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OXONIUM ION FORMATION IN FRIEDEL-CRAFTS CYCLIALKYLATION OF ω-HALOPHENONES

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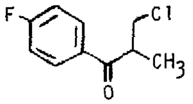
While studying the reaction of 3-chloro-4'-fluoro-2-methylpropiophenone (1) in the presence of $AlCl_3$ at 100° in situ in a ^{13}C NMR spectrometer, we observed signals which were attributed to oxonium ion 2[1]. We also found that 2 could be formed more readily from 4-chloro-4'-fluorobutyrophenone (3) in similar environment.



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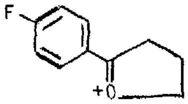

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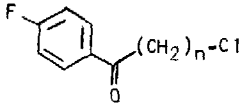
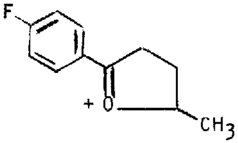


3(n=3); 4(n=4)
5(n=5)

Oxonium ions like 2 were not heretofore known in Friedel-Crafts cyclialkylations. They previously have been generated solvolytically[2], by cyclization of unsaturated[3,4] and cyclopropyl[5] ketones in proton acid-containing media, and by protonation of 4,5-dihydro-2-phenylfuran[2a]. Rearrangement of certain α-keto carbenium ions has served to generate some bicyclic examples[6]. Ward and Sherman[2a] also noted six-membered ring formation from a valerophenone; Olah's group[4] found only the five- even where six-membered oxonium ions might have been expected.

We became interested to see if six-membered homologs might also form in the Lewis acid media, and, if so, whether we could adduce evidence for ring size preference in formation (kinetic), and thermodynamic stability of the six- vs. five-membered rings.

When 4 was added to a cool slurry of 2 equiv. of $AlCl_3$ in CS_2 and the reactive layer transferred to the ^{13}C NMR spectrometer for observation at ambient temperature, the initial product was 6, which arose almost immediately. It remained unchanged even after several days, and only upon heating at 100° did rearrangement to tetralone 7 commence. The transformation to 7 was indeed slow; only ca. 20% conversion occurred after 20 hours at 100°. No evidence for isomeric indanones could be found even when quenched samples were scrutinized by chromatographic methods. The unreacted 6 was converted mainly to the carbinol 8 upon work-up.



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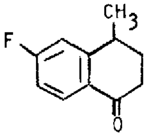

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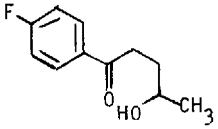

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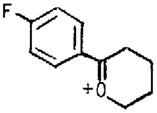
A similar reaction with the moderated catalyst $AlCl_3 \cdot CH_3NO_2$ proceeded not only more slowly, but it gave visible evidence for six-membered ring formation. At ~50°, both 6 and 9 accumulated slowly with the former in slight excess. Continued heating converted 9 to 6 which was stable at ~50° for several days.



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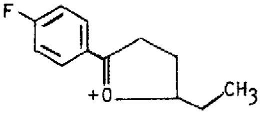
Homolog 5 was studied similarly. With $AlCl_3$, it showed rapid formation of both 10 and 11 in an initial ratio of 5-6:1 with the former predominating. After 16 hours, the six-membered ring 11 was converted to 10; higher temperatures converted both to the tertiary isomer, 12, which was apparently the thermodynamic sink. Intramolecular C-alkylation of 12 produced 4,4-dimethyl-6-fluoro-1-tetralone very sluggishly.



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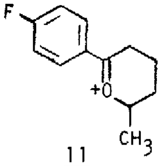

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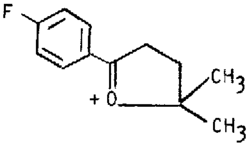

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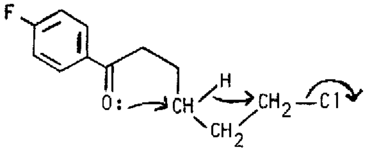
Most likely, the formation of these ions proceeds in a concerted manner concomitant with C-Cl bond cleavage. The most plausible alternatives would require either (a) initial generation of a primary carbenium ion, or (b) prior dehydrochlorination. The former fails to explain the considerable differences in reactivity of 4 and 5 vs. 3. Dehydrochlorination would not, in the case of 4, be expected to give the "primary" ion 9, nor the ethyl-substituted ion, 10, in the case of 5.

Comparisons from experiments with the moderated catalyst showed that the kinetic preference for the five membered ring system is not overwhelming. With 4, the ratio of 6 to 9 is less than two. In the case of 5, the initial ratio is ~3:1 favoring 10 vs. 11. 10 may form via a 1,3 hydride shift as depicted, and some rate enhancement may prevail. Few documented examples of 1,3 shifts in acyclic systems are known[8]. Labeling experiments could be definitive in this case.



Neighboring group effects alter the course of many reactions, sometimes with tremendous rate enhancement. No ^{13}C NMR evidence of any oxonium or other ionic species was found on treating a mixture of 4'-fluoroacetophenone and n-chloropentane with $AlCl_3$; only dehydrochlorination and polymerization of the alkyl compound was evident. Thus, the substitution of ion-forming cyclizations for rapid HCl elimination from the ω-chlorophenones clearly points to a unique set of mechanistic steps which we shall continue to study.

^{13}C chemical shifts of non-aromatic carbons are tabulated for the oxonium ions observed; other characterization of the products will be reserved for a full paper.

^{13}C Chemical Shifts; ppm from external TMS reference

Compound	$\overset{+}{C=O}$	α	β	γ	δ	ε
2	218.8	41.2	23.0	91.5	-	-
6	217.3	41.6	30.0	105.1	21.9	-
9	217.9	33.2	16.8	22.4	83.6	-
10	217.3	41.5	28.1	109.5	29.6	11.3
11	218.1	33.0	17.2	29.6	95.2	22.3
12	215.2	41.8	35.0	118.4	29.0	-

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