Aroyldiazomethanes by Mild Acyl Cleavage of Diaroyldiazomethanes Over Al_2O_3

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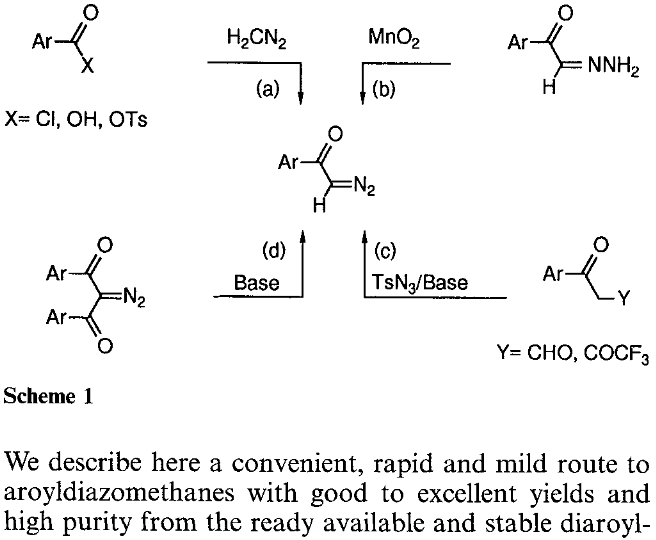
Dedicated to the memory of Prof. Irina K. Korobitsyna

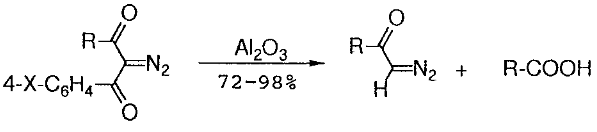
The synthesis of aroyldiazomethanes by the mild and rapid acyl cleavage of diaroyldiazomethanes on the surface of neutral alumina is reported.

The traditional synthesis of aroyldiazomethanes involves aroylation of diazomethane by the corresponding acid chlorides.[1] In some cases acids themselves[2] or other derivatives[3] have also been used [Route (a)]. Alternative methods are: (i) synthesis via acetophenone methyl group transformation to the hydrazone function, followed by MnO_2 oxidation [Route (b)],[4] or preparation of formyl[5] or trifluoroacetyl[6] derivatives, followed by a diazo transfer reaction [Route (c)]; and (ii) base-catalysed acyl cleavage of diaroyldiazomethanes [Route (d)] (Scheme 1).[7] However, these alternative methods have proved to be less than universal.



Scheme 1

We describe here a convenient, rapid and mild route to aroyldiazomethanes with good to excellent yields and high purity from the ready available and stable diaroyldiazomethanes. It was found that on contact with alumina diaroyldiazomethanes **1** readily underwent C–C cleavage resulting in the formation of aroyldiazomethanes **2** and benzoic acids **3**. The same processes can be observed on elution of the diazo compounds **1** on standard TLC plates coated with alumina.



1 **2** **3**

1	X	R
a	H	Ph
b	Me	4-Me-C_6H_4
c	Cl	4-Cl-C_6H_4
d	MeO	Ph
e	O_2N	Ph
f	O_2N	4-MeO-C_6H_4
g	H	Me

2,3	R
a	Ph
b	4-Me-C_6H_4
c	4-Cl-C_6H_4
d	4-MeO-C_6H_4
e	4-O_2N-C_6H_4
f	Me

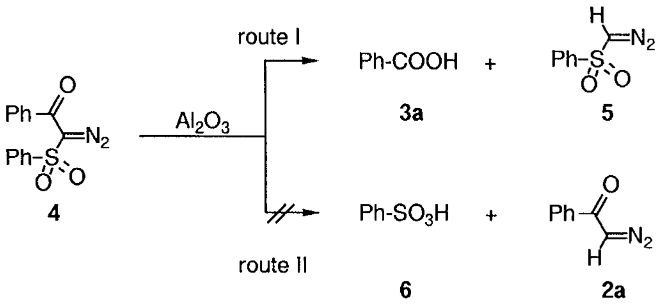
Scheme 2

Table 1. Acyl Cleavage of Diaroyldiazomethanes **1a–g** and **4**

Educt	Method	Products			
		Diazocomp.	Yield (%)	Acid(s)	Yield (%)
1a	A	**2a**	98	**3a**	98
	B	**2a**	94		
1b	A	**2b**	93	**3b**	97
	B	**2b**	87		
1c	A	**2c**	86	**3c**	97
	B	**2c**	75		
1d	A	**2a**	26	**3d**	26
		2d	58	**3a**	74
1e	A	**2a**	80	**3e**	77
		2e	17	**3a**	20
1f	A	**2d**	83	**3e**	91
		2e	5	**3d**	7
1g	A	**2a**	72[a]	**3f**	[b]
		2f	[b]	**3a**	22
4	A	**2a**	0	**6**	0
		5	66[c]	**3a**	72

[a] Unreacted **1g** (5%) was recovered.
[b] Not isolated.
[c] Unreacted **4** (26%) was recovered.

