Direct Alkylacylation of Arenes by Alkanes and Cycloalkanes in the Presence of Aprotic Superacids

Irena Akhrem,* Alexander Orlinkov and Mark Vol'pin

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 117813 Moscow, Russian Federation

Alkanes and cycloalkanes react with benzene and bromobenzene in the presence of the $RCO^+Al_2X_7^-$ complexes at 0–20 °C to give the products of arene alkylacylation in 60–87% yields after 5–30 min.

Selective single-stage functionalization of saturated hydrocarbons is of considerable interest as a direct synthetic route to fine organic chemicals from easily available raw hydrocarbon stocks.

The $RCO^+Al_2X_7^-$ (R = Alk, Ar; X = Cl, Br) aprotic organic superacids **I**[1] are found to acylate not only unsaturated compounds,[2–5] but also alkanes.[1,5,6] For this reason the possibility of arene alkylation in the presence of the complexes **I** seemed to be unlikely. However, the complexes **I** in the presence of an excess of alkyl halides were found to act as catalysts for benzene alkylation [eqn. (1)].

$$\mathrm{Pen^tCl} + \mathrm{C_6H_6} \xrightarrow[20\,^\circ\mathrm{C},\,1.5\,\mathrm{h}]{\mathrm{Ac^+Al_2Cl_7^-}} \underset{85\%}{\mathrm{Pen^tC_6H_5}} + \underset{10\%}{p\text{-}(\mathrm{Pen^t})_2\mathrm{C_6H_4}} \quad (1)$$

$$[C_6H_6]:[C_5H_{11}Cl]:[I] = 180:36:1;\ \mathrm{Pen} = \mathrm{pentyl}$$

Taking into account that complexes **I** easily generate carbenium ions from saturated hydrocarbons, we studied the possibility of the application of the latter as alkylating agents in reactions with aromatic compounds. Alkanes and cycloalkanes were found to alkylate effectively benzene and bromobenzene in the presence of complexes **I** yielding alkylated aromatic ketones. In these reactions the complexes **I** act as promotors of arene alkylation by alkanes and as traditional acylation agents for initially formed alkylbenzenes.

Single-stage benzene alkylacylation by iso- and linear-alkanes or cycloalkanes in the presence of **I** proceeds at 0–20 °C. The yields of alkylated ketones reach 68–87% in 5–30 min. The yields of products of competing reactions *viz.* non-alkylated aromatic ketones, are 0–20% and in the reactions with isobutane the yields reach 18–40%.

$$\mathrm{C_6H_6} + \mathrm{R'H} + 2\mathrm{RCO^+Al_2X_7^-} \xrightarrow[-\mathrm{HX}\ -\mathrm{RCHO}\ -\mathrm{Al_2X_6}]{0\text{–}20\,^\circ\mathrm{C}} p\text{-}\mathrm{R'C_6H_4\text{-}COR} \quad (2)$$

R' = Bu^i, Bu^n, Pen^i, Pen^n, 2,3-$Me_2C_6H_{12}$, c-C_5H_9Me, c-$C_6H_{11}Me$; R = Me, Pr, Ph; X = Cl, Br

Alkylacylation reactions with benzene can be carried out with good yields only by using an excess of the 'alkylation' system ($R'H + RCO^+Al_2X_7^-$) with the molar ration $[R'H]:[I]:[C_6H_6] = (10–15):(3–12):1$.

It is necessary to follow scrupulously the prescribed preparation procedure and in particular to add benzene to the mixture of $R'H + RCO^+Al_2X_7^-$ slowly. A rapid addition of benzene leads to a sharp increase of the non-alkylated aromatic ketone yields and changing the order of reagent mixing completely suppresses alkylation to give exclusively PhCOR.

