Dr. W. L. Wilson for helpful discussions. We are indebted also to Mr. H. Séguin of the National Research Council of Canada for performing the elemental microanalyses.

Friedel–Crafts Isomerization of Tetramethylacetophenones

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In 1952 Baddeley and Pendleton[1] reported that, in the presence of excess aluminum chloride at 100°, acetyldurene (2,3,5,6-tetramethylacetophenone) (**1**) was converted to acetylprehnitine (2,3,4,5-tetramethylacetophenone) (**7**, 80%), aromatic hydrocarbon (10%), and diacetyldurene (**6**, 10%). The formation of the latter two products was ascribed to fission of the acetyldurene into durene and acetyl cation, followed by electrophilic attack on a second molecule of acetyldurene to produce diacetyldurene. Transfer of the acyl group from one aromatic nucleus to another would be analogous to the well-known Friedel–Crafts transalkylation reaction.[2] More recently nmr studies have been conducted on ketones in the presence of Friedel–Crafts catalysts. Treatment of aliphatic,[3] alicyclic,[4] and aromatic ketones[5] with such strong acids as fluorosulfuric acid, fluorosulfuric acid–antimony pentafluoride, and related systems led in all instances to the observation of O-protonation producing stable cation systems.

We felt that these data were inconsistent and set about trying to resolve the question. The inconsistency is centered about the facts that the nmr data[3-5] require that, in the presence of acid, acetyldurene and related systems are O-protonated, whereas the transacylation data require a second protonation (Scheme I).

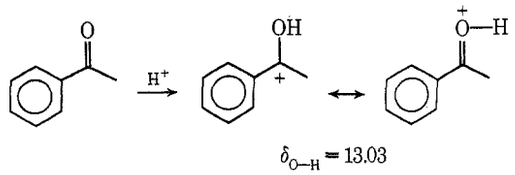
Although no benzenium ions such as **3** were observed by low-temperature nmr (protons in species such as **3** or **5** are observed at δ 4.5–5.5),[6] a small steady-state concentration would be stable under the reaction conditions. To effect transacylation **3a**, if present at all, must undergo the unlikely sequence outlined above: loss of $(CH_3CO)^+$ and H^+ followed by attack by the weak electrophile $(CH_3CO)^+$ on the *protonated* 2,3,5,6-tetramethylacetophenone to give **5** and finally **6**. On the other hand ions **3b–3d**, if present, are able to undergo intra- and intermolecular methyl shifts.

We have repeated the isomerization of acetyldurene with aluminum chloride with the results shown below.

We observed no hydrocarbon or diacetyltetramethylbenzene product as was reported in the earlier study,

