Thermal [2 + 3] cycloaddition of imino compounds to 3-aroylaziridines. Synthesis of imidazolidines

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3-Aroylaziridines react with a variety of imines and aryl-*N*-sulfonylimines in refluxing benzene to give imidazolidines in excellent yield. The orientation of the [2 + 3] cycloaddition of the intermediate azomethine ylids to the C=N double bond was proven by synthesis of specifically 5-deuterated imidazolidines. The reactions provide a convenient new general synthesis of imidazolidines.

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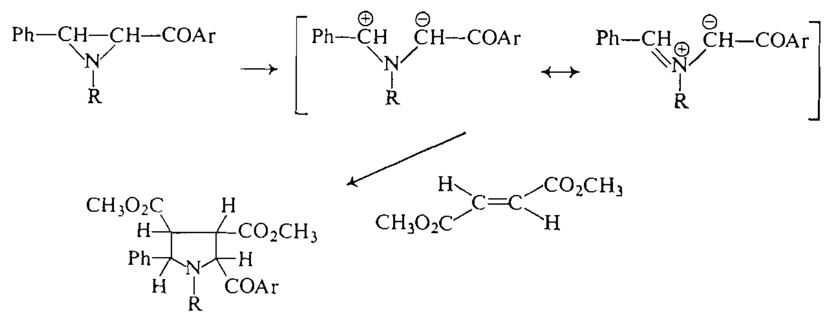
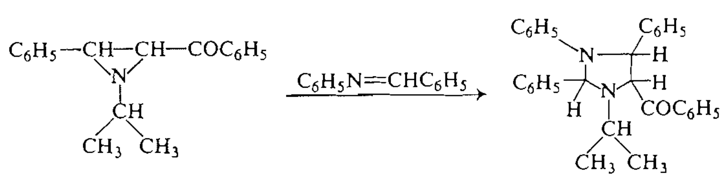
Many substituted aziridines will undergo thermal cleavage of the 2-3 bond to an azomethine ylid intermediate, and subsequent [2 + 3] cycloaddition can take place to the acetylenic bond and to activated alkenes, in many and stereospecifically (1–14).

We have reported the analogous thermally induced additions of 3-aroylaziridines to the polarized carbonyl bond of diphenylcyclopropenone with the formation of 4-aroyl-4-oxazolines (15) and to the C=S double bond of aryl isothiocyanates to form 4-aroyl-5-arylimino-4-thiazolines (16). In a continuing study of these additions to heteromultiple bonds, we report the [2 + 3] cycloaddition of 3-aroylaziridines to activated imino compounds which provides a new synthesis of imidazolidines.

Treatment of 3-benzoyl-1-isopropyl-2-phenylaziridine with an equimolar quantity of benzalaniline in refluxing toluene for 16 h, followed by chromatographic separation on alumina afforded the imidazolidine **1** as a white crystalline solid in 24% yield, m.p. 182°. The nuclear magnetic resonance (n.m.r.) spectrum of **1** shows the isopropyl methyl groups are non-equivalent, indicating proximity to an asymmetric center in accordance with the proposed structure. While the initial product consisted of an isomeric mixture corresponding to *cis* and *trans* arrangement of protons at the 4 and 5 positions as shown by the n.m.r. spectrum, only the isomer described above could be obtained in solid form. This was assigned the *cis* geometry at the 4,5 positions on the basis of an 8 Hz coupling constant for the AB





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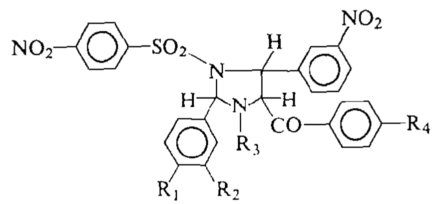
[1]NRCC Postdoctoral Fellow, 1967–1969.

TABLE I

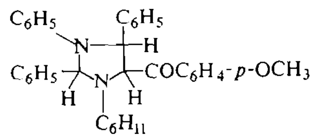
1-Alkyl-2,4-diaryl-5-aroyl-3-(*N*-arylsulfonyl)-imidazolidines (9)



No.	R_1	R_2	R_3	R_4	Melting point (°C)	Yield %	Observed C	Observed H	Observed N	Observed S	Observed Imidazole fragment ion	Calculated C	Calculated H	Calculated N	Calculated S	Calculated Imidazole fragment ion
a	H	H	CH_3	H	94–95	93	60.71	4.60	9.49	5.57	383.1272	60.82	4.86	9.78	5.60	383.1270
b	H	H	CH_3	CH_3	172	41	61.85	4.51	9.39	5.47	397.1424	61.44	4.47	9.55	5.47	397.1426
c	H	H	$(CH_3)_2CH$	H	159–160	61.5	61.95	4.84	9.57	5.27	411.1581	61.97	4.81	9.33	5.34	411.1583
d	H	H	$(CH_3)_2CH$	CH_3	156–157	58	62.32	4.84	9.01	4.96	425.1737	62.50	4.92	9.11	5.21	425.1739
e	H	NO_2	$(CH_3)_2CH$	H	173–175	51	59.91	4.62	10.24	4.74	456.1437	59.61	4.56	10.22	4.97	456.1434
f	H	H	$C_6H_5CH_2$	H	165–166	84	64.69	4.24	8.35	5.15	459.1584	64.79	4.35	8.64	4.94	459.1587
g	H	H	$C_6H_5CH_2$	CH_3	169	57	64.87	4.97	8.27	4.91	473.1741	65.24	4.56	8.45	4.84	473.1739
h	H	H	C_6H_{11}	H	160–161	94	63.73	5.09	8.53	5.40	451.1898	63.74	5.04	8.74	5.10	451.1896
i	H	H	C_6H_{11}	CH_3	165–167	54	64.33	5.54	8.54	4.75	465.2048	64.19	5.33	8.56	4.90	465.2052
j	NO_2	H	C_6H_{11}	H	183–184.5	14.5	59.91	4.62	10.24	4.61	496.1752	59.55	4.56	10.22	4.68	496.1747
k	H	NO_2	C_6H_{11}	H	112–113	80	59.85	4.68	9.98	4.58	496.1748	59.55	4.56	10.21	4.68	496.1747
l	H	H	C_6H_{11}	NO_2	160–161	79	59.83	4.93	9.38	4.49	496.1748	59.55	4.56	10.21	4.68	496.1747
m	CH_3O	H	C_6H_{11}	H	162–164	63	63.08	5.35	8.17	4.76	481.2000	62.67	5.11	8.35	4.78	481.2002
n	H	H	C_6H_{11}	CH_3O	152–153	34	62.58	5.39	8.16	4.78	481.1999	62.67	5.11	8.35	4.78	481.2002

