

## BENZYLIDENEMALONALDEHYDES: SYNTHESIS OF 4-ARYL-2-DIMETHYLAMINO-4H-1,3-OXAZINE-5-CARBOXALDEHYDE

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Reaction of substituted benzylidenemalonaldehydes *Ia–Ic* and thienylmethylenemalonaldehyde (*Id*) with dimethylcyanamide in boiling benzene afforded the corresponding 4-aryl-2-dimethylamino-4H-1,3-oxazine-5-carboxaldehydes *III*. Electronic requirements for this cyclization reaction are discussed in relation with general rules and further applicability.

Recently, we have elaborated a general approach to benzylidenemalonaldehydes and related compounds<sup>1–5</sup>. Besides their interesting physico-chemical properties, these novel unsaturated conjugated dialdehydes are extraordinarily reactive with nucleophilic reagents and in cycloaddition reactions<sup>6</sup>. We studied their cycloadditions with a wide variety of olefinic compounds and prepared thus many aldehydes of the dihydropyran type. Since the high reactivity of benzylidenemalonaldehydes promised their possible use in the synthesis of new heterocyclic compounds, we included into our cycloaddition studies some less frequent  $2\pi$ -components, particularly compounds containing a nitrile group.

Although the nitrile group has been already known to participate in many syntheses of pyridine compounds<sup>7</sup>, the reaction conditions and complexity make the obtained results only of limited validity. It has been found that the addition of tetraphenylcyclopentadienone to benzonitriles<sup>8</sup> is favourably influenced by a halogen atom in position 4 of the benzonitrile, whereas a dimethylamino group in this position suppresses this reaction. A markedly favourable effect of electronegative substituents was observed in the synthesis of 2-trifluoromethylpyridine from 1,3-butadiene and trifluoroacetonitrile<sup>9</sup>. Cycloaddition reactions of  $\alpha,\beta$ -unsaturated carbonyl compounds, the most common heterodienes<sup>10</sup>, were classified as Diels–Alder reactions with reversed electronic demands<sup>11</sup>. The available data on the reactivity of benzylidenemalonaldehydes lead to the conclusion that these derivatives are stronger electron acceptors than  $\alpha,\beta$ -unsaturated monocarbonyl compounds. On the basis of analogies<sup>12</sup> one can expect that the cycloaddition reaction would be facilitated by an enhanced electron donor character of the  $2\pi$ -component. For our studies



oxazine part of the molecule. Two of them, a typical aldehyde proton signal in the region  $\delta$  9.3 and the O—CH= proton signal at about  $\delta$  7.3, are practically independent of the substituent in the ring and they are located similarly as the signals of analogous protons in the dihydropyran ring<sup>6</sup>. The chemical shift of the remaining proton in the region  $\delta$  5.31–5.64 corresponds to the shift of protons in an analogous structural situation in aldehydes of 4*H*-pyran series<sup>13</sup> and also its relative sensitivity toward substitution agrees with the position 4 of this proton.

The synthesis of 4-aryl-2-dimethylamino-4*H*-1,3-oxazine-5-carboxaldehydes described in this communication represents a new entry into the 1,3-oxazine chemistry. Within the framework of chemistry of this heterocyclic system we may see an analogy between our cycloaddition reaction and the condensation of  $\beta$ -chloro ketones with nitriles<sup>14,15</sup> which, however, proceeds under different conditions (in the presence of tin tetrachloride). The observed high reactivity of the nitrile group in cyanamides might find a more general use in the cycloaddition reactions leading to heterocyclic compounds.

## EXPERIMENTAL

Melting points were determined on a Kofler block, analytical samples were dried over phosphorus pentoxide at 25°C/25 Pa. IR spectra were measured on a Zeiss UR 20 spectrophotometer, <sup>1</sup>H NMR spectra on a Tesla B 46 (60 MHz) instrument in deuteriochloroform with tetramethylsilane as internal standard. The starting dialdehydes *I* were prepared by the described methods<sup>3,4</sup>.