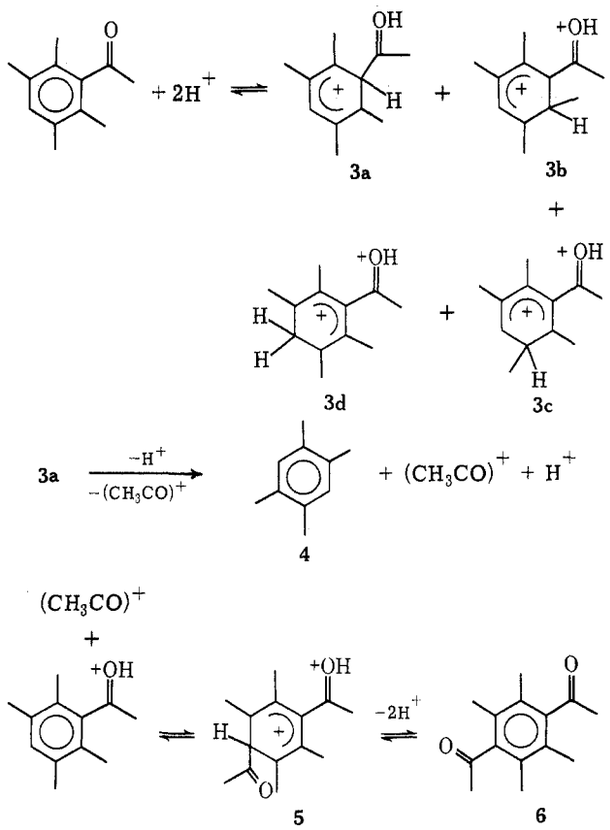
SCHEME I

A. Nmr[5]

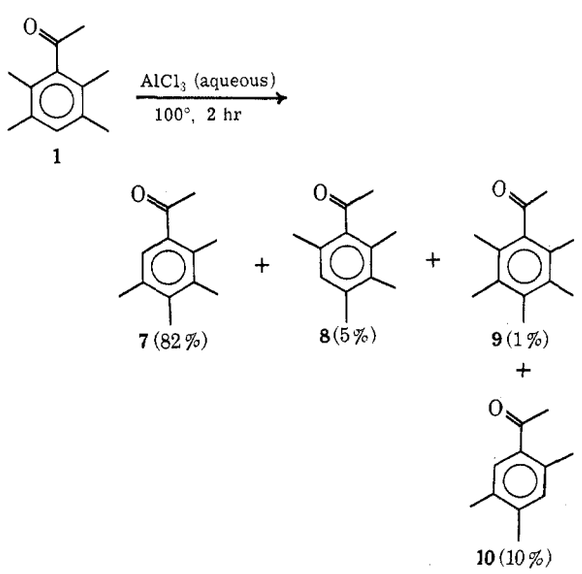


$\delta_{O-H} = 13.03$

B. Transacylation[1]



and believe our results are consistent with the nmr data presented above. A combination of Friedel–Crafts transalkylation and isomerization reactions can account for all products formed. Scheme II, which presents one possible pathway, indicates that indeed when enough



(1) G. Baddeley and A. G. Pendleton, *J. Chem. Soc.*, 807 (1952).
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(3) G. A. Olah, M. Calin, and D. H. O'Brien, *J. Amer. Chem. Soc.*, **89**, 3586 (1967).
(4) G. A. Olah and M. Calin, *ibid.*, **90**, 938 (1968).
(5) G. C. Levy and S. Winstein, *ibid.*, **90**, 3574 (1968); M. Brookhart, G. C. Levy, and S. Winstein, *ibid.*, **89**, 1735 (1967); T. Birchall and R. J. Gillespie, *Can. J. Chem.*, **43**, 1045 (1965).
(6) G. A. Olah, *J. Amer. Chem. Soc.*, **87**, 1103 (1965).