quartet due to these protons in the n.m.r. spectrum (8). This configuration of **1** is evidently quite stable since no epimerization occurred, and no deuterium was incorporated at the 5 position upon refluxing **1** with deuterium oxide containing potassium carbonate. Specifically 5-deuterated imidazolidines could however be synthesized by a different method (*vide infra*).

Similarly, benzalaniline reacted with 3-*p*-anisoyl-1-cyclohexyl-2-phenylaziridine to give imidazolidine **2**



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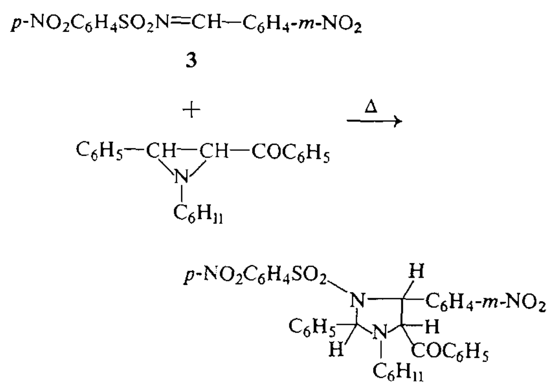
Addition of the more reactive *N*-(*m*-nitrobenzal)-*p*-nitrobenzenesulfonamide (**3**) to 3-benzoyl-1-cyclohexyl-2-phenylaziridine in refluxing benzene proceeded smoothly to give the imidazolidine **4** m.p. 160–161° in 94% yield.



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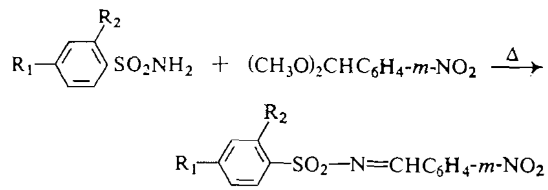
The scope of this new synthesis of imidazolidines was then explored. Several *N*-sulfonylimines were prepared by condensation of arylsulfonamides with the methyl acetal of *m*-nitrobenzaldehyde, following a method previously used by Kresze *et al.* (17, 18).

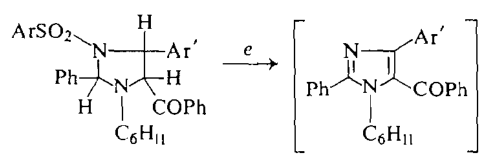
Excellent yields of imidazolidines were obtained by reaction of these sulfonylimines with a variety of aziridines containing different 2 and 3 substituents and with *N*-substituents of cyclohexyl, isopropyl, methyl, and benzyl. The sulfonylimines **3** and **5** gave excellent yields; **6** and **7** gave good to excellent yields, while **8**, containing



3 $R_1 = NO_2$, $R_2 = H$
5 $R_1 = —C{\equiv}N$, $R_2 = H$
6 $R_1 = Cl$, $R_2 = NO_2$
7 $R_1 = Cl$, $R_2 = H$
8 $R_1 = CH_3$, $R_2 = H$

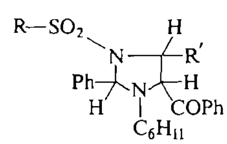
an electron releasing substituent in the arylsulfonyl group, was an exception and gave only poor yields. The analytical and spectral data on the product imidazolidines are summarized in Tables I–IV. Table V contains the analytical data on the new aryl-*N*-sulfonylimines.

The molecular ion cannot be observed in the high resolution mass spectrum of these imidazolidines. Fragmentation to the ion of the 5-aroylimidazole, although in low abundance relative to the aroyl ion, was highly characteristic of these compounds (see Tables I and III).



Three distinct structural and spectral problems connected with this synthesis of imidazolidines, required solution, namely, (*i*) orientation of addition, (*ii*) dependence of product configuration on the stereochemistry of the aziridine, i.e., possible stereospecificity of the reaction, and (*iii*) unambiguous assignment of the imidazolidine ring proton magnetic resonances, which consisted of one sharp singlet in the region of 6.0 δ and two weakly coupled broad singlets at higher field in the region of 5.5 and 5.1 δ.

