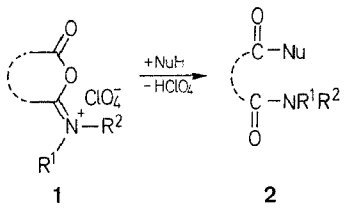
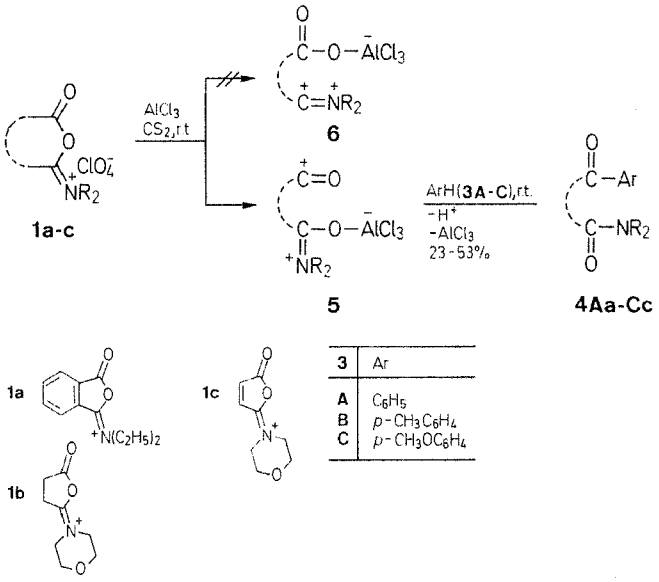


1 2

We report here our preliminary results regarding the acylation of aromatic compounds (Nu = Ar) by various cyclic isoimidium perchlorates **1** such as phthalisoimidium **(1a)**, succinisoimidium **(1b)** and maleisoimidium **(1c)** perchlorates. In view of the structural similarity between **1** and acid anhydrides, which are classical Friedel-Crafts acylating agents, we were interested whether compounds **1** are sufficiently electrophilic (or *vice versa* whether aromatic substrates **3** can act as sufficiently powerful nucleophiles) in order to afford the corresponding *N,N*-disubstituted *β*-aroylcarboxamides **4**. There is yet another analogy with a known reaction, namely the aroylaminoacylation of aromatics with azlactones yielding compounds which are easily converted into 2,5-diaryloxazoles.[4]



1a-c **6** **5** **4Aa-Cc**

3	Ar
A	C_6H_5
B	p-$CH_3C_6H_4$
C	p-$CH_3OC_6H_4$

A Novel Aromatic Electrophilic Substitution: Acylation of Aromatics with Cyclic Isoimidium Salts to Yield *N,N*-Disubstituted *β*-Aroylcarboxamides

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Cyclic isoimidium perchlorates derived from *N,N*-diethylphthalamic acid and the monomorpholides of succinic and maleic acid react with benezene, toluene or anisole in the presence of aluminium chloride to give the corresponding *β*-aroylcarboxamides in moderate yields.

The recently synthesized cyclic isoimidium perchlorates **1**[1] have proved to react with various nucleophiles (NuH), e.g. sodium azide,[2] affording easy access to derivatives **2** of amic acids. These derivatives are of considerable interest (especially as drugs) and their chemistry is rapidly expanding.[3]

In the presence of aluminium chloride, the isoimidium perchlorates **1a–c** reacted smoothly in carbon disulfide with benzene **(3A)**, toluene **(3B)** and anisole **(3C)** affording the corresponding aroylcarboxamides **4** in moderate yields (20–50%) as indicated in the Table.

When using dichloromethane instead of carbon disulfide, considerable amounts of diarylmethane derivatives resulted. This fact offers a comparison between the rates of acylation with isoimidium salts and Friedel-Crafts alkylation. Usually, acylation reactions proceed more rapidly than similar alkylation reactions,[5] the transition state for the former reactions is a 'late' one with strongly charge-developed structures resembling a *σ*-complex whereas for the latter reaction the transition state has a *π*-complex nature.[6] Thus isoimidium perchlorates appear as relatively weak acylation agents.

Under the same reaction conditions, chlorobenzene and bromobenzene did not yield the corresponding carboxamides.

Interestingly, the products **4Ac**, **4Bc** and **4Cc** obtained from maleisoimidium perchlorate have a *trans* double bond as shown by the large ^{1}H-NMR coupling constant (15 Hz). A similar *cis-trans* isomerisation has been observed in the reaction of

