K. Lloyd, R. Mason, and J. A. McCleverty, *J. Chem. Soc., Dalton Trans.*, 2039 (1973).
(11) Anal. Calcd for $C_{47}H_{39}BCl_2F_4NOP_2Rh$: C, 59.02; H, 4.11; N, 1.46. Found: C, 59.08; H, 3.98; N, 1.33. IR (CH_2Cl_2): 2020, 1724, 1689, 1065 (br) cm^{-1}. ^1H NMR (90 MHz) (CD_2Cl_2): δ 8.94 (1 H, d, J = 5 Hz), 5.33 (2 H, s), −10.70 (1 H, d of t, J_{P-H} = 6, J_{Rh-H} = 20 Hz). Of the two bands in the acyl region, the 1689-cm^{-1} one may be a quinoline band; however, see ref 4 for other instances of acyl groups in acylrhodium(III) complexes appearing as doublets.
(12) A. Wojcicki, *Adv. Organomet. Chem.*, **11**, 87–145 (1973).
(13) K. Sakai, J. Ide, O. Oda, and N. Nakamura, *Tetrahedron Lett.*, 1287 (1972); K. Sakai and O. Oda, *ibid.*, 4375 (1972); C. F. Lochow and R. G. Miller, *J. Am. Chem. Soc.*, **98**, 1281 (1976).
(14) P. Pino, F. Piacenti, and M. Bianchi in "Organic Synthesis via Metal Carbonyls", Vol. 2, I. Wender and P. Pino Ed., Wiley, New York, N.Y., 1977, pp 215–228; J. Schwartz and J. B. Cannon, *J. Am. Chem. Soc.*, **96**, 4721 (1974).

J. William Suggs
Bell Laboratories, Murray Hill, New Jersey 07974
Received September 26, 1977

A Priori Calculations on Isotopic Exchange Equilibria

Sir:

According to molecular orbital theory, the lowest lying acceptor orbital of a methyl group is CH antibonding.[1] It follows, therefore, that transfer of electron density into the group will lead to a weakening of its CH linkages. A like result derives from resonance arguments, $H_3C-X^- \leftrightarrow H_2C(H^-)=X \leftrightarrow$ etc., and has been aptly termed "negative hyperconjugation".[2] The observation of significant β-deuterium isotope effects for the gas phase ion–molecule equilibria (1–3 in Table I) has recently been cited as evidence for such an effect.[3] We now present theoretical results based on ab initio molecular orbital calculations which further support such an interpretation.

Equilibrium geometries and quadratic force constants, molecular parameters which, within the Born–Oppenheimer approximation, are invariant to isotopic substitution, have been evaluated with the split-valence-shell 4-31G basis representation[4,5] for the species in reactions 1 and 2.[6] Theoretical equilibrium constants (K_{theory}) for equilibria 1 and 2 have been calculated,[7] and are presented in Table I, along with the corresponding experimental quantities (K_{expt}). Also tabulated are the contributions made by the C–H bond stretching motions alone ($K_{stretch}$) to the total calculated equilibrium constants, obtained by the perturbation theory method of Singh and Wolfsberg.[8] (In this approach, the zeroth-order vibrational problem corresponds to uncoupled bond stretches and bond

0002-7863/78/1500-0641$01.00/0

Table I. Experimental and Calculated Equilibrium Constants for Isotopic Exchange Reactions

Reaction	K_{expt}	K_{theory}[a]	$K_{stretch}$[a]
(1) $CD_3NH^- + CH_3NH_2 \rightleftharpoons CD_3NH_2 + CH_3NH^-$	1.9 ± 0.3[b]	2.4	2.1
(2) $CD_3O^- + CH_3OH \rightleftharpoons CD_3OH + CH_3O^-$	2.3 ± 0.4[b]	2.9	2.7
(3) $CD_3S^- + CH_3SH \rightleftharpoons CD_3SH + CH_3S^-$	1.7 ± 0.2[b]		
(4) $CD_3NH_3^+ + CH_3NH_2 \rightleftharpoons CD_3NH_2 + CH_3NH_3^+$	0.8 ± 0.2[c]	0.8	0.8

[a] Calculated at 300 K, to correspond to room temperature experimental measurements. [b] Reference 3. [c] D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **98**, 311 (1976). The equilibrium constant for this reaction has also been determined in our laboratories (M. Taagepera and R. W. Taft, unpublished results) and is in good agreement with the above result. Note also a similar equilibrium constant for the related proton transfer reaction, $(CD_3)_3NH^+ + (CH_3)_3N \rightleftharpoons (CD_3)_3N + (CH_3)_3NH^+$, K_{eq} (per CD_3) = 0.84 ± 0.02 (R. W. Taft in "Proton Transfer Reactions", E. F. Caldin and V. Gold, Ed., Wiley-Halstead, New York, N.Y., 1975, p 50).

