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IMPROVEMENT OF A β-TETRALONE SYNTHESIS: 5-, 6-, 7- AND 8-METHYL-β-TETRALONES

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One of the best methods for synthesizing β-tetralones is that reported by Burkhalter.[1] The reaction consists of mixing a phenylacetyl chloride and $AlCl_3$ in carbon disulfide, then bubbling in ethylene for several hours at 0°. However, in our hands, the product obtained in this manner is dark and contains odorous sulfur compounds; in addition the yield of tetralone is less than satisfactory.

When the reaction is carried out in methylene chloride a dramatic improvement takes place. β-tetralone can be isolated in 84% yield with a reaction time of minutes rather than hours. We feel that two things, the relative inertness of methylene chloride and its ability to dissolve the acid chloride-aluminum chloride complex[2] thus giving a homogeneous reaction mixture, are responsible for the improvement.

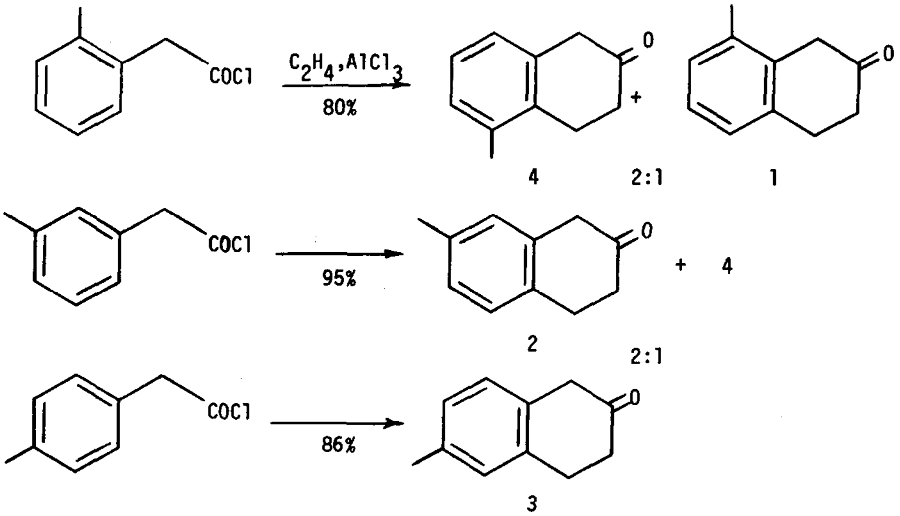
Treatment of o-methylphenylacetyl chloride as above led to a mixture of two methyl-β-tetralones, one crystalline (MP 72-3°) and one a liquid (BP 81-83°, 0.2 mm). A search of the literature revealed that 5-methyl-β-tetralone[3], a liquid, was the only known ar-methyl-β-tetralone. To prove the structures of our compounds we carried out the same reaction with m- and p-methylphenylacetyl chlorides.

The reaction of p-methylphenylacetyl chloride as above led to a single crystalline isomer (MP 25-6°). This compound was not identical with either of the isomers formed from o-methylphenylacetyl chloride. The new β-tetralone was assigned structure 3.

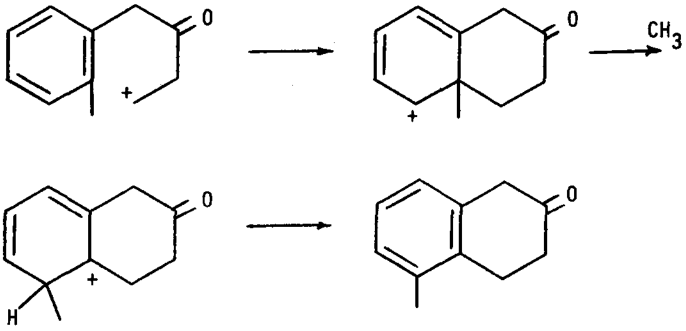
As expected, m-methylphenylacetyl chloride gave two isomeric β-tetralones, a liquid and a solid. The solid (MP 57-59°) was a new compound; the liquid was identical to the liquid formed from o-methylphenylacetyl chloride.

We now had in hand the four possible isomeric ar- methyl-β-tetralones. The compounds fell into two different classes of aromatic substitution, 1,2,3- and 1,2,4-trisubstituted benzene

Scheme I



Scheme II



derivatives. As such their infrared spectra showed predictable bands between 5.0 and 6.0μ[4] which established to which class each compound belonged. The single isomer 3 formed from *p*-methylphenylacetyl chloride showed bands characteristic of 1,2,4-substitution making its structure sure. The liquid isomer formed from both *o*- and *m*-methylphenylacetyl chlorides gave a 1,2,3-substituted type of spectrum and was thus assigned structure 4. The crystalline β-tetralone formed from *m*-methylphenylacetyl chloride was thus 2 and the remaining tetralone formed from *o*-methylphenylacetyl chloride was 1; each of these compounds gave consistent infrared spectra. In addition, the four tetralones gave ultraviolet spectra which were suggestive of two types of structure, the 1,2,4-substituted compounds 2 and 3 (Table 1) gave maxima at longer wave length with larger ε values than the 1,2,3 substituted compounds, 1 and 4. A perhaps fortuitous similarity has been observed with 1,2,3- and 1,2,4-trimethylbenzene[5]. The nmr spectra of the isomers were very similar (Table 1). The one anomaly being a 12 cps upfield shift of the methyl resonance of compound 1 relative to the others. This effect is presumably due to shielding by the carbonyl group[6].

A check on our structure assignment of the β-tetralones was carried out as follows. Catalytic hydrogenation of 7-methyl-2-naphthol[7], using the T-1 raney nickel catalyst[8,9] gave as expected 7-methyl-1,2,3,4-tetrahydro-2-naphthol. Oxidation of the naphthol with Jones reagent[10] yielded 7-methyl-β-tetralone identical with 2 in mp and spectral comparisons.

The unexpected rearrangement leading to 4 may be rationalized as outlined in Scheme 2. The electrophilic attack of the aromatic ring at a carbon substituted by a methyl group is unusual. It appears to be the first observation of such an attack in an alkylation type of reaction, although such attack at a ring carbon bearing an alkyl group is not uncommon for other electrophilic reagents. An example is the Jacobson rearrangement of polyalkylated aromatics in strong acid. The methyl migration is very similar to that observed in the well known dienone-phenol rearrangement.

TABLE 1

NMR[a] and UV SPECTRA OF AR-METHYL-β-TETRALONES

Compd.	CH_3	C_1	C_3	C_4	Arom	λ_{MAX}^{MEOH}	(ε)		
1	122 s	200 s	144 t	180 t	416 m	261	(294)	267	(252)
2	134 s	200 s	140 t	174 t	416 m	268	(897)	275	(705)
3	134 s	198 s	137 t	172 t	412 m	267	(652)	274	(614)
4	136 s	204 s	142 t	178 t	416 m	262	(313)	268	(271)

[a] chemical shifts, expressed as cps downfield from tetramethylsilane as an internal standard, were measured in $CDCl_3$: s, singlet; t, triplet; m, multiplet. $J_{3,4}$ - 7.0 cps in all compounds.

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