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The Synthesis of Several Dipivaloylpolymethylbenzenes[1)]

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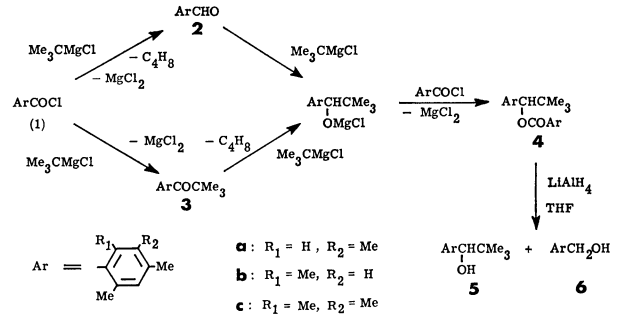
Synopsis. 2,4-Dipivaloyl-1,3,5-trimethylbenzene, 4,6-dipivaloyl-1,2,3,5-tetramethylbenzene, and 3,6-dipivaloyl-1,2,4,5-tetramethylbenzene were prepared by the Friedel-Crafts dipropionylation of the corresponding polymethylbenzenes, followed by the exhaustive methylation of the resulting diketones with potassium *t*-butoxide and methyl iodide in boiling benzene–*t*-butyl alcohol. The PMR and IR spectra are reported for these new compounds.

In connection with our work on the non-conventional reactions of polysubstituted aromatics, we needed hindered ketones of the (**8**) type, bearing a methyl group at the position flanked both sides by the bulky electron-withdrawing groups. To our knowledge, there is no published preparation of ketones with this particular structure. The traditional method for the direct synthesis of pivalophenones (2,2-dimethyl-1-phenyl-1-propanones) involves the reaction of pivaloyl chloride with arylmagnesium halides[2)] or with arenes in the presence of the Friedel-Crafts catalyst,[3)] and the reaction of pivalonitrile] with the appropriate Grignard reagent.[4)] Our attempts to convert hindered polymethylpivalophenones to the title diketones by the Friedel-Crafts method led to extensive deacylation as well as the formation of a complicated mixture of hydrocarbons and polymeric substances. The reactions of pivaloyl chloride with the Grignard reagent[5)] derived from bromopolymethylpivalophenones resulted only in the recovery of the parent polymethylpivalophenones. Likewise, attempts to prepare the diketones by the reaction of polymethylbenzenedicarbonitriles with *t*-butylmagnesium chloride failed, since no reaction took place.

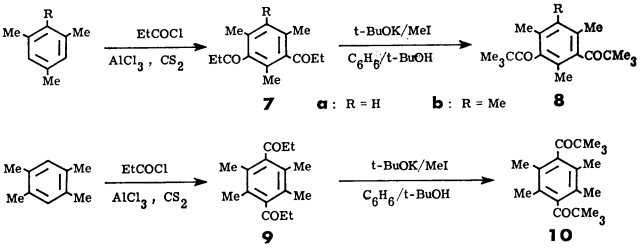
Next we planned to prepare the diketones starting from polymethylbenzene-1,3-dicarboxylic acids and following the reaction sequence: diacids — diacid dichlorides — dipivaloylbenzenes. In a search for a simple procedure for converting the hindered acid chloride groups into pivaloyl groups, we examined the reaction of several polymethylbenzoyl chlorides with *t*-butylmagnesium chloride with or without the use of transition metal catalysts.[6)] The results were unpromising, however. When polymethylbenzoyl chloride (**1b—c**) was treated with an excess of the Grignard reagent, the reductive 1,2-addition occurred sluggishly, giving an ester as the sole product.[7)] The analytical and spectral data of this compound were consistent with the highly crowded structure (**4b—c**) (Table 1). As expected, neither attempts to saponify this ester by heating it with ethanolic potassium hydroxide or concentrated hydrochloric acid, nor attempts to obtain an authentic specimen from the reaction of alcohol (**5**) and acid chloride (**1**), were successful. However, this ester underwent reductive cleavage with lithium aluminum hydride in boiling tetrahydrofuran, giving two benzylic alcohols (**5** and **6**) in accord with the assigned structure **4**. Two possible mechanisms for the formation of the ester are given in Scheme 1. In order to differentiate between these two pathways, the aldehyde (**2b**) and ketone (**3b**) were each treated with *t*-butylmagnesium chloride under the same conditions. The latter compound was recovered unchanged, while the former gave the expected alcohol **5b**, supporting the first mechanism, in which the reaction proceeds *via* the aldehyde as intermediate.