The question of orientation of addition, i.e., whether the products are of type **9** or **10** is not a trivial one, since Huisgen has pointed out that in 1,3-dipole addition reactions, one may not safely



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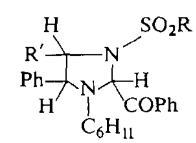

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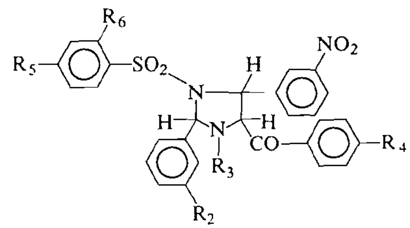
TABLE II

Spectroscopic properties of 1-alkyl-2,4-diaryl-5-aroyl-3-*N*-arylsulfonylimidazolidines (**9**)

No.	Infrared spectrum $CHCl_3$ (C=O)	Nuclear magnetic resonance spectrum $[(CD_3)_2SO]\delta$ Aryl protons	Ring proton 2	Ring proton 5	Ring proton 4	2-Aryl substituent	5-Aroyl substituent	*N*-Substituents	
a	1690	7.0–8.3(18H)m	5.80(1H)s	5.13(1H)s	4.93(1H)s	—	—	2.09(3H)s CH_3	
b	1693	6.9–8.1(17H)m	4.64(1H)s	4.84 AB quartet	5.62 (J = 8 Hz)		2.18(3H)s CH_3	1.93(3H)s CH_3	
c	1681	7.0–8.4(18H)m	5.84(1H)s	5.16(1H)s	4.98(1H)s	—	—	0.70, (3H)d; 0.58 (3H)d J = 6 Hz $(CH_3)_2$CH—	2.46–3.07(1H)m J = 6 Hz $(CH_3)_2CH$—
d	1677	7.0–8.4(17H)m	6.04(1H)s	5.30(1H)s	5.11(1H)s	—	2.37(3H)s CH_3	0.83(3H)d J = 6 Hz 0.72(3H)d J = 6 Hz $(CH_3)_2$CH—	2.61–3.65(1H)m $(CH_3)_2CH$
e	1684	7.0–8.5(17H)m	6.20(1H)s	5.53(1H)s	5.24(1H)s	—	—	0.83 (6H)d J = 4.5 Hz $(CH_3)_2$CH—	2.76–3.12(1H)m $(CH_3)_2CH$—
f	1690	6.7–8.3(23H)m	5.68(1H)s	5.07(1H)s	4.73(1H)s	—	—	3.25–3.81(2H)m Ph—CH_2	—
g	1687	6.7–8.3(22H)m	5.13(1H)s	4.86 AB quartet	5.84 (J = 8 Hz)	—	2.36(3H)s CH_3	3.48–4.10(2H)m Ph—CH_2	—
h	1681	7.1–8.9(18H)m	6.09(1H)s	5.39(1H)s	5.13(1H)s	—	—	0.37–1.87(10H)m C_6H_{11}	—
i	1675	7.2–8.6(17H)m	6.07(1H)s	5.33(1H)s	5.08(1H)s	—	2.40(3H)s CH_3	0.58–1.90(10H)m C_6H_{11}	—
j	1680	7.2–8.6(18H)m	6.19(1H)s	5.50(1H)s	5.16(1H)s	—	—	0.49–1.91(10H)m C_6H_{11}	—
k	1681	7.0–8.5(17H)m	6.04(1H)s	5.35(1H)s	5.01(1H)s	—	—	0.25–1.80(10H)m C_6H_{11}	—
l	1693	7.2–8.3(17H)m	6.02(1H)s	5.43(1H)s	5.22(1H)s	—	—	0.30–1.90(10H)m C_6H_{11}	2.9–3.3(1H)m 1-cyclohexyl CH
m	1680	7.27–8.50(17H)m	6.06(1H)s	5.37(1H)s	5.13(1H)s	3.79(3H)s —OCH_3	—	0.48–1.81(10H)m C_6H_{11}	—
n	1674	6.70–8.60(17H)m	6.13(1H)s	5.33(1H)s	5.12(1H)s	—	3.92(3H)s —OCH_3	0.38–1.90(10H)m C_6H_{11}	

TABLE III

1-Cyclohexyl-2,4-diaryl-5-aroyl-3-(*N*-arylsulfonyl)-imidazolidines (**9**)



No.	R_2	R_4	R_5	R_6	Melting point (°C)	Yield %	Observed C	Observed H	Observed N	Observed Cl	Observed S	Observed Imidazole fragment ion	Calculated C	Calculated H	Calculated N	Calculated Cl	Calculated S	Calculated Imidazole fragment ion
o	H	H	CH_3	H	Oil	13	68.96	6.10	6.86	—	5.00	451.1898	68.95	5.80	6.89	—	5.26	451.1896
p	H	H	Cl	NO_2	155–157	62	60.51	4.64	7.98	5.54	4.81	451.1898	60.45	4.63	8.30	5.25	4.75	451.1896
q	H	H	Cl	H	163–164	85	65.00	5.20	6.74	5.30	4.91	451.1903	64.80	5.11	6.67	5.60	5.09	451.1896
r	H	H	C≡N	H	181–182	72	67.86	4.98	9.31	—	5.05	515.1740*	67.72	5.20	9.03	—	5.00	515.1753
s	H	CH_3	Cl	NO_2	168–169	10.5	61.13	4.78	8.17	4.86	4.84	465.2046	60.99	4.83	8.13	5.15	4.65	465.2052
t	H	CH_3	C≡N	H	193–194	76.5	67.92	5.65	8.70	—	4.95	515.1740*	68.11	5.39	8.82	—	5.05	515.1753
u	H	NO_2	Cl	H	171.5–173	54.5	60.60	4.75	8.30	5.57	4.84	496.1748	60.47	4.63	8.30	5.25	4.75	496.1747
v	NO_2	H	C≡N	H	180–182	93	63.15	5.14	10.65	—	4.83	496.1753 560.1611*	63.14	4.70	10.52	—	4.82	496.1747 560.1604

*Fragment ion corresponding to loss of 5-aroyl moiety.