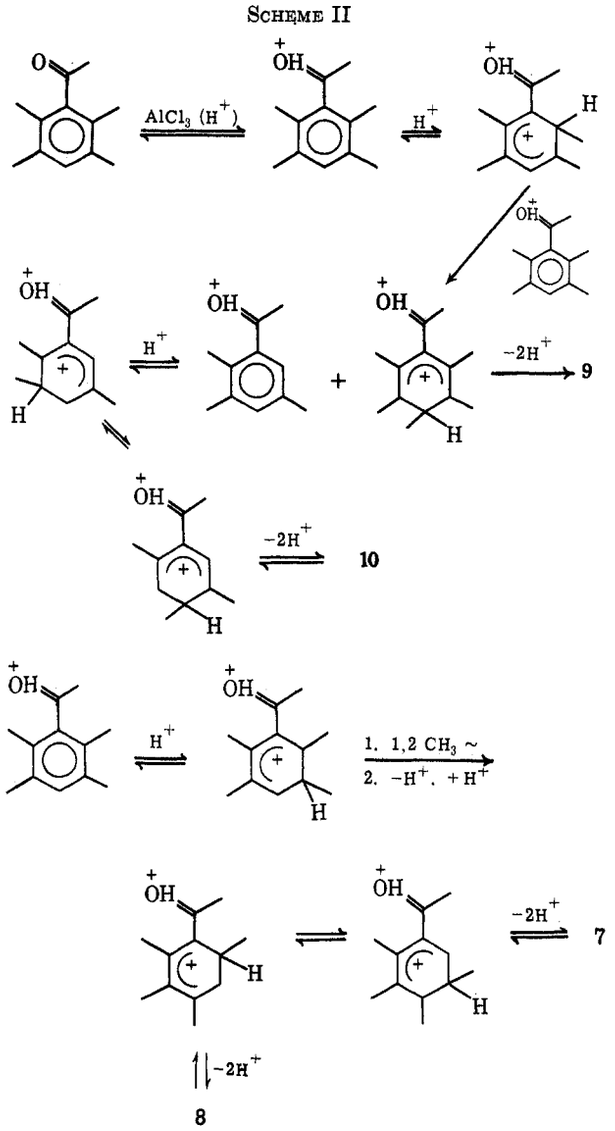
TABLE I

ACETYLATIONS OF POLYMETHYLBENZENES[a]

Substrate	Compd	$\nu_{C=O}$, cm^{-1}	Nmr: ArH, δ	Nmr: CH_3CO, δ	Nmr: CH_3, δ	Retention time, min[b]
1,2,3,4-Tetramethylbenzene	7	1694	7.23	2.45	2.09 (C_2, C_3, or C_4) 2.23 (C_3 or C_4) 2.35 (C_5)	5.9
1,2,3,5-Tetramethylbenzene	8	1695	6.78	2.30	2.08 (C_2) 2.13 (C_3) 2.20 (C_4, C_6)	4.2
1,2,4-Trimethylbenzene	10	1695	6.97 (H_3) 7.53 (H_6)	2.50	2.23 (C_2, C_4, or C_5) 2.55 (C_4 or C_5)	2.4
Pentamethylbenzene	9	1694 (CCl_4)		2.66	2.41 (C_2, C_6) 2.48 (C_3, C_5) 2.52 (C_4)	7.0

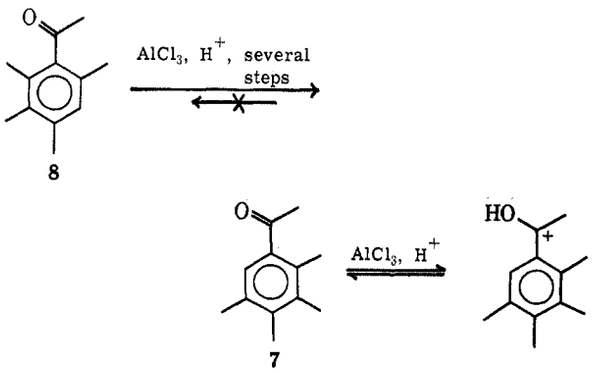
[a] All acetylations carried out as described for the acetylation of 1,2,4,5-tetramethylbenzene. [b] Retention times measured on a 150 ft MBMS capillary column at 160° and 30 psig He.

SCHEME II



methyl groups are present the ring is basic enough to be protonated despite the fact that the carbonyl is already protonated.

Two additional transacylations were attempted. Acetylprehnitine (**7**) was stable to the rection conditions, while 2,3,4,6-tetramethylacetophenone (**8**) was converted to **7** under the reaction conditions.



These results reflect the fact that under equilibrium conditions 2,3,4,5-tetramethylacetophenone is the most stable of the three tetramethylacetophenones.

With the above evidence in hand, we decided to further investigate the possibilites of Friedel–Crafts transacylations. The following ketone–aromatic hydrocarbon trapping agent mixtures were studied: acetophenone–anisole, acetophenone–naphthalene, acetyldurene–benzene, acetyldurene–anisole, 2-acetylthiophene–benzene, and 2-acetylfuran–benzene. A number of very strong acid catalysts were employed in these reactions, including aluminum chloride, aluminum chloride–water,[7] and 5:1 (mol/mol) hydrogen fluoride–antimony pentafluoride. Reaction temperatures were varied from 25 to 100° and ketone/aromatic hydrocarbon/catalyst ratios ranged from 1:1:0.1 to 1:1:1.5.

In no case were we able to detect any transacylation product under these conditions.

Experimental Section

All nmr spectra were obtained on a Varian Associates Model A-60 nmr spectrometer. All ir spectra were obtained on a Perkin-Elmer Model 700 spectrophotometer. All aromatic hydrocarbons were obtained from Aldrich Chemical Co., Milwaukee, Wis., and were used without further purification.

