TABLE I
AMIDE FORMATION FROM CARBOXYLIC ACID AND AMINE WITH SILICON TETRACHLORIDE–PYRIDINE AS COUPLING REAGENT

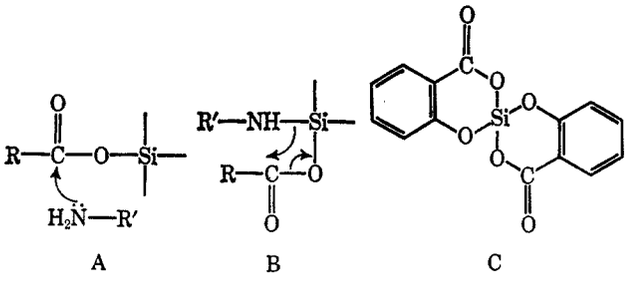
| Acid | Amine | Conditions | Product (yield,[a] %) |
|---|---|---|---|
| Acetic | Aniline | R.t., 10 hr | Acetanilide (60) |
| Stearic | Aniline | R.t., 10 hr | Stearanilide (70) |
| Benzoic | Aniline | Reflux, 1 hr | Benzanilide (70) |
| *p*-Toluic | Aniline | R.t., 10 hr | *p*-Toluanilide (40) |
| *p*-Toluic | Aniline | Reflux, 1 hr | *p*-Toluanilide (70) |
| *p*-Hydroxybenzoic | Aniline | Reflux, 1 hr | *p*-Hydroxybenzanilide (50) |
| Salicylic | Aniline | Reflux, 1 hr | <1%[b] |
| Benzoic | Cyclohexylamine | R.t., 10 hr | N-Cyclohexylbenzamide, (25) |
| Benzoic | Cyclohexylamine | Reflux, 1 hr | N-Cyclohexylbenzamide (90) |
| Benzoic | *t*-Butylamine | Reflux, 1 hr | N-*t*-Butylbenzamide (65) |
| Benzoic | 2,4,6-Mesidine | Reflux, 1 hr | N-2,4,6-Trimethylphenylbenzamide (80) |
| Acetic | N-Methylaniline | Reflux, 1 hr, $N_2$ | N-Methylacetanilide (75) |

[a] Isolated yield. [b] Salicylic acid was recovered quantitatively.

reaction is silica, which is insoluble in all common solvents, and thereby avoids the problem of contamination by side product.[8]

$$2RCO_2H + 2R'NH_2 + SiCl_4 \longrightarrow 2RCONHR' + (SiO_2)_n + HCl$$

Some comments can be made about the mechanism of this reaction. Both carboxylic acids[9] and amines[10] are known to displace chlorine from chlorosilanes to form the acyloxy- or aminosilanes. Two modes of condensation can be postulated to take place. One involves a nucleophilic attack by amine on what may be considered as a mixed anhydride (A). The other involves an intramolecular four-centered reaction (B). At present, we favor the latter mode of reaction. This is based on the observation that *p*-hydroxybenzoic acid reacted with aniline to give the anilide, whereas under identical conditions, salicyclic acid was recovered after hydrolysis.[11] Salicyclic acid forms a stable chelate with silicon (C)[12] and thus prevents the formation of B.



A B C

### Experimental Section

**Example A. Acetanilide.**—To a solution of acetic acid (2.5 g) and aniline (3.8 g) in anhydrous pyridine (50 ml), silicon tetrachloride (4.0 g) was introduced. The mixture was stirred at room temperature for ten hours and was poured onto crushed ice. The precipitate was filtered and the filtrate was concentrated to yield 3.3 g of crystalline acetanilide, mp 113°.

**Example B. N-*t*-Butylbenzamide.**—To a solution of benzoic acid (1.0 g) and *t*-butylamine (0.60 g) in anhydrous pyridine (30 ml), silicon tetrachloride (1.0 g) was introduced. The mixture was refluxed for one hour, and was poured onto crushed ice. The precipitate was filtered and triturated with hot ethanol. The ethanol solution was concentrated to yield 0.90 g of N-*t*-butylbenzamide, mp 134–136°.

