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# Domino Knoevenagel Hetero-Diels-Alder/Ene Reactions with 1 $\lambda^6$ .2.6-Thiadiazine-3.5-Diones

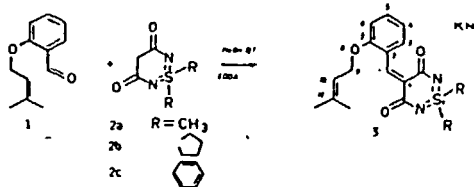
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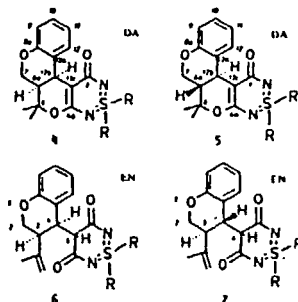
From thiadiazinediones **2** via one-pot intra- and intermolecular Domino-Knoevenagel/Hetero-Diels-Alder/Ene reactions polyheterocycles are obtained with high diastereoselectivities.

**Keywords:** 1 $\lambda^6$ .2.6-Thiadiazine-3.5-diones; Domino-Knoevenagel/Hetero-Diels-Alder/Ene reactions; polyheterocyclic sulfodiimines

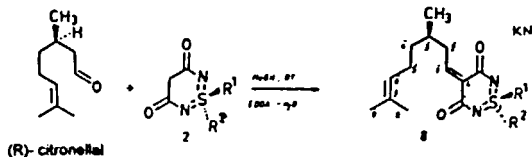
The development of Domino reactions by L.F. Tietze and coworkers<sup>1</sup> prompted us to investigate the potential of 1 $\lambda^6$ .2.6-thiadiazine-3.5-diones<sup>2</sup> **2** for the construction of polyheterocyclic systems via the reaction pathways indicated in the schemes. With aldehyde **1** as well as with (R)-citronellal, for example, the educts **2a-d** have been converted into condensation (KN) products of type **3** and **8** as well as intramolecular Hetero-Diels-Alder (DA) and Ene (EN) reaction products of type **4-7** and **9-11**. The ratios of EN/DA as well as cis/trans isomers have been determined via HPLC and NMR-analysis. The diastereomers **4** and **5** can be resolved on a  $\beta$ -cyclodextrin column into their enantiomers. The EN-isomers are converted into DA-isomers in the presence of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  catalyst.



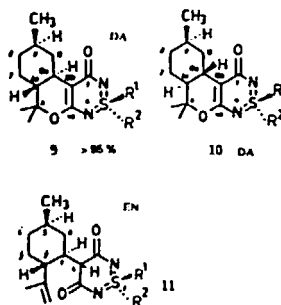
| educt | reaction time | product | yield (%) | isomer ratio      | de (%) |
|-------|---------------|---------|-----------|-------------------|--------|
| 2a    | 14 d          | 11A     | 72        | 78:30 (cis:trans) | 40     |
|       |               | 11N     | 19.5      | 88:20 (trans:cis) | 60     |
| 2b    | 14 d          | 11A     | 78        | 78:30 (cis:trans) | 40     |
|       |               | 11N     | 23        | 79:21 (trans:cis) | 58     |
| 2c    | 50 h          | 11A     | 46        | 83:17 (cis:trans) | 66     |
|       |               | EN      | 18.5      | 88:12 (trans:cis) | 76     |



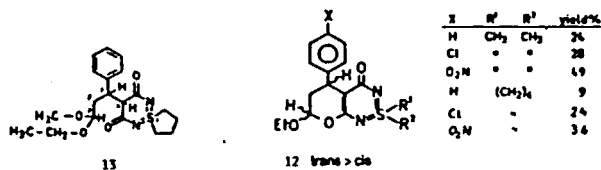
With (R)-citronellal 100% non-induced diastereoselectivity (only trans-isomers) is observed. The asymmetric induction further causes high induced diastereoselectivity (i.e. ca. 90% for 9/10). According to prochiral sulfur in educt 2d the two expected diastereomers 9d and 9e have been isolated which only differ in configuration on sulfur.



| educt | R <sup>1</sup>  | R <sup>2</sup>  | reaction time        | product  | yield (%)                 |
|-------|-----------------|-----------------|----------------------|----------|---------------------------|
| 2a    | CH <sub>3</sub> | CH <sub>3</sub> | 7 d                  | DA<br>EN | 44<br>32                  |
| 2b    |                 |                 | 7 d                  | DA<br>EN | 44<br>34                  |
| 2c    |                 |                 | 24 h                 | DA<br>EN | 39,3<br>34,3              |
| 2d    |                 | CH <sub>3</sub> | 14 d RT/<br>5 h 80°C | DA<br>EN | 4<br>6,2 (fraction 2, 5d) |



Domino KN/DA reactions have further been carried out intermolecular on a three component basis in methanol employing 2a-d, aromatic aldehydes and ethylvinylether as dienophile to give corresponding heterocycles of type 12 in addition to solvolysis products, for example 13.



| X                | R <sup>1</sup>                  | R <sup>2</sup>  | yield% |
|------------------|---------------------------------|-----------------|--------|
| H                | CH <sub>3</sub>                 | CH <sub>3</sub> | 26     |
| Cl               | "                               | "               | 28     |
| O <sub>2</sub> N | "                               | "               | 49     |
| H                | (CH <sub>2</sub> ) <sub>4</sub> | "               | 9      |
| Cl               | "                               | "               | 24     |
| O <sub>2</sub> N | "                               | "               | 34     |

## References

- [1] L. F. Tietze, *Chem. Rev.*, **96**, 115-136 (1996).
- [2] M. Haake, *Angew. Chem.*, **82**, 391-392 (1970).