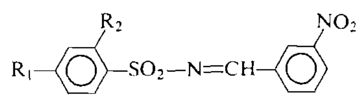
TABLE IV

Spectroscopic properties of 1-cyclohexyl-2,4-diaryl-5-aroyl-3-*N*-aryl-sulfonylimidazolidines (**9**)

Infrared		Nuclear magnetic resonance spectrum [$(CD_3)_2SO$]δ							
No.	(C=O) $CHCl_3$	Aryl protons	Ring proton 2	Ring proton 5	Ring proton 4	3-*N*-Aryl-sulfonyl substituent	5-Aroyl substituent	1-*N*-substituent	
o	1683	7.0–8.3(18H)m	6.10(1H)s	5.26(1H)s	5.02(1H)s	2.42(3H)s $CH_3C_6H_4SO_2$—	—	0.40–1.90 (10H) m C_6H_{11}	2.99–3.53 (1H) m $C_5H_{10}CH$—N<
p	1682	7.1–8.5(17H)m	6.31(1H)s	5.53(1H)s	5.31(1H)s	—	—	0.36–2.02 (10H) m C_6H_{11}	—
q	1680	7.2–8.3(18H)m	5.97(1H)s	5.28(1H)s	4.95(1H)s	—	—	0.50–1.87 (10H) m C_6H_{11}	—
r	1677	7.1–8.5(18H)m	5.98(1H)s	5.27(1H)s	5.03(1H)s	—	—	0.33–1.83 (10H) m C_6H_{11}	—
s	1674	7.2–8.3(16H)m	6.02(1H)s	5.38(1H)s	5.13(1H)s	—	2.37(3H)s CH_3	0.50–1.93 (10H) m C_6H_{11}	—
t	1673	6.9–8.1(17H)m	5.90(1H)s	5.21(1H)s	4.89(1H)s	—	2.32(3H)s CH_3	0.24–1.66 (10H) m C_6H_{11}	—
u	1688	7.1–8.3(17H)m	5.90(1H)s	5.34(1H)s	4.91(1H)s	—	—	0.31–1.85 (10H) m C_6H_{11}	—
v	1690	7.2–8.4(17H)m	6.13(1H)s	5.42(1H)s	5.07(1H)s	—	—	0.37–1.81 (10H) m C_6H_{11}	—

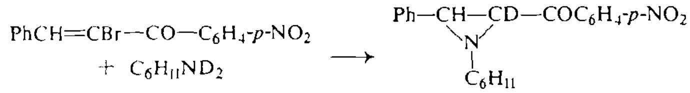
TABLE V

Aryl-*N*-sulfonylimines



R_1	R_2	Melting point (°C)	Yield (%)	C	H	N	Cl	S	Molecular ion (found)	C	H	N	Cl	S	Molecular ion (calcd.)
CH_3	H	120–122	83*	55.18	4.22	8.81	—	10.75	304.0519	55.25	3.98	9.21	—	11.03	304.0518
Cl	NO_2	152.5–154	91†	42.20	2.40	11.37	9.92	9.03	368.9814	42.23	2.18	11.37	9.59	8.67	368.9807
Cl	H	163–164	81.5†	48.06	2.78	8.59	10.87	9.68	323.9972	48.08	2.80	8.63	10.92	9.87	323.9972
C≡N	H	136–137	57†	53.32	2.82	13.25	—	10.16	315.0310	53.32	2.88	13.32	—	10.16	315.0314

*From benzene/hexane.
†From ethyl acetate.

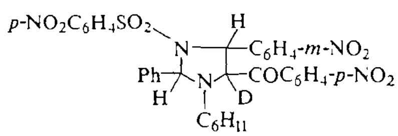


11

predict the orientation of addition on the basis of assignment of nucleophilic and electrophilic centers in the 1,3-dipole (19).

1-Cyclohexyl-3-deutero-2-phenyl-3-*p*-nitrobenzoylaziridine (**11**) was prepared by the reaction of 2-bromo-2-*p*-nitrobenzoyl-1-phenylethylene with cyclohexylamine-ND_2 in anhydrous ether. Examination of the integral of the aziridine ring protons in the n.m.r. spectrum showed, by comparison with the protium compound, about 50–60% deuterium incorporation at the 3-position.

Reaction of **11** with the sulfonylimine **3** gave an imidazolidine corresponding to **12** in structure.



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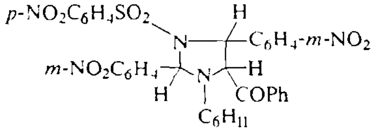
The n.m.r. spectrum of **12** showed a sharp singlet at 6.0 δ (1H), now assignable to the 2 proton; and two broad and weakly coupled singlets at 5.43 (0.75H) and 5.22(1H) δ now assigned unambiguously to the 5 and 4 imidazolidine ring protons respectively in **12**. An examination of several integrals showed an average of 24% deuterium incorporation in **12**.

The possible dependence of the course of the [2 + 3] cycloaddition on the stereochemistry of the aziridine was examined by reacting the *N*-sulfonylimine **3** in separate experiments with stereoisomerically pure samples of *cis*- and *trans*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine.

In both cases the only product isolated in good yield was the imidazolidine **13**.



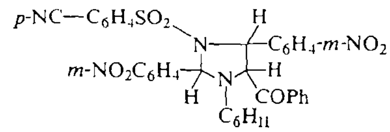
13

The n.m.r. spectrum showed a sharp singlet for the 2-imidazolidine proton at 6.04 δ and two broadened and weakly coupled singlets for the 4 and 5 protons at 5.01 and 5.35 δ respectively, and was therefore assigned the *trans* arrangement for the 4,5 protons because the small coupling constant is characteristic of *trans* coupling in a five membered ring (8).