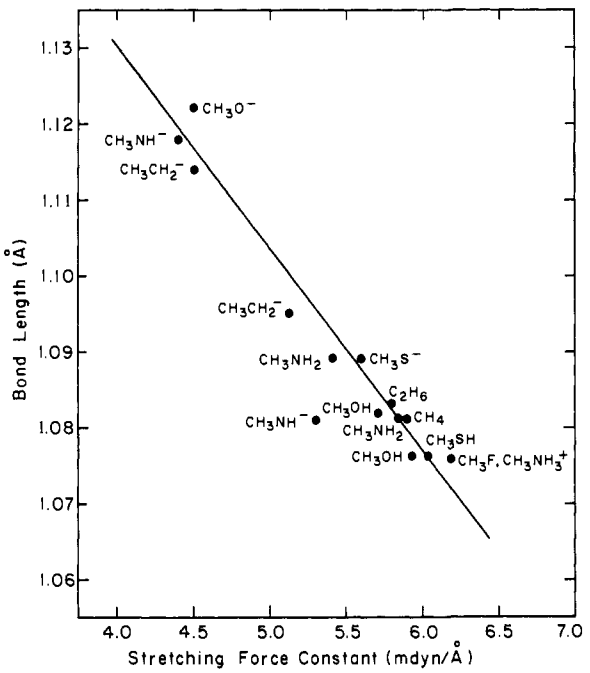


Figure 1. Calculated (4-31G level) methyl group C-H bond lengths (Å) vs. corresponding stretching force constants (mdyn/Å). Multiple entries indicate individual parameters for nonequivalent C-H bonds.

angle and torsional deformations, the coupling of which in the potential and kinetic vibrational energy expressions serves as the perturbation. The contributions of diagonal force constants to the total isotope effect are then amenable to dissection in terms of the zeroth-order problem.[9])

We have also calculated the equilibrium constant for the related isotopic exchange reaction (4) involving the formal transfer of a proton between CH_3NH_2 and CD_3NH_2. Our theoretical result is included in the table, along with that of a recent experimental determination.

The following points are worthy of mention.

(1) Simple levels of ab initio molecular orbital theory yield isotope effects in nearly quantitative agreement with experiment. It is recognized that equilibrium constants for isotopic exchange reactions reflect *changes in force constants* at the position of isotopic substitution much more strongly than they reflect the absolute values of the force constants.[10] Thus, for reaction 1 the important quantities are the differences in the force constants associated with the methyl group in CH_3NH^- and CH_3NH_2. While absolute values of force constants calculated (using theoretically obtained equilibrium geometries) with the 4-31G method tend to be somewhat in error,[11,12] the high level of agreement between theoretical and experimental equilibrium constants indicates that differences in force constants are better described.

(2) The perturbation theory analysis demonstrates that it is the methyl C-H stretching force constants which largely determine the isotope effect. This finding supports the suggestion of the simple molecular orbital and resonance pictures that hyperconjugative interactions weaken the C-H bonds in these systems. In this connection reference should be made to Figure 1, where an approximate linear relationship between calculated methyl group C-H bond lengths and the corresponding stretching force constants is depicted.[13] Thus, the equilibrium constants for the reactions studied may be interpreted as direct evidence in support of the notion that the C-H bonds in the methylamine and methoxy anions are longer than those in their neutral precursors.

(3) The theoretical and experimental results for reaction 4, involving proton transfer between CH_3NH_2 and CD_3NH_2, provide further evidence for the importance of "negative hyperconjugation". Here the amino substituent in neutral methylamine is a much stronger electron donor than the NH_3^+ group in the protonated molecule. The observed direction of the equilibrium isotope effect follows. As in the previous examples, the perturbation approach suggests that changes in C-H stretching force constants play the dominant role in dictating the magnitude of the total effect.

In conclusion, it appears that quantitative molecular orbital theory may now be employed as a means of interpreting the direction and magnitude of observed secondary isotope effects. Such applications of the quantitative theory are not yet routine, but, in view of the substantial improvements which have been made in recent years in computer algorithms for carrying out the nonempirical calculations, it seems that they will be within this decade.

