Efficient *O*-Acylation of Anions of Monoimines from 1,2-Dicarbonyl Compounds

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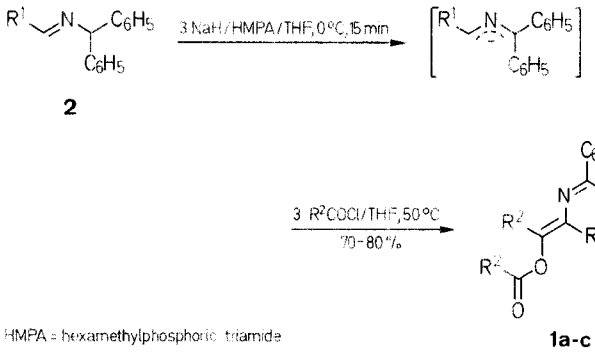
The facile synthesis of a series of 4-acyloxy-2-azabuta-1,3-dienes by the *O*-benzoylation and *O*-acetylation of the anions of the readily accessible monoimines of phenyl glyoxal, diacetyl, benzil, and 1-phenyl-propan-1,2-dione is described. This route provides easy access to 2-azabuta-1,3-dienes with substituents other than aryl groups on C-1, C-3, and C-4 of the diene skeleton.

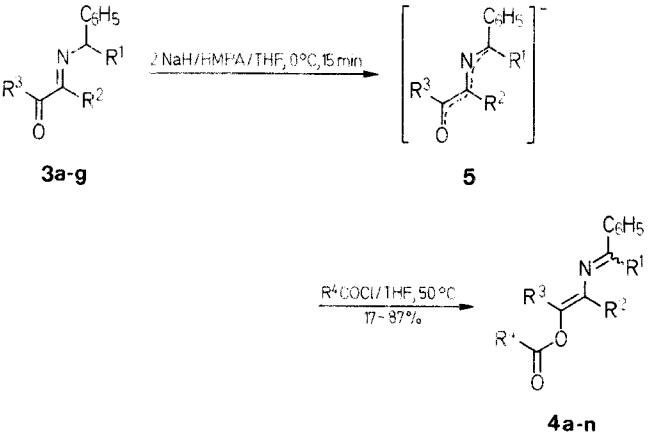
2-Azabuta-1,3-dienes have provided several thermal reactions of use in the synthesis of heterocyclic compounds such as 2-azabicyclo[2.2.1]hept-2-ene,[1] pyridines,[2,3] dihydropyridines,[2] and azoles.[3] We have also been interested in synthetic routes to heterocyclic compounds *via* reactions of 2-azabuta-1,3-dienes and have shown[4] that the azadienes of the type represented by **1** were photochemically reactive and could be converted in high yield into derivatives of 2,5-dihydro-oxazole. However, our novel and only synthetic method to date for the synthesis of 4-acyloxy-2-azabuta-1,3-dienes **1** does not allow for much variation in the substitution pattern on the diene skeleton[5] since the substituents on C-3 and C-4 must always be aryl and the aryl group on C-4 is always the same as the aryl ester group. This has obvious restrictions on the scope of the cyclization of the 2-azadienes and so a new method for synthesis was sought.

The limitations of the previous synthetic approach to the 2-azadienes is illustrated in the three new examples **1a–c** shown here (Table). These were prepared by the double aroylation of the anions generated by action of sodium hydride in hexamethylphosphoric triamide/tetrahydrofuran on the imines **2** (Scheme **A**). These results highlight the similarity in the substituents on the skeleton and also exemplify the fact that only aroyl chlorides can be used to aroylate



Scheme **A**

the anions from **2** and attempts to use acetyl chloride were completely unsuccessful. The new route to 2-azadienes is based on the facile *O*-acylation of carbanions derived from the known monoimines of 1,2-dicarbonyl compounds (Scheme **B**). The monoimines are readily prepared from the corresponding dicarbonyl compound and the appropriate amine. Thus the monoimines **3a–d** are prepared by reaction of benzhydryl amine with benzil,[6] 1-phenylpropan-1,2-dione,[7] biacetyl,[8] and phenyl glyoxal.[9] Other amines such as 1-phenylethylamine or benzyl amine can also be used to yield the corresponding monoimines **3e–g**.



