2-Amino-1-azetines, a New Class of Strained Amidines

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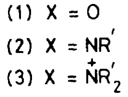
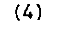
Summary The reaction of amide chlorides with *N*-benzhydrylimines yields azetidin-2-iminium salts, which, upon hydrogenolysis and treatment with base, are converted into 2-amino-1-azetines.

IN spite of much work on the β-lactams (**1**), very few studies have been devoted to the corresponding imines (**2**) and iminium salts (**3**). We have previously described[1,2] a procedure for the synthesis of (**3**). However, the method

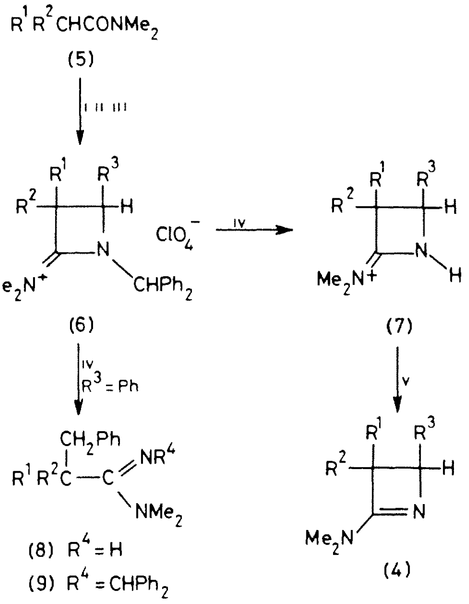


(1) $X = O$
(2) $X = NR'$
(3) $X = \overset{+}{N}R'_2$



(4)

did not apply to the synthesis of *N*-unsubstituted azetidin-2-iminium salts (**3**) (R = H) which are potential sources of the virtually unknown[3] 2-amino-1-azetines (**4**)



Scheme 1
- **a** $R^1 = R^2 = Me$, $R^3 = Ph$
- **b**, $R^1 = Me$ $R^2 = H$, $R^3 = Ph$
- **c** $R^1 = H$, $R^2 = Me$, $R^3 = Ph$
- **d**, $R^1 = R^2 = H$, $R^3 = Ph$
- **e**, $R^1 = R^2 = Me$, $R^3 = CO_2Me$
- **f** $R^1 = Me$, $R^2 = H$, $R^3 = CO_2Me$
- **g**, $R^1 = H$, $R^2 = Me$, $R^3 = CO_2Me$
- **h**, $R^1 = R^2 = H$ $R^3 = C_6H_{11}$

Reagents i, $COCl_2$ ii $R^3CH{=}NCHPh_2$–NEt_3, iii, $NaClO_4$ iv, H_2, Pd/C–MeOH, v, KOH–MeOH or DBN–Et_2O (DBN = 1,5-diazabicyclo[4 3 0]non-5 ene)

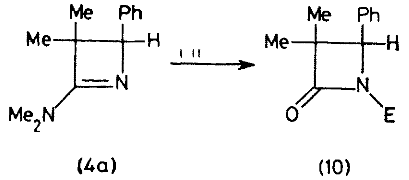
We report here a simple route to these new strained amidines The *N*-benzhydrylazetidin-2-iminium perchlorates (**6**) were readily obtained from the reaction of the amides (**5**) with phosgene[4] followed by treatment of the crude amide chlorides with a Schiff's base and triethylamine Hydrogenolysis of (**6**) yielded the *N*-unsubstituted azetidin-2-iminium salts (**7**) However, when R^3 = phenyl, cleavage of the benzylic C(4)–N bond leading to (**8**) or (**9**) competed with removal of the benzhydryl group, at least for the less substituted azetidin-2-iminium salts (**6c**) and (**6d**)

Finally, treatment of (**7**) with bases quantitatively yielded the 2-amino-1-azetines (**4**) (Scheme 1, Table) as stable liquids, fully characterized by their spectral properties The azetines (**4**) react readily with alkylating and acylating agents, or with Michael acceptors such as acrylonitrile, to give, after hydrolysis,[1] the *N*-substituted azetidin-2-ones (**10**) (Scheme 2)

Table % Yields of products obtained in the preparation of the 2-amino-1-azetines (**4**)

	Adducts[a] (**6**)	Hydrogenolysis products[a] (**7**)	(**8**)	(**9**)	2-Amino-1-azetines (**4**)
a	80	80	0	0	100[d]
b	90[b]	100	0	0	100[d]
c		0	70	0	—
d	88	0	23	48	—
e	60	100	0	0	100[e]
f	20[c]	92	0	0	100[e]
g	25[c]	99	0	0	100[e]
h	80	95	0	0	100[d]

[a] Yields are for the purified perchlorates [b] Mixture of *cis* (25%) and *trans* (75%) isomers [c] Yields are for the pure isomers separated by crystallization in ethanol [d] From the reaction of (**7**) with KOH in MeOH [e] From the reaction of (**7**) with DBN in diethyl ether



Scheme 2
- **a**, E = Me (90% yield)
- **b**, E = $CH_2CH{=}CH_2$ (95% yield)
- **c** E = PhCO (50% yield)
- **d** E = CH_2–CH_2–CN (70% yield)

i, (a) MeI, (b) $CH_2{=}CH$–CH_2Br, (c) PhCOCl (d) $CH_2{=}CH$–CN, ii, KOH–MeOH or NaOH aq –CH_2Cl_2

The sequence (**5**)—(**10**) represents a potentially useful method for the synthesis of a variety of *N*-substituted azetidinones

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