In practice, filtration of symmetrically substituted **1a–c** through a layer of Al_2O_3 over 15–60 min (Methods A and B) provided 75–98% yields of **2a–c** (see Table 1). An investigation of the crude products, after filtration, by NMR spectroscopy shows the purity to be more than 95%. The melting points of the crude products were only slightly lower than those reported in the literature.[5] No traces of starting diazoketones **1a–c** were detected either on slow elution through a chromatography column (Method B), or on rapid filtration through a thin layer of Al_2O_3 (Method A). Benzoic acids **3** in their anionic form are strongly retained on alumina and could not be eluted even with such polar solvents as methanol or water. However, they can be easily regenerated in high yields on acidification of the alumina followed by extraction with a suitable solvent. Similar results were found in the unsymmetrically substituted diazomethane series. Filtration of diaroyldiazomethanes **1d–f** through a layer of alumina (Method A) results in complete cleavage of the starting diazocompounds and provides mixtures of monosubstituted diazomethanes **2** in 84–97% yields (see Table 1). Due to the difference in adsorption, they can be easily separated by chromatography on alumina. Acyl cleavage and complete separation of the diazoketone mixtures formed were achieved simultaneously by slow elution through a chromatography column of Al_2O_3 (Method B). Replacement of one of the phenyl groups by a methyl group (diazoketone **1g**) or of a carbonyl function by a sulfonyl group (diazoketone **4**) prevented complete reaction and unreacted starting diazo compounds were recovered in 5 and 26% yields. Moreover the acetyl group proved to be more reactive than the benzoyl group since treatment of **1g** with Al_2O_3 resulted in the formation of **2a** predominantly. The sulfonyl group in **4** shows no reactivity towards Al_2O_3 (route II, Scheme 3) and acyl cleavage took place exclusively to afford the (diazomethyl) sulfone **5** (route I, Scheme 3).



Scheme 3

A similar result has been obtained in only one publication, where alumina was used for the cleavage of acetyl(*p*-nitrobenzenesulfonyl)diazomethane when the starting diazo compound was recovered in 20.6% yield and the resulting *p*-nitrobenzenesulfonyldiazomethane was isolated in 45% yield as the single product.[8] Also, the rapidity of acyl cleavage is subject to the nature of the sorbent used, since no reaction occurred using silica and slower rates were observed using magnesium oxide as alternatives to alumina (see Table 2). According to the known theories[9] dehydrated alumina will have on its surface partially exposed oxide anions which will react with one of the carbonyl groups of diazodiketones **1** in accordance with the charge value. We found no difference in the rate of degradation between symmetrically substituted diazoketones **1a–c**. In the unsymmetrically substituted compounds **1d–f** the carbonyl group next to the more electron donating aromatic ring was less reactive, and aroyldiazomethanes with the more electron donating aromatic ring were formed predominantely. However, the regioselectivity of the reaction was not complete even in the case when strong donor and acceptor groups (OMe and NO_2) were used simultaneously (compound **1f**). It is unclear why the acetyl group decreased the general reactivity of diazodiketone **1g** since it is known that the acetyl group is more reactive than the benzoyl group.[7] The sulfonyl group is less reactive towards mild alkali compared with a carbonyl group[8] and thus the cleavage of **4** on alumina shows an excellent chemoselectivity. We can recommend the route **4** → **5** for the preparation of diazomethyl sulfones.

Table 2. Comparison of Behaviour of **1a** in the Presence of Different Adsorbents[a]

Adsorbent	Method	Yield (%)	Ratio **1a**/**2a**
Al_2O_3[b]	C	75	0 : 100
Al_2O_3[c]	C	78	29 : 71
Al_2O_3[d]	C	79	42 : 58
MgO[e]	C	99	97 : 3
MgO[e]	B	99	94 : 6

[a] Yields of isolated products, ratio by high field NMR.
[b] Al_2O_3 (Lachema) column (L 100/250), neutral.
[c] Al_2O_3 (Woelm) TLC, neutral.
[d] Al_2O_3 (Woelm) TLC, acid.
[e] MgO (Krasnui Khimik) 99.99%, neutral, activated at 150 °C (4 h).

Aroyldiazomethanes **2** themselves are also not stable on alumina and underwent some transformations to unidentified products. The reactivity of these compounds [4-X-$C_6H_4C(O)CH=N_2$] towards alumina increased thus: $NO_2 \simeq H < Me < Cl < MeO$ (see Table 1).

