

DIENAMIDES AS VERSATILE PRECURSORS OF POLYCYCLIC PYRIDINES AND ISOQUINOLINES

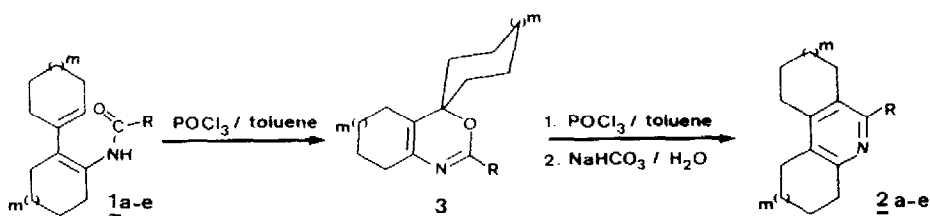
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Abstract - The treatment of aromatic and aliphatic dienamides with a cyclodehydrating agent (POCl₃) leads to a variety of polycyclic pyridines and isoquinolines.

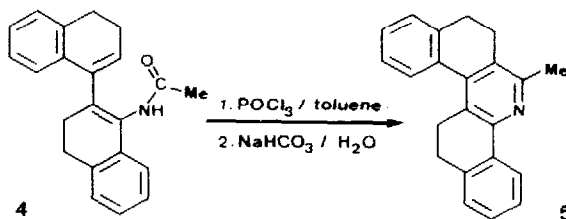
Enamides are undoubtedly a class of conjugated systems possessing a wide variety of synthetic interests¹ but paradoxically dienamides have been the subject of only very few and fragmental studies. We have recently developed a general and efficient method for the elaboration of diversified bicyclic aromatic and aliphatic dienamides which recommends the direct condensation under acidic conditions of 2-(cycloalken-1-yl)cycloalkanones with various aromatic and aliphatic primary amides^{2,3}. We have subsequently established that these dienamides can be regarded as excellent precursors of oxazines^{2,3}, thiazines and selenazines⁴ with a spiroheterocyclic framework. The present paper deals with the synthetic potential of these polyenic compounds and their use in the elaboration of a variety of polycyclic pyridines and isoquinolines.

Thus the treatment of the bicyclic dienamides 1a-d with a standard cyclodehydrating agent such as phosphorus oxychloride gives rise to the polyhydrophenanthridines 2a-d with fairly good yields (Scheme 1, Table).



Scheme 1

This particular reactivity of aromatic and aliphatic dienamides is not conditioned by the size of the different ring contained in the models as exemplified by the annelation of 1e (Table). It is equally insensitive to the geometry of the parent model since the treatment of the polycyclic dienamide 4⁴ with POCl₃ affords the cyclodehydrated product 5 with an excellent yield (Scheme 2, Table).



Scheme 2

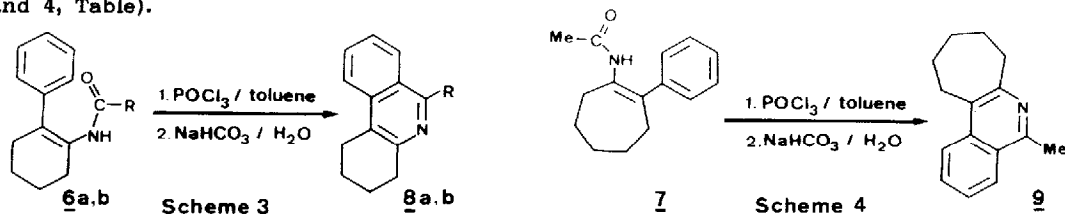
Table - Results of the Different Reactions of the Dienamides 1a-e, 4, 6a,b and 7⁵

Product	R	m	Reaction Time ^a	Compounds (Ratio, yield%)	mp °C
<u>1a</u>	Ph	1	15min	<u>2a</u> , <u>3a</u> (60/40, 69)	97-98 (<u>3a</u>)
			30min	<u>2a</u> , <u>3a</u> (83/17, 82)	-
<u>1b</u>	pOCH ₃ Ph	1	1h	<u>2a</u> (98/-, 92)	81-82
			2h	<u>2b</u> (79)	96-98
<u>1c</u>	CH ₃	1	1h	<u>2c</u> (87)	60-62
<u>1d</u>	CH ₂ Ph	1	1h	<u>2d</u> (85)	72-74
<u>1e</u>	CH ₃	3	1h30	<u>2e</u> (82)	64-66
<u>3a</u>	Ph	1	1h	<u>2a</u> (89)	-
<u>4</u>	Ph		2h	<u>5</u> (88)	229-230
<u>6a</u>	Ph		2h	<u>8a</u> (93)	99-100
<u>6b</u>	pOCH ₃ Ph		2h	<u>8b</u> (91)	102-103
<u>7</u>			2h	<u>9</u> (87)	98-99

a) Dienamide (4mmol) is refluxed in a mixture POCl₃ (10 mol. equiv.)-toluene (25 ml)

It is likely that the thermal reactions involve a large participation of the spirooxazines 3. Indeed, as it is reported in Table for the dienamide 1a, an intermediate analysis at different reaction times clearly indicates the presence of the spirocyclic iminoether 3a. The prolonged chemical processing of 1a leads exclusively to the octahydrophenanthridine 2a. The obtention of this fused heterocyclic compound by direct treatment of the oxazine 3a with phosphorus oxychloride corroborates this hypothesis.

The introduction of an aromatic unit in the models does not notably modify their chemical behavior as illustrated by the annelation of the dienamides 6a,b³ and 7⁵ (Scheme 3 and 4, Table).



The reactions reported here undoubtedly reflect the great versatility of aromatic and aliphatic dienamides, a class of scarcely studied compounds. Furthermore they illustrate a new and promising extension of the Bischler-Napieralski synthesis⁷ since one can elaborate a wide variety of polycyclic pyridine ring systems from easily available precursors. These fused nitrogen compounds are now only accessible by a few limited and sophisticated methods⁸.

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