Acknowledgments. This research was supported in part by the U.S. Energy Research and Development Administration (EY-76-S-03-0034, P.A. No. 188), the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

References and Notes

(1) For pictorial representations, see W. L. Jorgensen and L. Salem, "The Organic Chemist's Book of Orbitals", Academic Press, New York, N.Y., 1973.
(2) For examples, see (a) D. Holtz, *Prog. Phys. Org. Chem.*, **8**, 1 (1971); (b) W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry", W. A. Benjamin, New York, N.Y., 1969, p 18 ff; (c) D. J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York, N.Y., 1965, p 68 ff.
(3) D. J. DeFrees, J. E. Bartmess, J. K. Kim, R. T. McIver, Jr., and W. J. Hehre, *J. Am. Chem. Soc.*, **99**, 6451 (1977).
(4) R. Ditchfield, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).
(5) All calculations have been performed using the Gaussian-70 series of computer programs (W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, program no. 236, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Ind.).
(6) The calculated force constants correspond to the theoretical equilibrium geometry and have been obtained in the manner suggested by Newton et al. (M. D. Newton, W. A. Lathan, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, **52**, 4064 (1970)). It has been suggested (R. H. Schwendeman, *ibid.*, **44**, 2115 (1966)) that theoretical force constants (second derivatives) be evaluated at the experimental rather than the theoretical equilibrium geometry. Without taking a position on this suggestion, our choice of using the theoretical geometry was clearly dictated by a lack of experimental structural data for the ions.
(7) M. Wolfsberg and M. J. Stern, *Pure Appl. Chem.*, **8**, 225 (1964). The harmonic approximation has been employed. See J. Bigeleisen and M. G. Mayer, *J. Chem. Phys.*, **15**, 261 (1947).
(8) G. Singh and M. Wolfsberg, *J. Chem. Phys.*, **62**, 4165 (1975).
(9) S. A. Skaron and M. Wolfsberg, *J. Am. Chem. Soc.*, **99**, 5253 (1977).
(10) For a discussion, see M. Wolfsberg, *Acc. Chem. Res.*, **5**, 225 (1972).

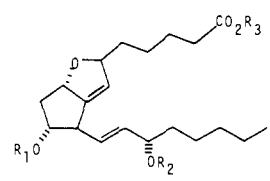
(11) W. A. Lathan, W. J. Hehre, L. A. Curtiss, and J. A. Pople, *J. Am. Chem. Soc.*, **93**, 6377 (1971).
(12) The recent work of Schlegel and Wolfe (H. B. Schlegel and S. Wolfe, unpublished results) should be noted. These authors have calculated fundamental vibrational frequencies of methanol and methylamine in good agreement with experiment by evaluating the energy derivatives at the observed rather than the theoretical equilibrium geometry. We thank Professor Wolfe for communicating these results to us prior to publication.
(13) There is, of course, a long history of correlations between force constants and geometrical parameters. For a discussion, see L. Pauling, "The Nature of the Chemical Bond", 2nd ed, Cornell University Press, Ithaca, N.Y., 1948, p 171.

D. J. DeFrees, D. Z. Hassner, W. J. Hehre*
E. A. Peter, M. Wolfsberg*
Department of Chemistry, University of California
Irvine, California 92717
August 24, 1977

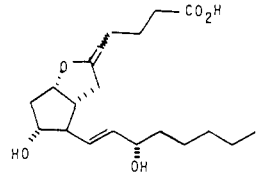
Concerning the Chemical Identity of 6,9α-Oxido-11α,15α-dihydroxyprosta-7(8),(*E*)13-dienoic Acid

Sir:

In 1971, Pace-Asciak and Wolf[1] reported the isolation of two novel prostanoic acid derivatives during the biosynthetic conversion of arachidonic acid into prostaglandins by rat stomach homogenates. The major product was characterized as 6,9α-oxido-11α,15α-dihydroxyprosta-7(8),(*E*)13-dienoic acid (**1**), primarily on the basis of mass spectrometric evidence of several derivatives and products derived from oxidative ozonolysis. A minor product, identified as an isomer of **1**,



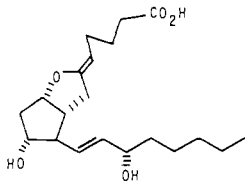
1 $R_1 = R_2 = R_3 = H$
6 $R_1 = R_2 = TMS$; $R_3 = CH_3$



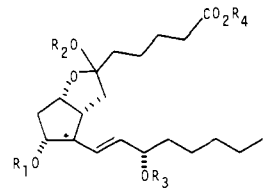
2

6,9α-oxido-11α,15α-dihydroxyprosta-5(6),(*E*)13-dienoic acid (**2**) was postulated as an intermediate in its formation.