Table. Aroylcarboxamides 4 Prepared

Product	Yield (%)	m.p. (°C)	Molecular Formula[a] or Lit. m.p. (°C)	^{1}H-NMR ($CDCl_3$/TMS) δ (ppm)
4Aa	34	55	55–56[7]	0.99 (t, 6H, J = 7 Hz, 2 × $CH_2\underline{CH_3}$); 3.33 (q, 4H, J = 7 Hz, 2 × $\underline{CH_2}CH_3$); 7.28 (s, 4H$_{arom}$); 7.67, 8.07 (2m, 3H and 2H, C_6H_5)
4Ba	48	65–66	$C_{19}H_{21}NO_2$ (295.4)	1.08 (t, 6H, J = 7 Hz, 2 × $CH_2\underline{CH_3}$); 2.40 (s, 3H, Ar–$\underline{CH_3}$); 3.45 (q, 4H, J = 7 Hz, 2 × $\underline{CH_2}CH_3$); 7.23, 7.73 (AA′BB′, 2H each, J = 8.5 Hz, $\underline{Ar}$–CH_3); 7.47 (s, 4H$_{arom}$)
4Ca	23	oil	$C_{19}H_{21}NO_3$ (311.4)	1.09 (br t, 6H, 2 × $CH_2\underline{CH_3}$); 3.40 (br q, 4H, 2 × $\underline{CH_2}CH_3$); 3.82 (s, 3H, OCH_3); 6.80, 7.72 (AA′BB′, 2H each, J = 9 Hz, $\underline{Ar}$–OCH_3); 7.40 (s, 4H$_{arom}$)
4Ab	53	83	85–87[8]	2.73 (t, 2H, J = 7 Hz, $C_6H_5COCH_2\underline{CH_2}$); 3.35 (t, 2H, J = 7 Hz, $C_6H_5COCH_2\underline{CH_2}$); 3.64 (s, 8H, morpholyl-CH_2); 7.43, 8.00 (2m, 3H and 2H, C_6H_5)
4Bb	45	83–84	85[9]	2.38 (s, 3H, Ar–$\underline{CH_3}$); 2.73 (t, 2H, J = 7 Hz, $ArCOCH_2\underline{CH_2}$); 3.32 (t, 2H, J = 7 Hz, $ArCOCH_2\underline{CH_2}$); 3.63 (s, 8H, morpholyl-CH_2); 7.91 (AA′BB′, 2H each, J = 8 Hz, C_6H_5)
4Cb	30	oil	86–87[8]	2.70 (t, 2H, J = 7 Hz, $ArCOCH_2\underline{CH_2}$); 3.30 (t, 2H, J = 7 Hz, $ArCOCH_2\underline{CH_2}$); 3.63 (s, 8H, morpholyl-CH_2); 3.83 (s, 3H, OCH_3); 6.87, 7.97 (AA′BB′, 2H each, J = 9 Hz, C_6H_5)
4Ac	48	129–130	$C_{14}H_{15}NO_3$ (245.3)	3.70 (s, 8H, morpholyl); 7.33 (d, 1H, J = 15 Hz, $C_6H_5COC\underline{H}$ =CH); 7.50, 7.97 (2m, 3H and 2H, C_6H_5); 7.92 (d, 2H, J = 15 Hz, C_6H_5COCH =$C\underline{H}$)
4Bc	42	122–123	$C_{15}H_{17}NO_3$ (259.3)	2.43 (s, 3H, CH_3); 3.75 (s, 8H, morpholyl-CH_2); 7.33, 7.98 (AA′BB′, 2H each, J = 9 Hz, Ar–CH_3); 7.45 (d, 1H, J = 15 Hz, $ArCOC\underline{H}$=CH); 8.03 (d, 1H, J = 15 Hz, ArCOCH =$C\underline{H}$)
4Cc	26	127	$C_{15}H_{17}NO_4$ (270.3)	3.75 (s, 8H, morpholyl-CH_2); 3.93 (s, 3H, OCH_3); 7.04, 8.11 (AA′BB′, 2H each, J = 9 Hz, $\underline{Ar}OCH_3$); 7.48 (d, 1H, J = 15 Hz, $ArCOC\underline{H}$=CH); 8.05 (d, 1H, J = 15 Hz, ArCOCH =$C\underline{H}$)

[a] Satisfactory microanalyses obtained: C ±0.32, H ±0.10, N ±0.15.

maleisoimidium salts with sodium azide, when the corresponding acyl azides **2** were *trans* compounds, however, in this case the mechanism involves a nucleophilic addition of azide anion.[2]

As seen from the Table, ^{1}H-NMR spectra and elemental analyses confirm the structure of products **4**. The assignment is facilitated by the singlet peaks of phthalyl and morpholyl protons. In agreement with previous observations, the structure of the products demonstrates that ring opening of the isoimidium perchlorate proceeds regiospecifically. We interpret this as being due to the higher stability of the intermediate **5** than of **6** which has two adjacent positive charges. In the case of maleiyl derivatives **4c**, a *cis* → trans isomerization accompanies the ring opening; this isomerization is facilitated by the "allylic" delocalization leading to a lowering of the C=C bond order.

Some of the aroylcarboxamides **4** were earlier reported as indicated in Table.[7–9] Compound **4Ab** ("AP36") is a strong depressant for the central nervous system and its pharmacological effects were studied.[10] The present reaction might prove to be attractive in synthesizing various compounds of this type as the aroyl moiety can be widely varied and is introduced in a one-step procedure.

4-(*p*-Tolyl)-4-oxo-butyric Acid Morpholide (4Bb); Typical Procedure:
Anhydrous aluminium chloride (4.0 g, 30 mmol) is suspended in a solution of toluene (8.3 g, 90 mmol) in dry carbon disulfide (25 ml). The isoimidium perchlorate **1b** (2.7 g, 10 mmol) is added to the stirred suspension at room temperature. Gentle evolution of hydrogen chloride accompanies the separation of the aluminium chloride complex. The mixture is stirred for 4 h at room temperature and is allowed to stand overnight. After decomposition of the complex with 10 normal hydrochloric acid (10 ml) under stirring, the product is extracted with ether (4 × 10 ml). The combined organic layer is washed with aqueous sodium hydrogen carbonate (20 ml) and concentrated under reduced pressure, where upon the carboxamide **4Bb** crystallized; yield: 1.30 g (45%); m.p. 78–81 °C. Recrystallization from isopropanol gives a pure sample with m.p. 83–84 °C (Lit.[9] m.p. 85 °C).

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