**Registry No.**—Silicon tetrachloride, 10026-04-7.

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(8) For example, the well-known coupling reagent dicyclochexylcarbodiimide sometimes gives acylurea as a side product which is difficult to separate.

(9) R. C. Mehrotra, *Pure Appl. Chem.*, **13**, 111 (1966).

(10) R. O. Sauer and R. H. Hasek, *J. Amer. Chem. Soc.*, **68**, 241 (1946).

(11) This differs from phosphonitrilic chloride, which activated salicyclic acid to form amide: L. Caglioti, M. Poloni and G. Rosini, *J. Org. Chem.*, **33**, 2979 (1968).

(12) R. C. Mehrotra and B. C. Pant, *J. Indian Chem. Soc.*, **40**, 623 (1963).

## Perchloric Acid Catalyzed Acylations. Occurrence of Carbon Acylation in Enol Lactones[1]

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We have published earlier a versatile procedure for preparing the enol lactones and enol acetates using a reagent composed of acetic anhydride and perchloric acid in ethyl acetate.[3,4] After detailed experimentation with reaction times and reagent composition, we have established that a 5-min reaction at room temperature with a reagent composed of 1 *M* acetic anhydride and $10^{-3}$ *M* perchloric acid in ethyl acetate converts a δ-keto acid such as 17β-hydroxy-4-nor-5-oxo-3,5-seco-3-andro-

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(2) (a) To whom all correspondence should be addressed. (b) Taken from the M.S. Thesis submitted by J. E. B. to St. Mary's University, San Antonio, Tex., May 1968.

(3) (a) P. Narasimha Rao and L. R. Axelrod, *Chem. Ind.* (London), 1838, (1963); (b) P. Narasimha Rao and L. R. Axelrod, *J. Chem. Soc.*, 1356 (1965).

(4) B. E. Edwards and P. Narasimha Rao, *J. Org. Chem.*, **31**, 324 (1966).

stanoic acid (I) to the corresponding 17β-acetoxy-3,5-enol lactone (II) in essentially quantitative yield without formation of other side products.[4] However, with increase in reaction time or concentration of perchloric acid, or both, a second reaction product was obtained as the major product in addition to the enol lactone II. Accordingly, when the keto acid (I) was treated with a reagent consisting of 2 *M* acetic anhydride and 0.15 *M* perchloric acid in ethyl acetate for one hour at room temperature, a second product of mp 190.5–191.5° was obtained. This reaction product was identified as 17β-acetoxy-6-acetyl-5-hydroxy-3,5-seco-4-norandrost-5-en-3-oic acid 3,5-lactone (III) on the basis of analytical and other spectral data. Compound III analyzed for $C_{22}H_{30}O_5$ and had a molecular weight of 374 as determined by mass spectrum[5] (molecular ion peak at *m/e* 374). The infrared spectrum demonstrated enol lactone (1755 $cm^{-1}$), 17β-acetate (1725 and 1265 $cm^{-1}$) and conjugated carbonyl (1677 $cm^{-1}$) bands. The ultraviolet absorption spectrum showed an absorption maximum at 252 mμ (ε 9874) and is in good agreement with the calculated value[6] of 254 mμ. The nmr spectrum of compound III ($CDCl_3$, TMS) showed peaks at δ 0.85 (C-18 methyl), 1.22 (C-19 methyl), 2.06 (17β-acetate), and 2.51 (conjugated C-6 acetyl) ppm.

The possibility of the acetyl group being in the A ring was ruled out by mass spectral data. The major fragmentation pattern of both III and the enol lactone II showed the loss of $C_3H_4O$ (56 mass units) as the first fragmentation product. If the acetyl group had been located in ring A, the fragmentation pattern would have been different since the $C_3H_4O$ fragment was due to the loss of carbons 1, 2, and 3 of the lactone.

