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Epoxide formation in the Friedel-Crafts reaction of adipoyl chloride and bromobenzene

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Abstract: The aluminium chloride catalysed Friedel-Crafts reaction between adipoyl chloride and bromobenzene has been re-examined. At elevated temperatures a number of side products are produced including a cyclopentane epoxide. The structure of this epoxide was elucidated by nmr and ir spectroscopy and its stereochemistry confirmed by x-ray crystallography.

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The Friedel-Crafts acylation of benzene and oligoaryl derivatives has been widely employed in liquid crystal synthesis.[1] As part of our studies on liquid crystal polymers we required large quantities of 1,6-bis(4-bromophenyl)hexane and decided to follow a literature procedure *via* acylation of bromobenzene with adipoyl chloride.[2] Attempts to optimise the procedure further included performing the reaction at elevated temperatures. One set of conditions involved reaction of adipoyl chloride and aluminium chloride (2.2 equiv.) with bromobenzene (used in excess as solvent) at reflux and was found to produce a complex mixture of products. The components were isolated by column chromatography and characterised spectroscopically.

The majority of isolated products were easily identified and follow from the straightforward scheme and mechanism (Path 1). Following formation of 1,4-bis(4-bromobenzoyl)butane **1** via double Friedel-Crafts acylation, cyclisation (Aldol reaction) occurs to give intermediate **2**. Elimination gives a cyclopentene (the major isolated product) which is assigned structure **3** based on nmr and ir spectra (CO stretch at 1690cm^{-1} indicates the product is not α,β-unsaturated).[3] It should be noted that **3** is not the thermodynamic isomer. In a separate experiment, **1** was cyclised by refluxing in glacial acetic acid/HCl producing the fully conjugated cyclohexene **9** with only a trace of **3** (**9**:**3** = >98:2).

One additional compound was also isolated. Initial spectroscopic characterisation and consideration of the reaction mechanism led to a tentative assignment of the structure as the alcohol formed by protonation of intermediate **2**. Closer examination of the data, however, revealed inconsistency with this assignment. The mass spectrum gave molecular ion peaks 2 amu lower than calculated for the alcohol and the ^{13}C DEPT clearly revealed only two signals for methylene carbons leading to the conclusion that epoxide **8** had in fact been formed in the reaction.[4] The stereochemistry of **8** was sunsequently confirmed by x-ray crystallography. A plausible mechanism for formation of **8** is depicted in Path 2. α-Bromination of **1** gives tribromide **6** (isolation of **4**, **5** and dibromobenzenes demonstrates the presence of bromonium ion equivalents in the reaction mixture[5]). Cyclisation gives intermediate **7** which yields the epoxide **8** by displacement of bromide. Previously the

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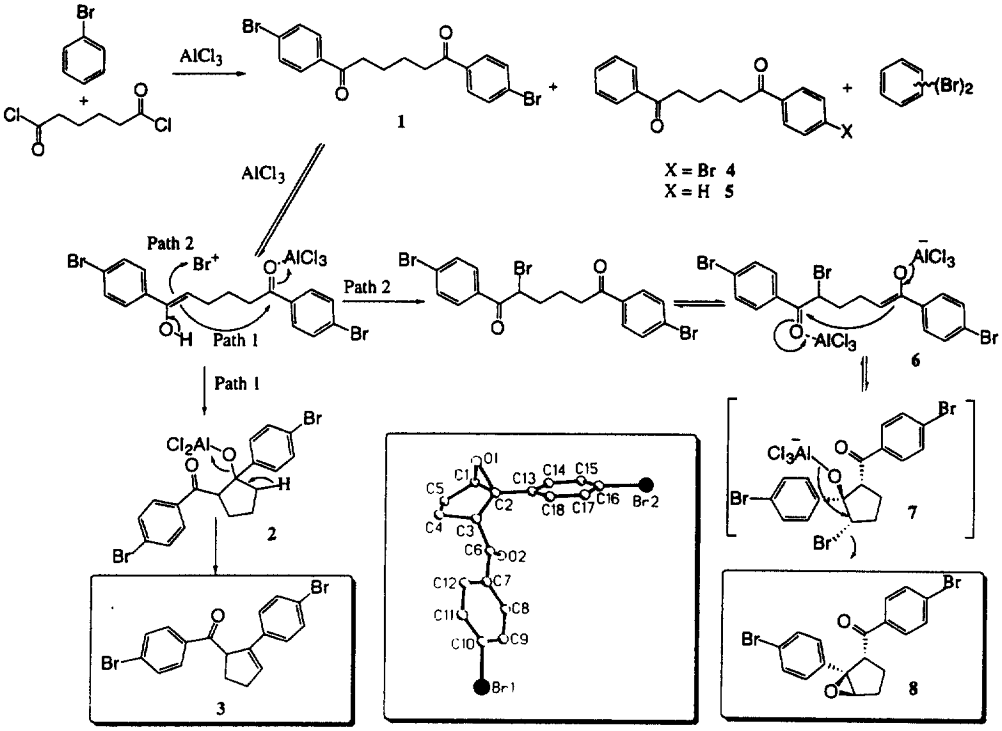
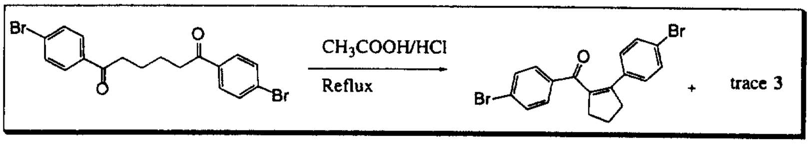
synthesis of related compounds has only been possible from α,α'-dihalogeno-1,6-diketones by Reformatsky reaction followed by epoxide formation.[6]

In conclusion we have found that, under carefully controlled conditions, a high (>85%) yield of 1,4-bis(4-bromobenzoyl)butane can be obtained by this procedure. At elevated temperatures, however, further reaction takes place to yield novel cyclopentene derivative **3** and, its formal oxidation product, **8**.





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References and Notes

1. For an overview see Hird, M.; Collings, P.J. "Introduction to Liquid Crystals", Taylor and Francis: London, 1997.
2. Jaunin, B.; Baer, T. *Helv. Chim. Acta* **1957**, *233*, 2245.
3. Selected data for **3**: ^{1}H nmr (270Mhz, $CDCl_3$) δ 7.88 (d, J=7.8Hz, 2H), 7.64 (d, J=7.8Hz, 2H), 7.37 (d, J=8Hz, 2H), 7.14 (d, J=8Hz, 2H), 6.45 (m, 1H), 4.85 (m, 1H), 2.62-2.5 (m, 3H), 2.12-2.02 (m, 1H); δc 199.9, 140.4, 134.9, 134.4, 132.1, 131.5, 131.2, 130.2, 128.5, 127.3, 121.0, 53.5, 32.5, 29.9.
4. Selected data for **8**: ^{1}H nmr (270Mhz, $CDCl_3$) δ 7.76 (d, J=7.3Hz, 2H), 7.60 (d, J=7.3Hz, 2H), 7.34 (d, J=8.2Hz, 2H), 7.14 (d, J=8.2Hz, 2H), 4.38 (d, J=8.2Hz, 1H), 4.0 (s, 1H), 2.2-2.0 (m, 3H), 1.8-1.7 (m, 1H); δc 199.4, 134.6, 132.1, 131.4, 129.9, 129.5, 128.9, 122.3, 77.2, 68.8, 64.1, 48.5, 26.8, 25.9.
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6. Fuson, R.C.; Farlow, M.J.W. *J. Am. Chem. Soc.* **1934**, *56*, 1593.