### 4-Aryl-2-dimethylamino-4*H*-1,3-oxazine-5-carboxaldehydes (*III*)

A mixture of the dialdehyde *I* (10 mmol), benzene (20 ml), and dimethylcyanamide (1.5 ml) was refluxed for the time specified in Table I. The solvent was evaporated *in vacuo* and the residue dissolved in ether and cooled with ice (in the case of *III*d with dry ice and ethanol). The product

TABLE II

Chemical shifts and multiplicities of <sup>1</sup>H NMR signals of 4-aryl-2-dimethylamino-4*H*-1,3-oxazine-5-carboxaldehyde (*III*)

<i>III</i>	-CH—O	CH—O	Ar	Ar—CH	(CH <sub>3</sub> ) <sub>2</sub> N
<i>a</i>	9.33 s, 1 H	7.38 s, 1 H	8.00–8.20 m, 2 H 7.31–7.61 m, 2 H	5.43 s, 1 H	2.97 s, 6 H
<i>b</i>	9.29 s, 1 H	7.32 s, 1 H	7.18–7.30 m, 4 H	5.31 s, 1 H	2.94 s, 6 H
<i>c</i>	9.32 s, 1 H	7.30 s, 1 H	7.20–7.38 m, 6 H	5.35 s, 1 H	2.93 s, 6 H
<i>d</i>	9.38 s, 1 H	7.32 s, 1 H	6.85–7.25 m, 3 H	5.65 s, 1 H	2.97 s, 6 H

TABLE III  
Infrared spectra of aldehydes III (CHCl<sub>3</sub>, cm<sup>-1</sup>)

III	$\nu(\text{C-H})$ $\text{N}(\text{CH}_3)_2$	$\nu(\text{C-H})$ $(\text{CH}=\text{O})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{O})$ $\nu(\text{C}=\text{N})$	$\nu(\text{ring})$	$\nu(\text{ring-})$ $\text{N}(\text{CH}_3)_2$	$\nu(\text{rock-})$ $\text{N}(\text{CH}_3)_2$	$\nu_{\text{sym}}(\text{CH}_3)_2\text{N}$	$\nu_{\text{as}}(\text{CH}_3)_2\text{N}$
<i>a</i>	2 838 w	2 746	1 715 m, sh 1 695 vs 1 682 vs, sh	1 639 m	1 601 m	1 368 m, sh	1 178 s	1 065 w 936 w	
<i>b</i>	2 840 w	2 744 w	1 734 w, sh 1 716 m, sh 1 683 vs 1 681 s, sh	1 639 w	1 595 w 1 493 m	1 368 m	1 177 s	1 063 w 943 w	
<i>c</i>	2 835 w	2 743 w	1 734 w, sh 1 716 m, sh 1 695 s 1 685 s, sh	1 641 m	1 494 w 1 500 vw	1 371 m	1 176 s	1 062 w 938 w	
<i>d</i>	—	—	1 716 m, sh 1 692 vs 1 682 vs, sg	1 637 m		1 370 m	1 179 s	1 065 w 935 w	

was collected on filter, washed with ether and purified by sublimation. For yields, melting points and spectral data see Tables I—III.

## REFERENCE

1. Arnold Z., Král V.: Czech. Appl. 8429—80 (1980).
2. Arnold Z., Král V., Dvořák D.: Tetrahedron Lett. 23, 1725 (1982).
3. Arnold Z., Král V., Dvořák D.: This Journal, 49, 2602 (1984).
4. Arnold Z., Dvořák D., Král V.: This Journal, 49, 2613 (1984).
5. Yanovskaya L. A., Kryshtal G. V., Dvořák D., Kárl V., Arnold Z.: This Journal, 50, 1300 (1985).
6. Dvořák D., Arnold Z.: Tetrahedron Lett. 23, 4401 (1982).
7. Needlman S. B., Chang Kuo M. S.: Chem. Rev. 62, 405 (1962).
8. Polaczkova W., Wolinski J.: Roczniki Chem. 26, 407 (1952); Chem. Abstr. 48, 11 359 (1954).
9. Jarrie J. M. S., Fitzgerald W. E., Jantz G. J.: J. Amer. Chem. Soc. 78, 978 (1956).
10. Desimoni G., Tacconi G.: Chem. Rev. 75, 651 (1955).
11. Sauer J.: Angew. Chem. 79, 76 (1967).
12. Bitter J., Leitich J., Partale H., Polansky O. E., Riemer W., Ritter-Thomas U., Schlamann B., Stilkerieg B.: Chem. Ber. 113, 1020 (1980).
13. Wille F., Schwab W.: Z. Naturforsch. 326, 733 (1977).
14. Lora-Tamayo M., Madronero R., Munoz G. G., Leipprand H.: Chem. Ber. 97, 2234 (1964).
15. Schmidt R. R.: Chem. Ber. 98, 334 (1965).

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