3	R^1	R^2	R^3	3	R^1	R^2	R^3
a	C_6H_5	C_6H_5	C_6H_5	e	CH_3	H	C_6H_5
b	C_6H_5	CH_3	C_6H_5	f	CH_3	C_6H_5	C_6H_5
c	C_6H_5	CH_3	CH_3	g	H	C_6H_5	C_6H_5
d	C_6H_5	H	C_6H_5				

Scheme **B**

Table. Azidienes **1a–c** and **4a–n** Prepared

Product	R^1	R^2	R^3	R^4	Yield[a] (%)	m.p. (°C)	Molecular Formula[b] or Lit. m.p. (°C)	IR (KBr) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ (ppm) R^1	R^2	R^3	R^4	^{13}C-NMR ($CDCl_3$/TMS) δ (ppm) C=N	C=O	MS m/e (M^+)
1a	p-$CH_3C_6H_4$	C_6H_5	–	–	70	160–161	$C_{35}H_{27}NO_2$ (493.6)	1730	2.10	–	–	–	170.4	166.0	493
1b	p-ClC_6H_4	C_6H_5	–	–	72	147–148	$C_{34}H_{24}ClNO_2$ (514.0)	1730	–	–	–	–	170.3	165.3	512
1c	p-CNC_6H_4	p-CNC_6H_4	–	–	80	205–206	$C_{37}H_{22}N_4O_2$ (554.6)	1735	–	–	–	–	172.7	163.6	554
4a	C_6H_5	C_6H_5	C_6H_5	C_6H_5	69	156	$C_{34}H_{25}NO_2$ (479.3)[5]	1725	–	–	–	–	170.3	165.4	479
4b	C_6H_5	C_6H_5	C_6H_5	CH_3	69	170–172	$C_{24}H_{21}NO_2$ (355.4)	1745	–	–	–	2.01	170.5	169.7	417
4c	C_6H_5	CH_3	C_6H_5	C_6H_5	45	124–126	$C_{29}H_{23}NO_2$ (417.5)	1725	–	1.71	–	–	167.7	164.8	417
4d	C_6H_5	CH_3	C_6H_5	CH_3	20	oil[c]	–[d]	1750	–	2.06	–	1.60	169.14	167.7	355
4e	C_6H_5	CH_3	CH_3	C_6H_5	56	88–89	$C_{24}H_{21}NO_2$ (355.4)	1730	–	1.51	1.93	–	167.8	164.8	355
4f	C_6H_5	CH_3	CH_3	CH_3	28	85–86	$C_{19}H_{19}NO_2$ (293.4)	1745	–	1.33	1.81	2.03	167.8	168.9	293
4g	C_6H_5	H	C_6H_5	C_6H_5	69	139–140	$C_{28}H_{21}NO_2$ (403.5)	1730	–	7.01	–	–	167.4	165.2	403
4h	C_6H_5	H	C_6H_5	CH_3	57	121–122	$C_{23}H_{19}NO_2$ (341.4)	1735	–	6.78	–	2.23	167.3	169.4	341
4i	CH_3	H	C_6H_5	C_6H_5	33	125–126	$C_{23}H_{19}NO_2$ (341.4)	1725	2.40	–	–	–	164.7	165.2	341
4j	CH_3	H	C_6H_5	CH_3	17	74–75	–[d]	1745	2.40	–	–	2.33	164.6	169.8	279
4k	CH_3	C_6H_5	C_6H_5	C_6H_5	87	192–193	$C_{29}H_{23}NO_2$ (417.5)	1730	2.16	–	–	–	168.1	165.9	417
4l	CH_3	C_6H_5	C_6H_5	CH_3	38	87–89	$C_{24}H_{21}NO_2$ (355.4)	1745	2.16	–	–	2.10	168.1	169.7	355
4m	H	C_6H_5	C_6H_5	C_6H_5	77	144–145	$C_{28}H_{21}NO_2$ (403.5)	1715	7.98	–	–	–	159.7	165.3	403
4n	H	C_6H_5	CH_3	CH_3	47	109–110	$C_{23}H_{19}NO_2$ (341.4)	1740	7.98	–	–	2.15	159.9	169.4	341

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ± 0.10, H ± 0.10, N ± 0.10.
[c] Unstable.
[d] These azadienes are moisture sensitive and gave unreliable microanalytical data.