Acetylation of 1,2,4,5-Tetramethylbenzene.—A solution of 15.8 g (0.20 mol) of CH_3COCl in 15 ml of CH_2Cl_2 was added dropwise at 5° to a suspension of 26.6 g (0.20 mol) of anhydrous $AlCl_3$ in 15 ml of CH_2Cl_2 and the mixture was stirred for 10 min. At the same temperature, a solution of 26.8 g (0.20 mol) of 1,2,4,5-tetramethylbenzene in 50 ml of CH_2Cl_2 was added dropwise over 45 min. The mixture was stirred for 1 hr, poured onto ice, washed (H_2O, saturated $NaHCO_3$ and H_2O), and dried

(7) Water (0.005 mol) added as a promoter and to keep [H_2O] constant. See, *e.g.*, G. A. Olah and J. A. Olah, *J. Org. Chem.*, **32**, 1612 (1967).

(Na_2SO_4). After removal of the solvent *in vacuo* the yield of solid product was 20.4 g (0.114 mol, 58%) of a white substance, 2,3,5,6-tetramethylacetophenone (1), mp 72–73° (lit.[8] mp 73°), whose gc (150 ft MBMS capillary column at 160°, He pressure 30 psig) showed only a single peak (retention time 3.5 min). The compound gave an nmr spectrum (CCl_4) which consisted of singlets[9] at δ 2.05 (6 H, C_2 and C_6 methyls), 2.18 (6 H, C_3 and C_5 methyls), 2.32 (3 H, acetyl), and 6.85 (1 H, aromatic). The infrared spectrum (CCl_4) showed $\nu_{C=O}$ at 1698 cm^{-1}. Other acetylation data are summarized in Table I.

Isomerization of 2,3,5,6-Tetramethylacetophenone (1).—The procedure follows that of Baddeley and Pendleton.[1] 2,3,5,6-tetramethylacetophenone (1) (7.5 g, 0.043 mol), anhydrous $AlCl_3$ (15 g, 0.11 mol), H_2O (0.005 mol), and NaCl (1 g, 0.02 mol) were stirred together at 100° for 2 hr. The reaction mixture was cooled, poured onto ice, and neutralized with saturated $NaHCO_3$ solution. The organic material was extracted with a total of 30 ml of C_6H_6, washed (H_2O, saturated $NaHCO_3$ solution, and H_2O) and dried (Na_2SO_4). Analysis of the mixture by gc (150 ft MBMS column at 160°, He pressure 30 psig) showed five peaks: retention time 2.4 min (10%), 3.5 min (trace) 4.2 min (5%), 5.9 min (82%), and 7.0 min (1%). Comparison of retention time with that of authentic samples showed that these components were 2,4,5-trimethylacetophenone (10), starting material (1), 2,3,4,6-tetramethylacetophenone (8), 2,3,4,5-tetramethylacetophenone (7), and pentamethylacetophenone (9), respectively. Addition to this reaction mixture of pure samples of each of the components mentioned led to enhanced peak heights on the gas chromatogram.

Attempted Isomerization of 2,3,4,5-Tetramethylacetophenone (7).—Pure 7 was treated under the reaction conditions and was recovered intact as demonstrated by gc analysis.

Attempted Isomerization of 2,3,4,6-Tetramethylacetophenone (8)—Pure 8 was treated under the reaction conditions and gc analysis showed the conversion of 8 to 7.

Attempted Transacylation Reactions.—Typically, the attempted transacylations were run in the following manner illustrated for acetophenone–naphthalene. Acetophenone (1.20 g, 0.010 mol) and naphthalene (12.8 g, 0.10 mol) were mixed together in 20 ml of CCl_4. $AlCl_3$ (2.00 g, 0.015 mol) and water (0.005 mol)[7] were added and the reaction mixture was stirred at reflux overnight. The mixture was poured onto ice, washed (H_2O, saturated $NaHCO_3$ solution until basic, H_2O), dried (Na_2SO_4), and analyzed by gc (150 ft MBMS column at 100°, 20 psig He pressure). *In no case were any peaks observed except those for the starting materials.*

Registry No.—**1**, 2142-79-2; **7**, 34764-71-1; **8**, 2142-78-1; **9**, 2040-01-9; **10**, 2040-07-5.

