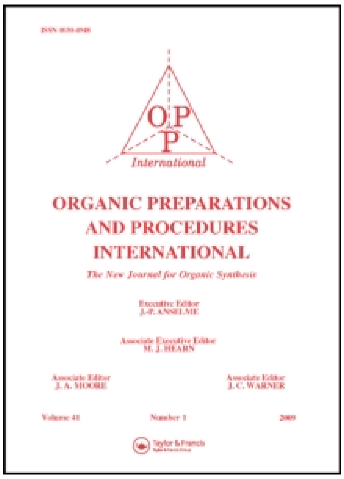

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# SYNTHESIS OF HINDERED AROMATIC DIKETONES—BY FRIEDEL-CRAFTS ACYLATION

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# SYNTHESIS OF HINDERED AROMATIC DIKETONES - BY FRIEDEL-CRAFTS ACYLATION

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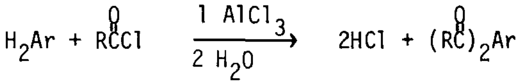
Three procedures have been recognized[1] for the Friedel-Crafts acylation:

1) The Elb, catalyst added as last reactant;
2) The Bouveault, acyl component added as final reactant;
3) The Perrier, a) aluminum chloride and acyl component mixed prior to final addition of substrate b) the reverse of (a), addition of preformed complex to substrate.

Although the Elbs procedure is most widely used, like the Bouveault it entails a continuous variation in the catalyst/acyl ratio (Q) and consequently, the rates of acylation and yields are dependent on the rate of addition of the final component and are non-reproducible. In contrast, results of the Perrier procedure are reproducible because the catalyst/acyl ratio is constant.

Although aromatic rings normally undergo only monoacylation under the usual Friedel-Crafts acylation methods, diacylation can take place with certain hindered aromatic compounds when a large excess of aluminum chloride is employed.[2,3]



$$H_2Ar + R\overset{O}{\overset{\|}{C}}Cl \xrightarrow[2\ H_2O]{1\ AlCl_3} 2HCl + (R\overset{O}{\overset{\|}{C}})_2Ar$$

Thus, acetophenone was the only product obtained from acetylation of benzene using aluminum chloride or other catalysts and solvents under various conditions.[4] Presumably the ring is deactivated toward further substitution by the coordinated acetyl group. Baum and Meyer[5] were apparently the first to obtain a diketone (diacetodurene) by Friedel-Crafts acetylation of durene, although the yield and procedure were not reported. The following year Meyer[4] reported an 80% yield of diacetodurene (procedure was not given); Weil[6] prepared several diacylmesitylenes; again neither procedures nor yields were reported. Later papers refer to these early references but also do not give procedures. As is demonstrated in the present paper, a good yield of diacetodurene is markedly dependent on the procedure used (85% vs. 10%), in particular the method and order of addition of reactants. However, in the cases of the mesitylene and isodurene diketones, the yields are not as critically dependent on the procedure (for example for diacetomesitylene 80 vs. 68% and 79 vs. 71% respectively for dipropiomesitylene using the same two methods used for diacetodurene and dipropiodurene, respectively). Although Gore and Hoskins[7] conducted a detailed investigation of diacylation, their study dealt only with mesitylene and product analyses were by analytical techniques. The purpose of the present paper is to report and summarize synthetic aspects and isolation of products from diacylation of durene, mesitylene, and isodurene which are either unreported or inadequately described in published literature.

The results are summarized in the Tables. It should be noted that approximately 3:1 mol ratios of acetyl chloride to durene, mesitylene or isodurene and 2:1 of aluminum chloride to acetyl chloride were used in most cases. It has been noted[1] that use of the calculated amount of catalyst (based on the acyl component) gives the best yields and that too large an excess results in tar formation. The yields of both diacetodurene (85%) and diacetomesitylene (80%) are higher when method 2 (Perrier procedure) is used, i.e. addition of a carbon disulfide solution of durene or mesitylene to an acetyl chloride/aluminum chloride mixture. When a carbon disulfide solution of the acid chloride and durene is added to aluminum chloride (Method 1), a lower yield is obtained in these cases- markedly lower with durene.