That the lactone II was the intermediate in the formation of III was shown by treatment of the lactone II with the perchloric acid reagent and isolation of the 6-acetyl product III in excellent yield.

Recently, Liston and Toft[7] have also observed a similar carbon acylation of enol acetates with perchloric acid and acetic anhydride.

(5) The mass spectrum was recorded on Model MS9 instrument of Associated Electrical Industries, Manchester, England.

(6) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 19.

(7) A. J. Liston and P. Toft, *J. Org. Chem.*, **33**, 3109 (1968).

### Experimental Section[8]

**Perchloric Acid Reagent.**—To absolute ethyl acetate (30 ml) was added 72% perchloric acid (0.75 ml) and acetic anhydride (9.6 ml), and the solution was made up to 50 ml with ethyl acetate.

**17β-Acetoxy-6-acetyl-5-hydroxy-3,5-seco-4-norandrost-5-en-3-oic acid 3,5-Lactone (III).**—A sample of the keto acid (I, 200 mg) was treated with perchloric acid reagent (20 ml) for 1 hr at room temperature. The reaction mixture was then washed with saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate, and evaporated to dryness. The total crude material was then chromatographed on silica gel to give compound III (114 mg). The analytical sample was crystallized from acetone–hexane: mp 190.5–191.5°, $\nu_{max}^{KBr}$ 1755, 1725, 1677 and 1265 $cm^{-1}$, $\delta_{TMS}^{CDCl_3}$ 0.85, 1.22, 2.06 and 2.51 ppm, $\lambda_{max}^{MeOH}$ 252 mμ (ε 9,874).

*Anal.* Calcd for $C_{22}H_{30}O_5$: C, 70.56; H, 8.08. Found: C, 70.47; H, 8.08.

**17β-Acetoxy-6-acetyl-5-hydroxy-3,5-seco-4-norandrost-5-en-3-oic acid 3,5-Lactone (III) from II.**—A sample of the lactone II (31 mg) was treated with perchloric acid reagent (3 ml) for 40 min at room temperature. The crude product obtained after the usual work-up was chromatographed on silica gel to give compound III (27 mg), mp 190.5–191.5°, which was found to be identical in all respects with the authentic sample obtained earlier.

**Registry No.**—Perchloric acid, 7601-90-3; III, 20104-38-5.

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(8) Melting points were determined on a Thomas–Hoover capillary melting point apparatus and are uncorrected. Nmr spectra were recorded on a Varian A-60A spectrometer using TMS as internal standard. Infrared spectra were determined on a Perkin-Elmer Model 21 spectrometer. Ultraviolet absorption spectra were determined with a Cary recording spectrophotometer (Model 11 MS). Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

## The Acetolyses of Certain 3,5-Disubstituted 6-Oxo-5β-cholestanes[1a]

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When 3β-tosyloxy-5-hydroxy-5β-cholestan-6-one (**1d**) was solvolyzed in anhydrous ethanol, methanol, or dimethyl sulfoxide, the major product was 3β,5-epoxy-5β-cholestan-6-one (**3**).[2] The formation of the oxetane ring from *cis* functional groups is unusual. Furthermore, we have found that the C-3 epimer (**2d**) of **1d** is recovered unchanged when heated under reflux for 19.5 hr in ethanol.[3] The usual stereochemical considerations lead to the conclusion that **2d** and *not* **1d** would be more likely to undergo oxetane ring formation. We have attempted to determine if some type of participation by hydroxyl occurs in the conversion **1d** → **3** by

(1) (a) This work was supported by National Science Foundation Undergraduate Research Participation Grants GE-2760 and GE-9534; (b) NSF-URP, 1964-1965; (c) NSF-URP, Summer, 1965.

(2) A. T. Rowland, *Steroids*, **7**, 527 (1966).

(3) Unpublished observation in this laboratory.