Typical procedure: (*i*) isopentane (0.45 g, 6.1 mmol) was added to a stirred solution of $MeCOBr{\cdot}2AlBr_3$ (3.7 mmol) in 4.4 ml of CH_2Br_2. Then benzene (0.05 g, 0.62 mmol) in 0.5 ml of CH_2Br_2 was added dropwise over 2 min. The mixture was stirred for 3 min more, cooled, hydrolysed with ice–water, extracted with diethyl ether, washed, dried and then fractionated *in vacuo*.

(*ii*) Liquid isobutane (2 ml, 20 mmol) was added to a stirred suspension of $MeCOBr{\cdot}2AlCl_3$ (15 mmol) in 8 ml of CH_2Cl_2 at −30 °C. After warming to 17–19 °C benzene (0.11 ml, 1.22 mmol) in 0.9 ml of CH_2Cl_2 was added dropwise over 5 min. The reaction mixture was stirred at 17–19 °C for 35 min more and then worked up as described above.

The reaction with n-alkanes can be effective only if these hydrocarbons are previously kept in the presence of complex **I** long enough for isomerization completion (*ca.* 3 h). Lower alkanes C_1–C_3 whose carbenium ions are unstable do not form alkylacylation products with arenes.

The reaction discussed works for various $RCO^+Al_2X_7^-$ complexes although with R = Ph the yields are lower. Lower yields were also obtained for other complexes **I** with aromatic R radicals.[7]

The structure of the products obtained was established by the GLC–MS technique. The positions of substituents in arene rings were determined by ^{13}C NMR spectra.†

The reactions of benzene with isobutane and n-butane proceed regioselectively resulting in the single product, *viz.* the *para*-isomer of the corresponding *tert*-butyl-substituted ketone [eqn. (3)].

$$\mathrm{C_6H_6} + \mathrm{Bu^iH} + \mathrm{RCO^+Al_2X_7^-} \rightarrow p\text{-}\mathrm{Bu^tC_6H_4\text{-}COR} \quad (3)$$

The reaction of benzene with isopentane gives a mixture of two *para*-isomers (in 1:1 molar ratio), which differ in the pentyl group structure [eqn. (4)].

$$\mathrm{C_6H_6} + \mathrm{Pen^iH} + \mathrm{RCO^+Al_2X_7^-} \rightarrow p\text{-}\mathrm{Me_2(Et)CC_6H_4\text{-}COR} + p\text{-}\mathrm{Me(Pr^i)HCC_6H_4\text{-}COR} \quad (4)$$

The reactions with isohexanes, methylcyclopentane and methylcyclohexane afford a large number of isomers with different structrures of the alkyl (cycloalkyl) group.

Alkylacylation of bromobenzene proceeds with high yields of 74–82% and greater selectivity than alkylacylation of benzene. Thus the reaction with isobutane results in a single isomer, *viz.* 2-bromo-4-*tert*-butylacetophenone [eqn. (5)].

$$\mathrm{C_6H_5Br} + \mathrm{Bu^iH} + \mathrm{MeCO^+Al_2Cl_7^-} \rightarrow \mathrm{2\text{-}Br\text{-}4\text{-}Bu^tC_6H_3\text{-}COMe} \quad (5)$$

The reaction with isopentane again results in isomers differing in the pentyl group structure.

Activated arenes such as toluene, *p*-xylene and naphthalene also form alkylacylation products but in this case the yields of the latter do not exceed 10% relative to the yields of direct acylation arene products. On the other hand, arenes with electron-accepting groups (nitrobenzene, acetophenone) do not react under these conditions.