Table 1. Friedel-Crafts Diacylation by Different Procedures.

| | Aromatic Substrate[a] | Acid Chloride[a] | $\frac{RCOCl}{ArH}$ | $AlCl_3$[a] | $\frac{AlCl_3}{RCOCl}$[b] | Vol. Solv.[c] |
|---|---|---|---|---|---|---|
| 1 | Durene[d] (15g.,0.110) | 26.4g.(0.34) | 3.1 | 90(0.67) | 2.0 | 225 |
| 2 | Durene[e] (25g.,0.187) | 43.9g.(0.559) | 3.0 | 150(1.12) | 2.0 | 300 |
| 3 | Acetodurene (20g.,0.114) | 12.0g.(0.150) | 1.3 | 40(0.300) | 2.0 | 400[e] |
| 4 | Mesitylene (25.7g.,0.214) | 50.8g.(0.650) | 3.0 | 173(1.30) | 2.0 | 275 |
| 5 | Mesitylene (10g.,0.0830) | 19.8g.(0.252) | 3.0 | 66.8(0.500) | 2.0 | 140 |
| 6 | Durene (26.8g.,0.200) | 40.0g.(0.440)[e] | 2.2 | 131(0.98) | 2.2 | 500[f,g] |
| 7 | Durene (15g.,0.11) | 30.5g.(0.33)[e] | 3.0 | 90(0.68) | 2.1 | 300 |
| 8 | Mesitylene (3g.,0.025) | 7.0g.(0.076)[e] | 3.0 | 20(0.15) | 2.0 | 50 |
| 9 | Mesitylene (20g.,0.17) | 47g.(0.51)[e] | 3.0 | 134(1.00) | 2.0 | 300 |
| 10 | Isodurene (3g.,0.022) | 5.47g.(0.069) | 3.1 | 18(0.135) | 2.0 | 40 |
| 11 | Isodurene (3g.,0.022) | 5.40g.(0.068) | 3.1 | 17.9(0.134) | 2.0 | 40 |

a) Amount in g. (moles); b) Mole ratio Q[7]; c) Total Vol. solvent (ml.); d) Method 1; e) Method 2; f) 1,1,2,2-Tetrachloroethane; g) Propionyl chloride; acetyl chloride for others.

## EXPERIMENTAL

The sources, grades and purification of materials used were: Mesitylene, reagent grade, fractionated; acetyl chloride, Allied Chemical; propionyl chloride, Baker & Adamson or Aldrich reagent grade, redistilled; anhydrous aluminum chloride, Mallinckrodt analytical reagent; durene, 98% pure; carbon disulfide, Mallinckrodt analytical reagent; methylene chloride, reagent grade, redistilled; 1,1,2,2-tetrachloroethane, distilled; isodurene, Aldrich reagent grade. Melting points were obtained with an electrically-heated, mechanically-stirred Thiele tube and are corrected. Boiling points are uncorrected.

General Procedures. The two procedures used in the present work will be identified as follows: Method 1, one of the possible variations of the Bouveault procedure, refers to the addition of solution of the acid chloride and aromatic component to the aluminum chloride. Method 2 - the usual Perrier procedure - refers to the addition of a solution of the aromatic component to a mixture of the acid chloride and aluminum chloride. Detailed

Table 2. Yields and Physical Properties of Diketones from Friedel-Crafts Diacylation.

| | Product | Diketone Yield(%)$^{a}$ | Lit. Yield(%) | Mp(°C) (obs.) | Mp(°C) lit. |
|---|---|---|---|---|---|
| 1 | Diacetodurene$^{n}$ | 2.4g.(10) | $5^{b,c}$<br>$37^{d}$, $80^{e}$ | 177-178 | 182.5-183.0$^{d}$ |
| 2 | Diacetodurene$^{n}$ | 35g.(85) | | | $178^{b,j}$ |
| 3 | Diacetodurene$^{n}$ | 4.2g.(17) | | 177-178.5 | |
| 4 | Diacetomesitylene | 29.4g.(68) | $71^{f}$<br>$19^{b}$, $95^{g}$ | k | |
| 5 | Diacetomesitylene | 13.6g.(80) | quant$^{h,i}$ | 43-44 | $44^{l}$, $46^{h}$ |
| 6 | Dipropiodurene$^{n}$ | 9.35g.(19) | | 180-180.6 | |
| 7 | Dipropiodurene | 19g.(70) | quant$^{i,j}$ | 175-176 | $176^{j}$ |
| 8 | Dipropiomesitylene$^{o}$ | 4.1g.(71) | | 100-101 | 101-102$^{m}$ |
| 9 | Dipropiomesitylene$^{o}$ | 30g.(79) | | | |
| 10 | Diacetoisodurene$^{o}$ | 3.95g.(81) | $14^{b}$ | 119.5 | $121^{j}$ |
| 11 | Diacetoisodurene$^{o}$ | 3.55g.(73) | quant$^{h,i}$ | | |