Finally, we have found that the compounds of the **8** and **10** types are accessible *via* an indirect route involving the Friedel-Crafts dipropionylation of polymethylbenzenes,[8)] followed by the treatment of the resulting diketones with potassium *t*-butoxide and methyl iodide in boiling benzene/*t*-butyl alcohol (Scheme 2).[9)] The exhaustive methylation of the ketones, **7** and **9**, proceeded with ease, and the concurrent formation of the enol ethers was not significant.

All the dipivaloylpolymethylbenzenes obtained are well-crystallized solids melting between 128 and 232 °C with partial sublimation. They are moderately soluble in benzene, chloroform, and ether, and slightly soluble in carbon tetrachloride, hexane, and methanol. The PMR signals for pivaloyl groups in **8a,b** and **10** showed a slight splitting ($\Delta\delta<0.02$ ppm), and those for ring methyl groups appeared as a somewhat broad singlet, suggesting the occurrence of stereoisomerism as a result of the restricted rotation about the sp^2-sp^2 carbon-carbon bond at room temperature. Ring methyl signals for each pair of diketones **7/8** or **9/10** appeared nearly at the same chemical shifts, indi-



Scheme 1.



Scheme 2.

Table 1. Physical data for some diacylbenzenes and 1-aryl-2,2-dimethylpropyl benzoates

Compound	Mp (°C)	IR (ν_{max}, cm^{-1})	PMR (δ)	Yield[a] (%)
2,4-Dipropionyl-1,3,5-trimethylbenzene (**7a**)	99—101	865, 930, 1140, 1240, 1345, 1695	1.13(6H, t; J=7 Hz), 1.95(3H, s), 2.57(4H, q; J=7 Hz), 6.75(1H, s)	51
4,6-Dipropionyl-1,2,3,5-tetramethylbenzene (**7b**)	99—100	775, 930, 1110, 1340, 1400, 1690	1.13(6H, t; J=7 Hz), 1.90(3H, s), 2.07(6H, s), 2.13(3H, s), 2.57(4H, q; J=7 Hz)	65
3,6-Dipropionyl-1,2,4,5-tetramethylbenzene (**9**)[b]	170—172	945, 1000, 1113, 1335, 1405, 1700	1.18(6H, t; J=7 Hz), 2.05(12H, s), 2.60(4H, q; J=7 Hz)	26
2,4-Dipivaloyl-1,3,5-trimethylbenzene (**8a**)	128—130	865, 930, 1100, 1230, 1685	1.22(9H, s), 1.23(9H, s), 1.97(3H, s), 2.15(6H, s), 6.82(1H, s)	39
4,6-Dipivaloyl-1,2,3,5-tetramethylbenzene (**8b**)	166—168	910, 930, 1100, 1300, 1690	1.18(9H, s), 1.20(9H, s), 1.93(3H, s), 2.08(6H, s), 2.15(3H, s)	33
3,6-Dipivaloyl-1,2,4,5-tetramethylbenzene (**10**)[b]	230—232	948, 1085, 1270, 1680	1.22(9H, s), 1.23(9H, s), 2.07(12H, s)	40
1-(2,4,5-Trimethylphenyl)-2,2-dimethypropyl 2,4,5-trimethylbenzoate (**5a**)	208—209	1035, 1136, 1265, 1720	1.06(9H, s), 2.18(6H, s), 2.24(6H, s), 2.44(3H, s), 2.54(3H, s), 5.95 (1H, s), 6.89(1H, s), 6.96(1H, s), 7.14(1H, s), 7.76(1H, s)	~5
1-(2,4,6-Trimethylphenyl)-2,2-dimethylpropyl 2,4,6-trimethylbenzoate (**5b**)	126—128	1075, 1162, 1260, 1725	1.09(6H, s), 2.16(6H, s), 2.24(6H, s), 2.37(3H, s), 2.57(3H, s), 6.07 (1H, s), 6.80(4H, s)	56
1-(2,3,4,6-Tetramethylphenyl)-2,2-dimethylpropyl 2,3,4,6-tetramethylbenzoate (**5**)	130—131	1028, 1150, 1270, 1725	1.03(9H, s), 2.00(6H, s), 2.07(6H, s), 2.20(6H, s), 2.27(3H, s), 2.50 (3H, s), 6.35(1H, s), 6.70(2H, s)	50

a) Based on the isolated product. All new compounds gave satisfactory analyses. b) The PMR spectra were measured in deuteriochloroform.

cating that the preferred conformations of all the pairs of compounds are very similar.

