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CYCLOADDITIONS OF 4-OXAZOLIN-2-ONES

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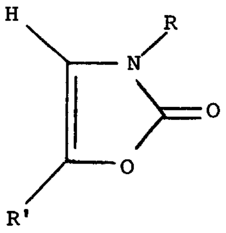
The β-amino alcohol structural unit is a key component of many important natural and synthetic substances. This group can also serve as a key precursor in further synthetic transformations. The classical routes to β-amino alcohols from epoxides and amino ketones have recently been supplemented by Sharpless's cis oxyamination procedure.[1] In this communication we would like to report a new approach based on cycloadditions of 4-oxazolin-2-ones.[2]



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a $R=R'=H$

b $R=COCH_3$, $R'=H$

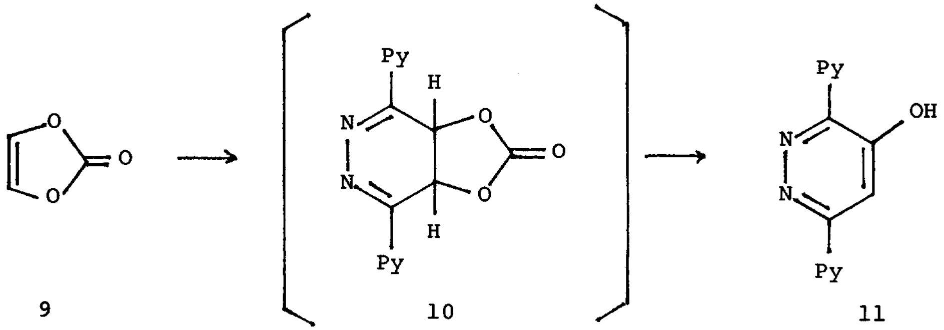
c $R=H$, $R'=C_6H_5$

d $R=COCH_3$, $R'=C_6H_5$

Reaction of 1a with an equivalent amount of hexachorocyclopentadiene gave 1:1 cycloadduct 2a.[6] Similar adducts were obtained, for example, from o-chloranil (3a) and 3,6-di(2'pyridyl)-1,2,4,5-tetrazine (4a) as indicated in Table I. In general, successful reactions of 1a were obtained with electron deficient dienes.[7] This reactivity characteristic and the instability of 1a at higher temperatures prohibited successful additions to more electron rich dienes (e.g. anthracene and cyclopentadiene).

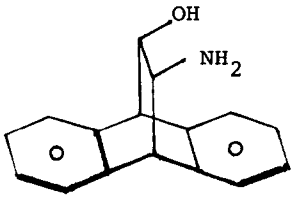
Acetylation of 1a converted it to a less electron rich dienophile. Thus, although 1b also reacted with 3,6-di(2'pyridyl)-1,2,4,5-tetrazine, forcing conditions were required and the product, 4b, decarboxylated under the reaction conditions to give 5b. Dienophile 1b was also added to cyclopentadiene and anthracene to give 6b and 7b respectively. Even the sterically hindered 1c,[8] which would not react with either type of diene, reacted as its acetyl derivative, 1d, with anthracene.

The reactivity of 1b appears to resemble that of vinylene carbonate (9). In contrast to 1a, 9 did not react at room temperature with 3,6-di(2'pyridyl)-1,2,4,5-tetrazine. Reaction of 9 with this dienophile did occur at 80° with a required reaction time in excess of 24 hours. The initial adduct, 10, was unstable under these conditions and decarboxylated to give 11.



9 10 11

Hydrolyses of the acetyl derivatives and oxazolidinones occur readily. For example, 7b could be converted to 7a (mp. 231-2°) in 91% yield at room temperature in ethanolic aqueous ammonia. Hydrolysis in refluxing ethanolic aqueous sodium hydroxide of either 7a (89%) or 7b (74%) yielded amino alcohol 12.



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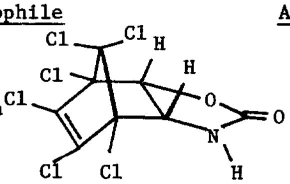
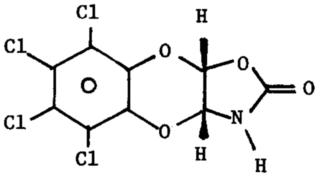
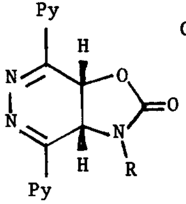
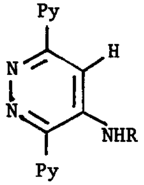
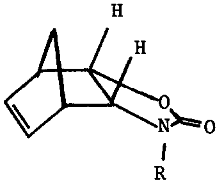
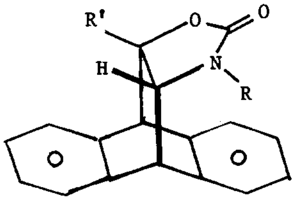
Our results demonstrate the utility and versatility of this synthetic approach to amino alcohols. Further application of these reactions and the chemistry of these adducts will be reported later.

TABLE I

Dienophile	Adduct	Conditions	mp	Yield
1a	 2a	ethyl acetate 79 hr. 77°	275-85°(dec.)	54%
1a	3a 	benzene 24 hr. 80°	265-75°(dec.)	86%
1a	 4a	ethyl acetate 24 hr. 25°	210-51°(dec.)	95%
1b	5b 	toluene 46 hr. 111°	242-43°	56%
1b	 6b	o-xylene 5 hr. 144°	oil	63%
1b	 7b	o-xylene 72 hr. 144°	189.5-90.5°	87%
1c	8c	p-cymene 60 hr. 177°	210.5-11.5°	67%

REFERENCES AND NOTES

1. K.B. Sharpless, D.W. Patrick, L.K. Truesdale, and S.A. Biller, J. Am. Chem. Soc., 97, 2305 (1975); K.B. Sharpless, A.O. Chong, and K. Oshima, J. Org. Chem., 41, 177 (1976).

2. The 4-oxazolin-2-ones 1a and 1b have recently been reported by Hartmann and co-workers.[3] We have prepared 1a by an alternate route, which will be reported later, modeled after Marckwald's preparation of 4-imidazolin-2-one.[4,5]

3. K.-H. Scholz, H.-G. Heine, and W. Hartmann, Justus Leibigs Ann. Chem., 1319 (1976).

4. W. Marckwald, Ber., 25, 2354 (1892).

5. R. Duschinsky and L.A. Dolan, J. Am. Chem. Soc., 68, 2350 (1946).

6. Satisfactory spectroscopic and microanalytic data were obtained for all compounds reported except 4a and 6b. Adduct 4a was too insoluble to characterize by nmr spectroscopy. Thermolysis of 4a in refluxing toluene afforded a mixture of 4-aminopyridazine (5a) and 4-hydroxy-pyridazine (11). Adduct 6b was smoothly deacylated to 6a at room termperature in ethanolic aqueous ammonia. Satisfactory spectroscopic and microanalytic data were obtained for 5a, 6a, and 11.

7. J. Sauer and H. Wiest, Angew. Chem. Intern. Ed. Engl., 1, 269 (1962); J. Sauer, ibid, 6, 16 (1967).

8. J. Strumza and D. Ben-Ishai, J. Heterocycl. Chem., 3, 459 (1966).