The proposed mechanistic alkylacylation scheme involves the generation of a carbenium ion from an alkane, alkylation of the arene by the carbenium ion with subsequent acylation of the alkylated aromatic compound [eqns. (6)–(8)].

$$\mathrm{R'H} + \mathrm{RCO^+Al_2X_7^-} \rightleftharpoons \mathrm{R'^+Al_2X_7^-} + \mathrm{RCHO} \quad (6)$$

† *Selected spectroscopic data*: ^{13}C NMR (Bruker WP200SY spectrometer, 50.3 MHz, rel. $SiMe_4$) for 2-Br-4-$Bu^tC_6H_3$ COMe (in CH_2Cl_2): 30.1 (q, ^1J 127 Hz, MeCO), 31.3 (q, ^1J 125, ^2J 4 Hz, Me_3C), 119.5 (m, ^2J 3, ^3J 6 Hz, C_{ar}–Br), 124.4 (dd, ^1J 160, ^3J 6 Hz, C_{ar}–H), 129.5 (d, ^1J 160 Hz, C_{ar}–H), 130.8 (dd, ^1J 160, ^3J 6 Hz, C_{ar}–H), 139.0 (t, ^3J 6 Hz, C_{ar}–COMe), 155.2 (d, ^2J 6 Hz, C_{ar}–Bu), 197.8 (s, MeCO); for *p*-$Bu^tC_6H_4$ COMe (in CCl_4): 25.8 (*Me*CO), 31.1 (Me_3C), 34.8 (*C*Me_3), 124.9 (C_{ar}–H), 128.0 (C_{ar}–H), 134.8 (C_{ar}), 155.4 (C_{ar}), 194.3 (CO).

Table 1 Single-stage alkylacylation of benzene and bromobenzene by alkanes and $RCO^+Al_2X_7^-$ complexes

Entry[a]	Alkane R'H	Arene C_6H_5Y	$RCO^+Al_2X_7^-$ **I** R	X	T/°C	t/min	Products, % from ArH $R'C_6H_3(Y)COR$	YC_6H_4COR
1	Bu^iH	C_6H_6	Me	Cl	0	30	62	35
2	Bu^iH	C_6H_6	Me	Cl	20	40	68	35
3	Bu^iH	C_6H_6	Me	Br	0	30	48	41
4	Bu^iH	C_6H_6	Pr	Br	0	30	54	23
5	Bu^iH	C_6H_6	Ph	Cl	0	30	35	18
6	Pen^iH	C_6H_6	Me	Br	20	5	87	3
7	Pen^iH	C_6H_6	Me	Br	20	5	65	12
8	Pen^nH	C_6H_6	Me	Cl	20	5	81	20
9	Pen^nH^b	C_6H_6	Me	Br	20	5	73	3
10	Isohexane	C_6H_6	Me	Cl	20	5	84	18
11	C-C_5H_9Me	C_6H_6	Me	Cl	20	5	58	11
12	Bu^iH	C_6H_5Br	Me	Br	0	60	82	4
13	Bu^iH	C_6H_5Br	Me	Cl	0	60	79	22
14	Pen^iH^b	C_6H_5Br	Me	Cl	0	20	74	Trace
15	Bu^nH^b	C_6H_5Br	Me	Cl	0	30	40	5

[a] [**I**]:[C_6H_5Y] = 12:1 in runs 1 and 2, 6:1 in the runs 3–6 and 8–15, 3–1 in the run 7. [b] Starting n-alkanes were initially kept with catalytical amounts of **I** for 3 h.

$$YC_6H_4 + R'^+ \xrightarrow{-H^+} YC_6H_4R' \quad (7)$$

$$YC_6H_4R' + RCO^+ \xrightarrow{-H^+} YC_6H_3(R')COR \quad (8)$$

Taking into account the high yield of products, good selectivity and simplicity of this single-stage reaction, availability of initial reagents and $RCO^+Al_2Cl_7^-$ complexes (prepared simply by mixing of acyl halides with aluminium halides)[1] we propose the method described here as a convenient route for laboratory syntheses. It is to be stressed that the traditional arene alkylation method by acid catalysts displays, as a rule, a low selectivity. The described *tert*-butylation of aromatic compounds by isobutane is of special interest as a method of introducing a directing group which provides the possibility for a selective aromatic substitution.[8,9]

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