Recently, Vane and his co-workers[2,3] reported the conversion of prostaglandin (PG) endoperoxides PGG_2 and PGH_2 by pig and rabbit aortic microsomes to a substance that inhibits platelet aggregation and causes relaxation of blood vessel walls, which they termed PGX. Its chemistry was elucidated by Johnson et al.,[4,5] who assigned to it structure **3**, 6,9α-oxido-11α,15α-dihydroxyprosta-(*Z*)5,(*E*)13-dienoic acid, and renamed it prostacyclin or PGI_2 (**3**). In aqueous and/or acidic media, **3** is readily hydrated to 6-keto-$PGF_{1\alpha}$ (hemiketal form, **4**). While 6-keto-$PGF_{1\alpha}$ (**4**) has been detected in various



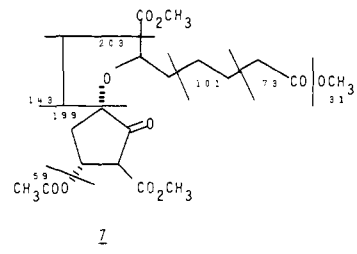
3



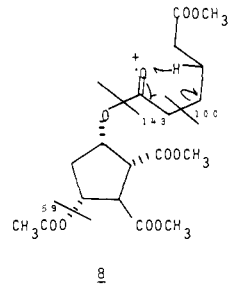
4 $R_1 = R_2 = R_3 = R_4 = H$
5 $R_1 = R_2 = R_3 = TMS$; $R_4 = CH_3$

tissues[6-8] after incubation with arachidonic acid, **1** appears to be confined to the rat stomach[1] and sheep seminal vesicle[9] systems. Incubation of [1-^{14}C]arachidonic acid with rat stomach homogenates in our laboratory[10] afforded [1-^{14}C]-6-keto-$PGF_{1\alpha}$ as the major product, but no **1** was detected. Further, it was reported[4] that the mass spectrum of the trimethylsilyl derivative of the hemiketal form of 6-keto-$PGF_{1\alpha}$ methyl ester (**5**) was found to be identical with that of the trimethylsilyl derivative of 6,9α-oxido-11α,15α-dihydroxyprosta-7(8),(*E*)13-dienoic acid methyl ester (**6**). These results raise considerable uncertainty as to the existence of **1**. In view of the potential physiological importance of natural prostacyclin-type compounds, we decided to reexamine the significant chemical evidences, used in establishing the proposed structure **1**, which is the subject of this communication.

One may suspect that the proposed structure for **1** had been erroneously assigned and that **1** may instead be **4**, since the mass spectra of the two derivatives **5** and presumed **6** were found to be identical. However, it should be emphasized that **1** and **2** had never been isolated in their pure forms; instead, they were always obtained as a mixture termed fraction A.[1] Thus, the value of the mass spectral data of derivatives of fraction A is in considerable doubt. The location of the double bonds in **1** was deduced from the results of the oxidative ozonolysis of the methyl ester and diacetate derivative of fraction A. Gas chromatography of the oxidative products after methylation gave two major fragments. One of these was identified as methyl α-acetoxyheptanoate; the other product showed a molecular ion at *m/e* 402 (M^+) with principal fragments at 371 (M − 31), 329 (M − 73), 311 (M − 60 + 31), 302 (M − (101 − H)), 297 (M − (73 + 32)), 242 (M − (60 + (101 − H))), 210 (242 − 32), 200 (M − (203 − H)), 199 (M − 203), 182 (M − ((2 × 60) + (101 − H))), 143, and 111, and was assigned the structure **7**. These data are clearly not



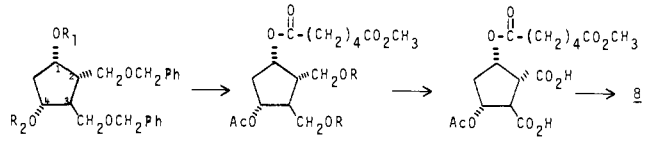
7



8

in accord with the supposition that **1** is simply the hemiketal form of 6-keto-$PFG_{1\alpha}$. However, a careful analysis of these mass spectral data reveals that an alternative structure **8** more suitably fits the fragmentation pattern. In particular, the loss of 100 was not adequately explained by Pace-Asciak and Wolf,[1] but one can readily envisage this fragment to be derived from a McLafferty rearrangement of the ester grouping resulting in β cleavage as shown in **8**. Also, the base peak, 143, can best be rationalized via the common α cleavage of the ester.

To test the validity of this hypothesis, we undertook the synthesis of **8** using the following sequence of reactions:



10 $R_1 = R_2 = Ac$
11 $R_1 = R_2 = H$
12 $R_1 = H$; $R_2 = Ac$
13 $R_1 = Ac$; $R_2 = H$

14 $R = CH_2Ph$
15 $R = H$

16

Deacetylation of **10**[11] using 2 N methanolic NaOH afforded **11** in quantitative yields. Compound **11** (25 mg) was reacted with a mixture of acetic anhydride–pyridine–ether (0.1:0.1:1.0 mL) for 2 days at 25 °C to yield two monoacetates **12** and **13**[12] and **11** in a ratio of 4:1:5. We assumed that the less hindered hydroxyl group at C-4 in **11** was preferentially acetylated. Also, chemical (CH_3OH-Et_3N-H_2O (2:1:1)) and microbial (*Aspergillus repens*) hydrolyses of **10** gave exclusively **13**, con-

0002-7863/78/1500-0643$01.00/0