Similarly reaction of *N*-(*m*-nitrobenzal)-*p*-cyanobenzenesulfonamide **5** with either *cis*- or *trans*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine gave only the *trans* imidazolidine **14**.

p-NC—$C_6H_4SO_2N{=}CHC_6H_4$-*m*-NO_2

5



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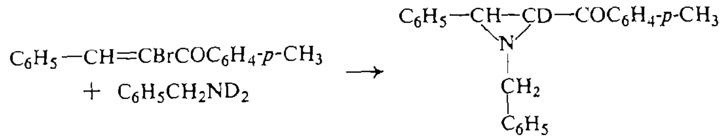
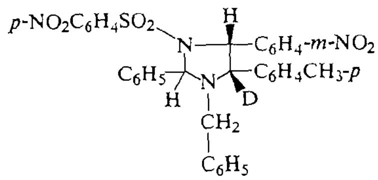
It seems probable that in these reactions, the [2 + 3] cycloaddition is stereospecific, but in the case of *cis*-imidazolidines is usually followed by post isomerization to the more stable *trans*-imidazolidine, as has been observed in other [2 + 3] cycloadditions with aziridines (1).

All the imidazolidines listed in Tables I and III which show small or zero 4,5 proton coupling have accordingly been assigned the *trans* configuration. The n.m.r. spectra of the imidazolidines obtained from *N*-benzyl and *N*-methylaziridines were different from the majority of the compounds listed in Tables I–IV, consisting of singlet at about 5.1 δ flanked by a strongly coupled AB quartet centered at ca. 4.9 and 5.8 δ with a coupling constant ($J \approx 8$ Hz) characteristic of *cis* vicinal proton coupling. An opposite orientation of addition of the azomethine ylids derived from these aziridines to the sulfonylimines was possible. Therefore 1-benzyl-3-deutero-2-phenyl-3-toluoylaziridine (**15**) was prepared as shown. Integration of the n.m.r. spectrum of **15** confirmed 71% deuterium incorporation in the 3-position of **15**. Reaction of **15** with the *N*-sulfonylimine **3** afforded an imidazolidine to which structure **16** was assigned unambiguously.

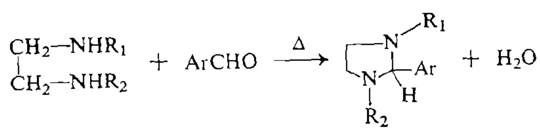




16

The n.m.r. spectrum of **16** showed a singlet at 5.13 (1H) δ and an AB quartet centered at 4.86(0.7H) and 5.84 (1H) δ, $J = 8$ Hz, and integration confirmed 29% deuterium incorporation in the 5-position of **16**. Therefore the orientation of addition of all the *N*-sulfonylimines to the 3-aroylaziridines is the same. The exceptional line positions for the heterocycle **16** and similar compounds derived from *N*-methylaziridine is attributed to screening factors operating in *cis* 4,5 configuration of the imidazolidine ring.

Imidazolidines are rare in the chemical literature and very few general syntheses exist (20–23). The principal method of synthesis consists of reaction of aldehydes with 1,2 diamines.



The [2 + 3] cycloaddition reactions described in this paper provide a convenient and versatile general synthesis of imidazolidines which nicely complements the existing routes in allowing for a wide variety of substituents in the imidazolidine ring.

Experimental

Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer model 421 spectrophotometer, and only the principal, sharply defined peaks are reported. Nuclear magnetic resonance spectra were recorded on Varian A-60 and A-100 analytical spectrometers. The spectra were measured on approximately 10–15% (w/v) solutions in $CDCl_3$, with tetramethylsilane as a standard. Line positions are reported in p.p.m. from the reference. Absorption spectra were recorded in 'spectro'-grade solvents on a Beckman DB recording spectrophotometer. Mass spectra were determined on an Associated Electrical Industries MS-9 double focussing high resolution mass spectrometer. The ionization energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15 000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for thin layer chromatography. Microanalyses were carried out by Dr. D. Daesslé, Organic Microanalysis Ltd., Montreal, Quebec and by Mrs. D. Mahlow of this department.

Reaction of 3-Benzoyl-1-isopropyl-2-phenylaziridine with Benzalaniline

A solution of 2.65 g (0.01 mole) of 3-benzoyl-1-isopropyl-2-phenylaziridine (16) and 1.81 g (0.01 mole) of benzalaniline in 15 ml of dry benzene was heated under reflux for 16 h when a deep orange color developed. The solution was passed down a column of Fisher alumina. Elution with benzene afforded one main fraction which upon evaporation of the solvent *in vacuo* gave a yellow gum, from which crystallized as a white powder, 5-benzoyl-1-isopropyl-2,3,4-triphenyl-(*cis*-4,5)-imidazolidine, 1.05 g (24% yield), m.p. 182°.

Anal. Calcd. for $C_{31}H_{30}N_2O$ (mol. wt. 446.2358): N, 6.27. Found (mol. wt. (mass spectrum) 446.2356): N, 6.20.

Infrared spectrum: ν_{max} (film): 1680 cm^{-1} (C=O). Nuclear magnetic resonance spectrum $\delta_{TMS}(CDCl_3)$: 0.85 and 1.15 (3H each, doublets $J = 6.5$ Hz, $(CH_3)_2CH$); 2.81–3.35 (1H, septet, $J = 6.5$ Hz, $(CH_3)_2CH$); AB quartet centered at 4.76 and 5.33 (2H, $J = 8$ Hz, 4 and 5 protons) 5.82 (1H, singlet, 2 proton); 6.60–8.40 (multiplet, 20H, aromatic protons).