The validity of this synthetic route to azadienes was demonstrated by the conversion of imine **3a** into the azadiene **4a**. This product was shown to be identical in all respects to the azadiene **4a** produced using our original synthetic approach.[5] The major difference in this new approach to azadienes is the ability to trap the carbanions using acetyl chloride. Thus the anion from imine **3a** was trapped using acetyl chloride yielding the new azadiene **4b**. The monoimines **3b–g** all undergo the analogous facile *O*-acylation with varying degress of efficiency as shown in the Table.

The new azadienes produced show varying degrees of moisture sensitivity but generally they are quite stable and can be stored for prolonged periods under anhydrous conditions.

The azadienes **4i–n** have unknown geometry around the imine double bond but we are certain that the alkene moiety is *trans* as illustrated in structures **1** and **4**. This certainty follows on the determination of the X-ray crystal structure of azadienes **1**[10] and **4g**[11] where the alkene bond was clearly shown to be *trans*.

In our previous study where *O*-acylation also occurred it could be argued that steric factors such as arylation of C-1 and C-3 could inhibit aroylation at these sites. This possibility can be discounted since *O*-acylation still occurs even when C-1 and C-3 are unsubstituted. Thus the experiments described by us not only have value in synthesis but also answer in a qualitative fashion some of the questions relating to the electronic distribution in the anions **5**.

Melting points were determined on a Buchi 510D apparatus in open capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer 257 spectrophotometer and are reported in wave numbers. UV spectra were recorded on a Perkin-Elmer 124 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on Varian T60 and Varian FT-80A spectrometers respectively. The mass spectra were recorded on a Varian MAT-711 spectrometer. Sodium hydride used was supplied by Merck, the weights quoted are those for pure sodium hydride. Elemental analyses were performed by the Consejo Superior de Investigaciones Cientificas, Madrid.

4-Aroyloxy-1,1,3,4-Tetraaryl-2-azabuta-1,3-dienes 1a–c; General Procedure:

A dispersion of sodium hydride (744 mg, 31 mmol) in anhydrous hexamethylphosphoric amide (60 ml), is placed under an atmosphere of nitrogen in a dried 250 ml three necked roundbottomed flask containing a magnetic stirring bar. Subsequently, a solution of the corresponding imine (9 mmol) in anhydrous tetrahydrofuran (6 ml) is added at room temperature. The highly-coloured reaction mixture is stirred at ambient temperature for 15 min after which it is cooled to 0 °C using an ice bath. A 4.5 molar solution of the acid chloride in tetrahydrofuran (5 ml) is introduced in a dropwise fashion. After the addition of approximately an equimolar amount of the aroyl chloride (*ca.* 2 ml, 9 mmol) the colour of the carbanion disappeared. The solution is warmed to 50 °C and stirred for 20–30 min after which the colour reappeared. The reaction mixture is then cooled to 0 °C and the addition of the acid chloride (*ca.* 1 ml, 4.5 mmol) is resumed until the intense colour has been discharged. The process is repeated up to five times until the colour did not redevelop after stirring for 1 h at 50 °C. A total amount of *ca.* 27 mmol of the acid chloride has been added. The reaction mixture is poured into ether (200 ml) and ice, to avoid partial hydrolysis of the product by local concentration of base. The ether layer is separated and the aqueous solution is extracted with ether (5 × 50 ml) and dried with magnesium sulfate. Ether is removed by rotary evaporation to yield orange oily product mixtures, which are separted by flash chromatography[12] on silica gel using ether/hexane (1:9) as eluent. All the solid azadienes are recrystallized from ethanol.

4-Acyloxy-2-aza-1,3-dienes 4a–n; General Procedure:

In general the same fundamental procedure as the above is used for the synthesis of the dienes **4a–n**. The minor changes relate to the quantities involved. Thus sodium hydride (432 mg, 18 mmol) in hexamethylphosphonic amide (60 ml) is placed in the flask and the imine (9 mmol) in tetrahydrofuran (10 ml) is added. The acid chloride (11.2 mmol) as a

solution in tetrahydrofuran is added as before but only three cycles of addition of acid chloride are required. Work-up of the mixture is identical to the above procedure.

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