The observed facts are in accordance with the acidic character of alumina, which on temperature activation will have on the surface partially exposed aluminium cations.[9] These Lewis acid centres will interact with negatively charged diazo-carbon atoms resulting in the formation of complex-type compounds and/or in decomposition of diazo compounds **2**. The formation of complexes between alumina and **2** was confirmed by the color of the sorbent during the elution, which was raspberry in the case of **5** and for similar compounds,[10] yellow in the cases of **2c, d, f**, and colorless in the cases of **2a, b, e, g**. No gas evolution was detected during the elution.

The work reported herein establishes a new approach to the synthesis of aroyldiazomethanes by the mild and rapid acyl cleavage of diaroyldiazomethanes on the surface of neutral alumina on filtration or column chromatography. The method is rather practical and efficient since all reactions occur with good yields. One would expect that the synthesis of diazomethylsulfones by the route **4** → **5** will also prove to be of great interest.

Organic solvents were dried and distilled before use. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX 400 instrument (^1H, 400.14 MHz; ^{13}C, 100.62 MHz). IR spectra were recorded on a PYE UNICAM SP^3-200 spectrometer. Analytical TLC was performed on Kieselgel 60 F 254 and aluminium oxide 60 F 254 neutral (Typ E) (Merck) plates. Aluminium oxide (Fluka) for chromatography (100–125 mesh, neutral) was used as a sorbent, which had been treated with pentane before use. Diaroyldiazomethanes **1a, g** were synthesized from the corresponding diaroylmethanes by the diazo transfer reaction catalysed with KF,[11] compounds **1b–f** and **4** were prepared analogously by the same method with the following yields (mp): **1b**, 96% (109–110 °C); **1c**, 95% (125–126 °C[12]); **1d**, 98% (oil); **1e**, 82% (100–101 °C[13]); **1f**, 84% (100–101 °C); **4**, 89% (124–125 °C[14]). Mps are uncorrected. For the new compounds satisfactory microanalyses were obtained: **1d** ($C_{16}H_{12}H_2O_3$), calc. C 68.57, H 4.32, N 9.99; found C 68.68, H 4.30, N 9.77; **1f** ($C_{16}H_{11}N_3O_5$), calc. C 59.08, H 3.41, N 12.91; found C 59.00, H 3.39, N 12.75.

Acyl Cleavage of Diazo Compounds 1a–g and 4 over Al_2O_3; General Procedure:

Method A (Filtration Through a Layer) and Method B (Column Chromatography):

To a solution of the corresponding diazodiketone **1** or **4** (150–180 mg) in dry CH_2Cl_2 (5 mL), Al_2O_3 (1 g) was added and the solvent was removed at r. t. under reduced pressure. The resulting solid was added to a layer of Al_2O_3 (6 g, 25 × 12 mm) (Method A)

Table 3. Selected Spectroscopic Data for Diazo Compounds **1**, **2**, **4** and **5**

Compound	^1H NMR ($CDCl_3$/TMS) δ[a]	^{13}C NMR ($CDCl_3$/TMS) δ	IR (CH_2Cl_2) ν ($C=N_2$) (cm^{-1})[b]
1a[c]			2147 s, 2113 s[13]
1b[d]	7.51 (m, 2H, H-2), 7.15 (m, 2H, H-3), 2.36 (s, 3H, Me)		2140 s, 2110 s[12]
1c	7.52 (m, 2H, H-2), 7.32 (m, 2H, H-3)	184.80 (C=O), 84.26 ($C=N_2$)	2149 s, 2113 s[12]
1d	7.60 (m, 2H, H-2′), 7.59 (m, 2H, H-2), 7.46 (m, 1H, H-4), 7.34 (m, 2H, H-3), 6.81 (m, 2H, H-3′), 3.82 (s, 3H, MeO)	186.70 (C=O), 184.94 (C′=O), 83.46 ($C=N_2$), 55.43 (MeO)	2147 s, 2110 s
1e	8.17 (m, 2H, H-2′), 7.69 (m, 2H, H-3′), 7.60 (m, 2H, H-2), 7.51 (m, 1H, H-4), 7.38 (m, 2H, H-3)	185.59 (C=O), 184.94 (C′=O), 85.28 ($C=N_2$)	2150 s, 2120 s[13]
1f	8.18 (m, 2H, H-2′), 7.71 (m, 2H, H-2), 7.61 (m, 2H, H-3′), 6.87 (m, 2H, H-3), 3.84 (s, 3H, MeO)	185.88 (C=O), 183.49 (C′=O), 84.08 ($C=N_2$), 55.59 (MeO)	2150 s, 2116 s
1g	7.64 (m, 2H, H-2), 7.58 (m, 1H, H-4), 7.49 (m, 2H, H-3), 2.58 (s, 3H, Me)	190.8 ($C=O_{alk}$), 185.08 ($C=O_{arom}$), 83.72 ($C=N_2$), 29.21 (Me)	2140 w, 2114 s[13]
2a[e]	7.76 (m, 2H, H-2), 7.54 (m, 1H, H-4), 7.44 (m, 2H, H-3), 5.92 (s, 1H, HCN_2)		2152 w, 2103 s[19]
2b	7.66 (m, 2H, H-2), 7.24 (m, 2H, H-3), 5.89 (s, 1H, HCN_2), 2.39 (s, 3H, Me)	186.16 (C=O), 53.87 ($C=N_2$), 21.58 (Me)	2150 w, 2102 s[19]
2c	7.70 (m, 2H, H-2), 7.42 (m, 2H, H-3), 5.88 (s, 1H, HCN_2)	184.95 (C=O), 54.40 ($C=N_2$)	2150 w, 2105 s[19]
2d[f]	7.73 (m, 2H, H-2), 6.92 (m, 2H, H-3), 5.88 (s, 1H, HCN_2), 3.84 (s, 3H, MeO)	185.19 (C=O), 55.48 (OMe), 53.47 ($C=N_2$)	2150 w, 2103 s[19]
2e	8.31 (m, 2H, H-2), 7.93 (m, 2H, H-3), 5.98 (s, 1H, HCN_2)	184.03 (C=O), 55.70 ($C=N_2$)	2158 w, 2108 s[19]
4	8.06 (m, 2H, H-2′), 7.65 (m, 1H, H-4′), 7.57–7.53 (m, 5H, PhCO), 7.43 (m, 2H, H-3′)	182.60 (C=O), 83.33 ($C=N_2$)	2130 w, 2108 s[14]
5[g]	7.88 (m, 2H, H-2), 7.63 (m, 1H, H-4), 7.58–7.54 (m, 2H, H-3), 5.31 (s, 1H, HCN_2)	57.64 ($C=N_2$)	2107 s[10]