A solution of 0.350 g (0.0008 moles) of 5-benzoyl-1-isopropyl-2,3,4-triphenylimidazolidine and 46 mg of potassium carbonate in a mixture of 10 ml of dry tetrahydrofuran and 3 ml of deuterium oxide was heated under reflux for 24 h, allowed to cool, and the organic material extracted with benzene. The combined extract was evaporated and the exchange process repeated with fresh deuterium oxide. Finally the recovered imidazolidine was purified by recrystallization from methanol m.p. 182°. An examination of the n.m.r. spectrum confirmed there had been no epimerization or deuterium incorporation.

Reaction of 3-p-Anisoyl-1-cyclohexyl-2-phenylaziridine with Benzalaniline

A solution of 3.35 g (0.01 mole) of 3-*p*-anisoyl-1-cyclohexyl-2-phenylaziridine (24) and 1.81 g (0.01 mole) of benzalaniline in 15 ml of dry benzene was heated under reflux for 48 h. The white solid which had precipitated 0.100 g (11% yield on the basis of unrecovered benzalaniline) was collected and purified by recrystallization from a large volume of benzene m.p. 182–184°, representing 5-*p*-anisoyl-1-cyclohexyl-2,3,4-triphenylimidazolidine.

Anal. Calcd. for $C_{35}H_{36}N_2O_2$ (mol. wt. 516.2777): C, 81.36; H, 7.03; N, 5.42. Found (mol. wt. (mass spectrum) 516.2773): C, 81.24; H, 6.96; N, 5.62.

Infrared spectrum ν_{max} ($CHCl_3$): 1677 cm^{-1} (C=O). Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 0.74–2.17 (10H, multiplet, cyclohexyl protons); 2.54–3.10 (1H, multiplet CH—N<); 3.73 (3H, singlet, —OCH_3); 5.51 (2H, singlet, 4,5 protons); 6.34 (1H, singlet, 2 proton); 6.38–7.80 (19H, multiplet, aromatic protons).

Preparation of Aryl-N-sulfonylimines

(i) m-Nitrobenzaldehyde Methyl Acetal

It was prepared in 85% yield by the method of Claisen (25), b.p. 139°/5 mm (lit. b.p. 145–146°/9 mm).

(ii) Preparation of N-(m-Nitrobenzal)-p-nitrobenzenesulfonamide

The following general method of preparation of this and similar aryl-*N*-sulfonylimines listed in Table V is due to Kresze *et al.* (18).

A mixture of 7.6 g (0.038 mole) of *p*-nitrobenzenesulfonamide and 8.2 g (0.042 mole) of *m*-nitrobenzaldehyde methyl acetal was heated to 150° until no more methanol was evolved. About 5 ml of 1:1 benzene/nitrobenzene mixture was added and the solution concentrated to ca. 20 ml and allowed to cool when the residue crystallized. The pure aryl-*N*-sulfonylimine was obtained by recrystallization from a 1:1 mixture of *o*-xylene and dimethylformamide in 84% yield, m.p. 212–214° (lit. 210–212° (18)).

General Method of Preparation of 1-Alkyl-2,4-diaryl-5-aroyl-3-(N-arylsulfonyl)-imidazolidines

The following experimental procedure is typical and was used to prepare all 22 imidazolidines listed in Tables I and III.

5-Benzoyl-1-cyclohexyl-3-(N-p-nitrobenzenesulfonyl)-4-m-nitrophenyl-2-phenylimidazolidine

A suspension of 1.53 g (0.005 mole) of 3-benzoyl-1-cyclohexyl-2-phenylaziridine and 1.68 g (0.005 mole) of *N*-(*m*-nitrobenzal)-*p*-nitrobenzenesulfonamide in 100 ml of dry benzene was stirred and heated under reflux for 24 h during which time the aryl-*N*-sulfonylimine gradually went into solution. The solvent was removed *in vacuo* and the residual yellow oil induced to crystallize as a pale yellow crystalline solid, 3.01 g (94% yield), m.p. 161–162°. The product was decolorised by treatment with charcoal in benzene and then purified by recrystallization from 3:2 hexane/benzene giving a white solid, m.p. 160–161°.

Anal. Calcd. for $C_{34}H_{32}N_4O_7S$: C, 63.74; H, 5.04; N, 8.74; S, 5.10. Found: C, 63.73; H, 5.09; N, 8.53; S, 5.40.

Mass spectrum calcd. for $C_{28}H_{25}N_3O_3$ (imidazole fragment ion): 451.1896. Found: 451.1898. Infrared spectrum ν_{max} ($CHCl_3$): 1681 cm^{-1} (C=O). Nuclear magnetic resonance spectrum δ_{TMS} ($(CD_3)_2SO$): 0.37–1.87 (10H, multiplet, cyclohexyl protons); 5.13 (1H, singlet, 4 proton); 5.39 (1H, singlet, 5 proton); 6.09 (1H, singlet, 2 proton); 7.1–8.7 (18H, multiplet, aromatic protons).

Preparation of 1-Cyclohexyl-2-phenyl-3-deutero-3-p-nitrobenzoylaziridine

(a) 2-Bromo-2-p-nitrobenzoyl-1-phenylethylene

A slurry of 4.13 g (0.01 mole) of 1,2-dibromo-1-phenyl-2-*p*-nitrobenzoylethane and 1.410 g (0.011 mole) of potassium acetate in 500 ml of 95% ethanol was heated under reflux for 12 h. The resulting pale yellow solution was evaporated to ca. 30 ml poured into 500 g of ice water and the organic material extracted with ether. The combined ether extract was dried ($MgSO_4$) and evaporated to give a pale yellow oil which readily solidified on cooling. Crystallization from benzene/heptane gave 2-bromo-2-*p*-nitrobenzoyl-1-phenylethylene, 2.1 g (63% yield), m.p. 108°.