a) Yields in g; % yields in parentheses based on aromatic component; b) Ref 8; c) Using acetic anhydride; d) Ref. 9; e) Ref. 4; f) Ref. 2; g) Ref. 7; h) Ref. 3; i) Quantitative crude yields were obtained in the present work also; j) Ref. 5; k) Bp 164-170°/6-7 torr; lit$^{l}$ 154°/6 torr; l) P. H. Gore, J. A. Hoskins, R. J. W. LeFevre, L. Radom, and G. L. D. Ritchie, J. Chem. Soc. (B), 485 (1969); m) Ref. 6; n) Recrystallized from benzene; o) Recrystallized from ethanol.

procedures are given for one example of each method and for the two different solvents used; the same procedures were used for the other examples for which the data is tabulated with any changes from the procedures noted in the table.

Diacetodurene.

Method 1. From Durene. - Aluminum chloride (90 g, 0.67 mol) was transferred to a 3-necked flask and covered with 150 ml of carbon disulfide. The mixture was stirred mechanically and heated to gentle reflux. A solution of durene (15 g, 0.11 mol) and acetyl chloride (26.4 g, 0.34 mol) in carbon disulfide (ca. 75 ml) was added slowly. In all of the diacylation reactions, a yellow color which formed initially slowly turned to red. The mixture was stirred and refluxed overnight, and then poured into crushed ice. Concentrated hydrochloric acid was added until the mixture was acidic to pH indicator (Accutint) paper (pH 1-3). Methylene chloride (ca. 100 ml) was added to the mixture and aqueous and organic portions were separated. The aqueous layer was washed with two 60 ml portions of methylene chloride and the washings added to the organic layer. The organic layer was washed with 5-10% aqueous sodium carbonate, distilled water, and saturated sodium chloride solution and finally dried over anhydrous sodium sulfate. The solvent was removed by distillation and the red solid was recrystallized from benzene to give 2.4 g (10% average of two runs), mp. 177-178°, lit. mp. 178°[4,5,8], 182.5-183.0[9].

Method 1. From Acetodurene. - ††Acetodurene was prepared by addition of a methylene chloride solution of durene (27 g, 0.20 mol) and acetyl chloride (16.5 g, 0.210 mol) to a mixture of anhydrous aluminum chloride (60 g, 0.45 mol) and methylene chloride (500 ml total volume) previously cooled to 0° by means of an ice-salt mixture. The addition was carried out so that the temperature did not rise above 10°. The reaction mixture was decomposed with ice-hydrochloric acid and worked up in the usual manner. On removal of solvent, acetodurene was obtained in 84% yield. A 61% yield was obtained after recrystallization from methanol as white plates, mp. 73-74°, lit.[8] 80% using acetic anhydride, mp. 72.5-73.5°.

A solution of acetodurene (20.0 g, 0.114 mol) and acetyl chloride (12.0 g, 0.150 mol) in 1,1,2,2-tetrachloroethane was added to anhydrous aluminum chloride (40.0 g, 0.300 mol) at a room temperature of 22° over a period of 1 hr. The temperature rose to 32°. The mixture was then heated with stirring for 12 hrs at 50°. At the end of this time, the reaction mixture was a deep-red color which was not observed during the monoacetylation of durene. The mixture was decomposed with ice and hydrochloric acid and the organic layer dried with anhydrous sodium sulfate. The solvent was removed by distillation and the residue recrystallized from benzene. Diacetodurene was obtained in 17% yield, mp. 177.0-178.5° lit.[8] 10% using acetic anhydride, mp. 178°. Unreacted acetodurene (9.5 g, 47.5%) was recovered from the benzene.

Method 2. From Durene. - Acetyl chloride (43.9 g, 0.560 mol) and aluminum chloride (150 g, 1.12 mol) were added to 200 ml of carbon disulfide and the mixture was gently refluxed overnight. Durene (25.0 g, 0.187 mol) in 100 ml of carbon disulfide was then added slowly with stirring to the refluxing solution. Thereafter the procedure was the same as in Method 1. The mp of recrystallized material was 177-178°. The recrystallized yield was 35 g (85%),(Lit. mp 178°[4,5,8], 182.5-183.0[9], 5%[8,10], 37%[9]; 80%[4]).

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