[a] The aromatic protons form the AA′MXX′ (Ph group) or AA′XX′ (1,4-substituted ring) systems.

[b] Abbreviations: s = strong, w = weak.

[c] ^1H and ^{13}C NMR (with $CDCl_3$ as a solvent and as an internal standard) are reported (see ref.[16]).

[d] ^{13}C NMR (in $CDCl_3$) is reported (see ref.[17]).

[e] ^1H NMR (in $CDCl_3$) is reported (see ref.[7]), ^{13}C NMR (in $CDCl_3$) is reported (see ref.[18]).

[f] For the corresponding protons (HCN_2) $\delta = 5.39$, and (MeO) $\delta = 3.87$ (in $CDCl_3$) are reported (see ref.[3]).

[g] For the corresponding proton (HCN_2) $\tau = 4.61$ (in $CDCl_3$) is reported (see ref.[10]).

or to the chromatography column with Al_2O_3 (6 g, 10 × 90 mm) (Method B) and the following solvents were used consecutively as the eluents: pentane (100 mL); pentane/Et_2O (9:1, 100 mL; 4:1, 100 mL; 1:1, 100 mL); Et_2O (250 mL). The rate of elution was 30 mL/min (Method A) or 5 mL/min (Method B). Diazo compounds **2** and **5** were obtained upon concentration of corresponding fractions and the crude products were investigated by ^1H NMR. After recrystallisation from petroleum ether bp 40–70 °C, the following mps were found: **2a**, 48–49 °C; **2b**, 49–50 °C; **2c**, 114–115 °C; **2d**, 90–91 °C; **2e**, 114–115 °C (same as reported, see ref. 5); **5**, oil (same as reported, see ref. 10). Yields and spectroscopic data, see Table 1 and 3).

Method C (Stirring of the Suspension):

To a solution of 2-diazo-1,3-diphenylpropane-1,3-dione (**1a**; 102 mg, 0.41 mmol) in dry CH_2Cl_2 (5 mL) at r.t. the corresponding Al_2O_3 (1 g) or MgO (1 g) was added and the mixture was stirred for 28 h. The solids were filtered off, the solvent was removed at reduced pressure at r.t. and the product was analysed by TLC and ^1H NMR, see Table 2.

Isolation of Benzoic Acids 3:

The suspension of Al_2O_3 in water (10 mL) after the elution (Methods A, B) was acidified with excess of 5% aq HCl (30 mL) and extracted with Et_2O (7 × 10 mL). The combined organic extracts were dried (Na_2SO_4), concentrated at reduced pressure and the crude products were investigated by ^1H NMR. After recrystallisation from H_2O the following mps were found: **3a**, 120–121 °C; **3b**, 177–179 °C; **3c**, 240–242 °C; **3d**, 182–184 °C; **3e**, 237–239 °C (same as reported, see ref. 15). Yields, see Table 1.

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