Infrared spectrum ν_{max} ($CHCl_3$): 1670 (α,β unsaturated ketone) 1600 (C=C stretching); 1540 and 1350 cm^{-1} (aromatic —NO_2). Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 7.15 (singlet, 1H, —CH); 7.3–8.5 (multiplet, 9H, aromatic protons). Mass spectrum showed molecular ion at 331.

This material had previously been reported by Weygand as a pale yellow oil (26).

(b) Reaction of 2-Bromo-2-p-nitrobenzoyl-1-phenylethylene with Cyclohexylamine-ND_2

A solution of 2.495 g (0.05 mole) of redistilled dry cyclohexylamine (27) in 25 ml of anhydrous ether was shaken vigorously with 3 ml of deuterium oxide (99.97%), separated, and the ethereal layer washed with further quantities of deuterium oxide (5 × 1 ml), then removed and dried ($MgSO_4$). The ether solution was filtered directly into a dried ($MgSO_4$) solution of 1.66 g (0.005 mole) of 2-bromo-2-*p*-nitrobenzoyl-1-phenylethylene in 100 ml of ether. The mixture was stirred at room temperature for 24 h before being filtered to remove the precipitated cyclohexylamine hydrobromide 0.7 g; (78% of theoretical). The filtrate was washed with water and dried ($MgSO_4$). Evaporation of the ether gave a pale yellow oil which after trituration with hexane gave the solid aziridine 1.26 g (72% yield) pure enough for further use.

Mass spectrum: *m/e* 349 (3%); (undeuterated material $M - 1$); *m/e* 350 (44%) (undeuterated material M); *m/e* 351 (40%) (deuterated material M'); *m/e* 352 (9%) (deuterated material, $M' + 1$).

Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 1.0–2.0 (multiplet, 10H, cyclohexyl protons); 2.5 (multiplet, 1H, $C_5H_{10}CHN$); 3.2 and 3.55 (2 broad singlets 1.35 H; aziridine ring protons); 7.0–8.5 (multiplet, 9H, aromatic protons). The integral indicates about 60% deuterium incorporation of the 3 position.

Reaction between 1-Cyclohexyl-2-phenyl-3-deutero-3-p-nitrobenzoylaziridine and N-(m-Nitrobenzal)-p-nitrobenzenesulfonamide

Reaction of 0.329 g (0.93 mmole) of 1-cyclohexyl-2-phenyl-3-deutero-3-*p*-nitrobenzoylaziridine (containing about 60% deuterium incorporation) and 0.314 g (0.93 mmole) of *N*-(*m*-nitrobenzal)-*p*-nitrobenzenesulfonamide in the manner described in the general procedure above gave 1-cyclohexyl-5-deutero-3-(*N*-*p*-nitrobenzenesulfonyl)-4-*m*-nitrophenyl-5-*p*-nitrobenzoylimidazolidine in 41.3% yield, m.p. 160–161°. Examination of the n.m.r. spectrum showed the position and extent of deuterium incorporation. The product was identical in all other respects to the protium analogue listed in Table I.

Nuclear magnetic resonance spectrum: δ_{TMS}($CDCl_3$): 0.30–1.90 (10H, multiplet, cyclohexyl protons); 2.9–3.3 (1H, multiplet, CH—N); 5.22 (1H broad singlet, 4-ring proton); 5.43 (0.7H, broad singlet, 5 ring proton); 6.02

(1H, sharp singlet, 2-ring proton); 7.2–8.3 (17H, multiplet, aromatic proton).

Averaging of 6 integrals confirmed 24–25% deuterium incorporation at position 5.

cis- and trans-3-Benzoyl-1-cyclohexyl-2-m-nitrophenylaziridines

A solution of 50 g (0.121 mole) of 3-*m*-nitrophenyl-2,3-dibromopropiophenone (28) in 500 ml of benzene at 0° was treated dropwise with stirring with a solution of 35.9 g (0.363 mole) of cyclohexylamine in 100 ml of benzene. The mixture was stirred at room temperature for 24 h, the precipitated cyclohexylamine hydrobromide was collected, and the filtrate washed with water (3 × 100 ml) and dried ($MgSO_4$). The solvent was evaporated and the residual oil treated with 50 ml of benzene and 100 ml of heptane and chilled when 6.5 g of *cis*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine, m.p. 124–126° (17% yield), precipitated.

Anal. Calcd. for $C_{21}H_{22}N_2O_3$ (mol. wt. 350.1630): C, 72.00; H, 6.29; N, 8.00. Found (mol. wt. (mass spectrum) 350.1630): C, 71.70; H, 6.17; N, 8.02.

Infrared spectrum ν_{max} ($CHCl_3$): 1680 cm^{-1} (C=O of *cis* isomer). Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 1.00–2.05 (10H, multiplet, cyclohexyl); AB quartet centered at 3.44 and 3.24, J = 7 Hz (2H, *cis* 2,3 protons (30)); 7.2–8.3 (9H, multiplet, aromatic protons).

The filtrate from the above separation was treated with a further 100 ml of heptane and kept at 0° for 4 weeks when 17.5 g (41.4% yield) of *trans*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine, m.p. 82–84°, was obtained.