On treatment with nitric acid in dichloromethane, **8b** underwent preferential attack upon the 2-methyl group at the most hindered position. This and other aspects of the reaction of this new compound will be reported in detail separately.

Experimental

The melting points were taken on a hot-stage apparatus and are uncorrected. The IR spectra were run as Nujol mulls on a Hitachi 215 spectrophotometer, and only prominent peaks were recorded. The PMR spectra were measured in carbon tetrachloride with a Varian T-60 spectrometer, using TMS as the internal standard, unless otherwise stated. The mass (MS) spectra were obtained on a Hitachi RMS-4 mass spectrometer with an ionizing potential of 70 eV.

The polymethylbenzoyl chlorides (**1a—c**) were prepared from the corresponding benzoic acids[10] by treatment with thionyl chloride. The dipropionylpolymethylbenzenes (**7a—b** and **9**) were prepared from the corresponding hydrocarbons according to the Perrier procedure of the Friedel-Crafts acylation.[8] The aldehyde (**2b**) and ketone (**3b**) were prepared as has previously been reported.[3,11] The physical properties and yields of dipropionyl- and dipivaloylpolymethylbenzenes (**7a—b** and **9**, and **8a—b** and **10**, respectively), and 1-(polymethylphenyl)-2,2-dimethylpropyl polymethylbenzoates (**4a—c**) obtained are summarized in Table 1. The general preparation of the hindered diketones and esters is illustrated below by the synthesis of **8b** and **4b**.

4,6-Dipivaloyl-1,2,3,5-tetramethylbenzene (8b). A mixture of the **7b** diketone (1.5 g; 0.006 mol), potassium *t*-butoxide (5.5 g; 0.050 mol), benzene (15 ml), and *t*-butyl alcohol (6 ml) was stirred, and then a solution of methyl iodide (15 g; 0.102 mol) in benzene (30 ml) was slowly added during the course of 30 min. Stirring was continued for 4 h under reflux, and then the reaction mixture was treated with water. The organic layer was separated and washed thoroughly with water, and the solvent was removed under reduced pressure. The residue was purified over a column of silica gel (hexane), giving **8b** as colorless plates (0.6 g; 33%); mp 166—168 °C. MS: *m/e* 302 (M^+), 287 (M^+-CH_3), and 245 (base peak; $M^+-C_4H_9$). Found: C, 79.67; H, 10.15%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%.

Compounds **8a** and **10** were obtained in a similar manner from 1,3,5-trimethylbenzene and 1,2,4,5-tetramethylbenzene respectively. **8a**: Found: C, 79.19; H, 9.74%. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78%. **10**: Found: C, 79.48; H, 10.13%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%.

1-(2,4,6-Trimethylphenyl)-2,2-dimethylpropyl 2,4,6-Trimethylbenzoate (4b). Into a solution of the Grignard reagent prepared from *t*-butyl chloride (5.0 g; 0.054 mol) and magnesium (1.3 g; 0.054 atom) in ether (30 ml), 2,4,6-trimethylbenzoyl chloride (5.9 g; 0.032 mol) in ether (20 ml) was stirred under ice-water cooling during the course of 0.5 h. After the acid chloride had then been added, the mixture was gently refluxed for 4 h and then treated with aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed successively with aqueous sodium hydrogencarbonate and water, dried over magnesium sulfate, and evaporated. After standing overnight in a refrigerator, the oily residue gave an ester as a white solid which, on several recrystallizations from hexane, melted at 126—128 °C. Yield, 3.2 g (56%). MS: *m/e* 352 (M^+) and 295 (base peak; $M^+-C_4H_9$). Found: C, 82.05; H, 9.19%. Calcd for $C_{24}H_{32}O_2$: C, 81.77; H, 9.14%.

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