Acknowledgments.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the State Universities of Wisconsin Research Fund, and to a National Science Foundation Institutional Grant for support of this research.

(8) L. I. Smith and G. Guss, *J. Amer. Chem. Soc.*, **59**, 804 (1937).

(9) All nmr spectra show slight broadening of ring methyls and ring hydrogens due to small long-range coupling.

Degradation of Solasodine

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A simple, high-yielding procedure for degrading solasodine (I) to 3β-acetoxy-5,16-pregnadien-20-one (VII) in steroid hormone production is desirable. It has previously been demonstrated[2] that I can be degraded in excellent overall yields (*ca.* 60%) to VII by conversion of the *O,N*-diacetate of the alkaloid with acid into the pseudoacetylamino derivative followed by oxidation and hydrolysis.

We have now found that the treatment of solasodine acetate (Ia) with phosgene in a basic milieu affords a number of intermediates which can be readily converted into a pseudoformamido derivative (VI) that can be transformed into VII.

Thus, when acetylsolasodine[3] (Ia) was treated with a cold benzene solution of phosgene and then refluxed with pyridine followed by a treatment with dimethylamine, two products were obtained. The analytical as well as spectroscopic data suggested the structure of the major product to be the epimino-*N*-carboxy compound V. This was confirmed by reduction of Va to the isomeric 5,6,22,23-tetrahydro derivatives, IX and IXa, the former of which agreed in properties with a synthetic specimen[3] prepared from phosgene and tetrahydrosolasodine acetate (VIII). The site of unsaturation in V, aside from the C-5 double bond, was placed at C-22 from nmr data. The spectra of both compound V and the product Va derived from the interaction of 5,6-dihydro-3β-acetylsolasodine (3β-acetylsoladulcidine) with phosgene–pyridine possessed a vinyl proton at 4.83 ppm[4] which was not present in the tetrahydro product IX. It is of some interest to note that the 16β,26-*N*-carboxy system in V proved refractory toward alkali or sodium borohydride reduction and only the C-3 free alcohol was obtained. The major product V (*ca.* 50%) was followed by about 15% of 26-*N'*,*N'*-dimethylcarbamido-5,20(22)-furostadien-3β-ol acetate (VI). The compound possessed a vinyl ether absorption[5] (1694 cm^{-1}) characteristic of a $\Delta^{20(22)}$-furostene structure and an amide-II band [3488 (NH), 1518, 1669 cm^{-1} (NNHCO)] in the infrared region. Chromic acid oxidation of the furostene derivative VI in aqueous acetic acid (80%) followed by hydrolysis of the acyloxy side chain with acetic acid[6] produced VII in good yield.

The reaction of solasodine acetate (Ia), on the other hand, with phosgene in triethylamine in lieu of pyridine proceeds to yield the very unstable *N'*,*N'*-dimethylaminoformylsolasodine acetate (II). The lability of the compound interfered in our attempts at purification and the structure was derived mainly from the infrared spectrum: 1735, 1245 (OAc), 1667 (-CON), 979, 911 cm^{-1} (spiro amino ketal linkage. A notable feature of compound II was its ease of isomerization to the pseudoformamido (furostadiene) derivative, VI, with glacial acetic acid. The second component, III, from the reaction mixture possessed an infrared spectrum quite similar to that of compound VI but exhibited a slightly less polar chromatographic behavior (tlc). It was assigned the isomeric $\Delta^{22(23)}$ structure III, since brief treatment with acetic acid or even hot methanol isomerized it readily to the pseudoformamido compound VI. In addition to II and III, a

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(4) We are indebted to Dr. H. J. C. Yeh of the Microanalytical Services and Instrumentation Section of the Laboratory for taking the nmr spectra of compounds V, Va, and IX on the Varian HR-220 spectrometer.

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