Mol. wt. Calcd. for $C_{21}H_{22}N_2O_3$: 350.1630. Found (mass spectrum): 350.1630. Infrared spectrum ν_{max} ($CHCl_3$): 1663 cm^{-1} (C=O of *trans* isomer). Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 0.89–2.02 (10H, multiplet, cyclohexyl protons); 2.30–2.87 (1H, multiplet, $CH{-}N\langle$); 3.64 (2H, singlet, *trans* 2,3 protons (30)); 7.3–8.3 (9H, multiplet, aromatic protons).

Reaction of N-(m-Nitrobenzal)-p-nitrobenzenesulfonamide with Stereoisomerically pure cis- and trans-3-Benzoyl-1-cyclohexyl-2-m-nitrophenylaziridines

(*a*) Reaction of 1.68 g (0.005 mole) of *N*-(*m*-nitrobenzal)-*p*-nitrobenzenesulfonamide and 1.75 (0.005 mole) of *cis*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine in the manner described in the general procedure above gave 2.73 g (80% yield) of 5-benzoyl-1-cyclohexyl-2,4-di(*m*-nitrophenyl)-3(-*N*-*p*-nitrobenzenesulfonyl)-imidazolidine, m.p. 112–113°.

(*b*) A similar reaction of 1.68 g (0.005 mole) of *N*-(*m*-nitrobenzal)-*p*-nitrobenzenesulfonamide and 1.75 g (0.005 mole) of *trans*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine gave the identical imidazolidine, 2.61 g (76.5% yield), m.p. 111–112°.

Reaction of N-(-m-Nitrobenzal)-p-cyanobenzenesulfonamide with Stereoisomerically pure cis- and trans-3-Benzoyl-1-cyclohexyl-2-m-nitrophenylaziridine

(*a*) Reaction of 1.662 g (0.0053 mole) of *N*-(*m*-nitrobenzal)-*p*-cyanobenzene sulfonamide and 1.846 g (0.0053 mole) of *cis*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine in the manner described in the general procedure above gave 3.25 g (93% yield) of 5-benzoyl-3-(*N*-*p*-cyanobenzenesulfonyl)-1-cyclohexyl-2,4-di(*m*-nitrophenyl)-imidazolidine, m.p. 180–182°.

(*b*) A similar reaction of 0.784 g (0.0025 mole) of *N*-(*m*-nitrobenzal)-*p*-cyanobenzenesulfonamide and 0.871 g (0.0025 mole) of *trans*-3-benzoyl-1-cyclohexyl-2-*m*-nitrophenylaziridine gave the identical imidazolidine 1.257 g (68% yield), m.p. 180–182°.

Preparation of 1-Benzyl-3-deutero-3-p-toluoyl-2-phenylaziridine

A solution of 7.64 g (0.070 mole) of redistilled dry benzylamine in 70 ml of anhydrous ether was shaken vigorously with 9 ml of deuterium oxide (99.97%), separated, and the organic layer washed with further quantities of deuterium oxide (4 × 3 ml), then removed and dried ($MgSO_4$). The ether solution was filtered directly into a dried ($MgSO_4$) solution of 4.30 g (0.014 mole) of 2-bromo-2-*p*-toluoyl-1-phenylethylene (26) in 200 ml of ether. The mixture was stirred at room temperature for 24 h before being filtered to remove the precipitated benzylamine hydrobromide ca. 1 g. The filtrate was washed with water and dried ($MgSO_4$). Evaporation of the ether gave a yellow oil which upon trituration with 2:1 heptane/benzene gave 1-benzyl-3-deutero-3-*p*-toluoyl-2-phenylaziridine 2.105 g (45% yield), m.p. 108–110° (lit. (29) m.p. 113–114°). Examination of the n.m.r. spectrum showed the position and extent of deuterium incorporation. The aziridine was identical in all other respects to the protium compound.

Nuclear magnetic resonance spectrum δ_{TMS}($CDCl_3$): 2.30 (3H, singlet, aryl CH_3); 3.30 (1.3H, multiplet, aziridine ring protons). AB quartet centered at 3.73 and 4.05, J = 14 Hz (2H, $PhCH_2$); 7.0–8.0 (14H, multiplet, aromatic protons). Averaging of integrations confirmed 71% deuterium incorporation in position 3.

Reaction between 1-Benzyl-3-deutero-3-p-toluoyl-2-phenylaziridine and N-(m-Nitrobenzal)-p-nitrobenzenesulfonamide

Reaction of 0.290 g (0.89 mmole) of 1-benzyl-3-deutero-3-*p*-toluoyl-2-phenylaziridine (71% deuterium incorporation) and 0.300 g (0.89 mmole) of *N*-(*m*-nitrobenzal)-*p*-nitrobenzene sulfonamide in the manner described in the general procedure above gave 1-benzyl-5-deutero-3-(*N*-*p*-nitrobenzenesulfonyl)-4-*m*-nitrophenyl-5-*p*-toluoylimidazolidine, 0.231 g (39.3% yield), m.p. 160°. Examination of the n.m.r. spectrum showed the position and extent of deuterium incorporation. The product was identical in all other respects to the protium analogue listed in Table I.

Nuclear magnetic resonance spectrum: δ_{TMS} ($(CD_3)_2SO$): 2.36 (3H, singlet, aryl CH_3); 3.48–4.10 (2H, quartet, J = 15 Hz, $PhCH_2$); AB quartet centered at 4.86 (0.7H) and 5.84 (1H), J = 8 Hz, (now assigned unambiguously to the 5 and 4 imidazolidine ring protons respectively); 5.13 (1H, singlet, 2 proton); 6.7–8.3 (22H, multiplet, aromatic protons). Averaging of the integrations confirmed 29% deuterium incorporation in position 5.

Acknowledgments

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