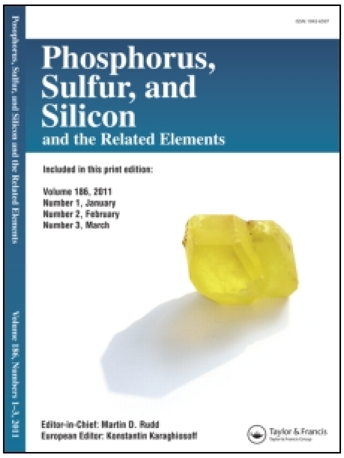

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Haake, Manfred and Holz, Heidi(1999) 'Domino Knoevenagel Hetero-Diels-Alder/Ene Reactions with 1λ^6.2.6-Thiadiazine-3.5-Diones', Phosphorus, Sulfur, and Silicon and the Related Elements, 153: 1, 407 — 408
To link to this Article: DOI: 10.1080/10426509908546494
URL: http://dx.doi.org/10.1080/10426509908546494

Phosphorus, Sulfur and Silicon, 1999, Vol. 153-154, pp. 407-408
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Domino Knoevenagel Hetero-Diels-Alder/Ene Reactions with 1λ^6.2.6-Thiadiazine-3.5-Diones

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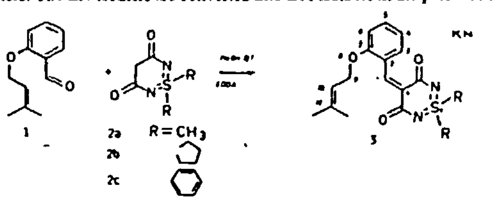
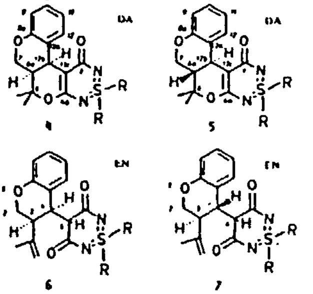
From thiadiazinediones 2 via one-pot intra- and intermolecular Domino-Knoevenagel/Hetero-Diels-Alder/Ene reactions polyheterocycles are obtained with high diastereoselectivities.

Keywords: 1λ^6.2.6-Thiadiazine-3.5-diones; Domino-Knoevenagel/Hetero-Diels-Alder/Ene reactions; polyheterocyclic sulfodiimines

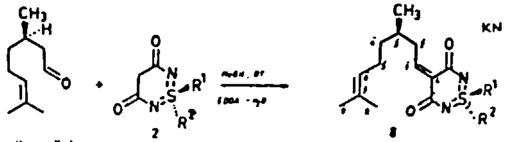
The development of Domino reactions by L.F. Tietze and coworkers[1] prompted us to investigate the potential of 1λ^6.2.6-thiadiazine-3.5-diones[2] 2 for the construction of polyheterocyclic systems via the reaction pathways indicated in the schemes. With aldehyde 1 as well as with (R)-citronellal, for 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 ß-cyclodextrin column into their enantiomers. The EN-isomers are converted into DA-isomers in the presence of $BF_3 \cdot Et_2O$ catalyst.



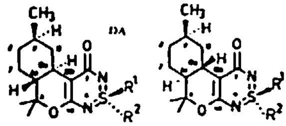
educt	reaction time	product	yield (%)	isomer ratio	de (%)
2a	14 d	DA	72	70 : 30 (cis : trans)	40
		EN	19,5	80 : 20 (trans : cis)	60
2b	14 d	DA	70	70 : 30 (cis : trans)	40
		EN	23	79 : 21 (trans : cis)	58
2c	50 h	DA	48	83 : 17 (cis : trans)	66
		EN	18,5	88 : 12 (trans : cis)	76



With (R)-citronellal 100% non-induced diastereoselectivity (only trans-isomers) is observed. The asymmetric induction further causes high induced diastereoselectivity (i-de 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.

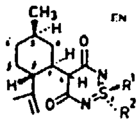


(R)- citronellal



9 >95% 10 DA

educt	R^1	R^2	reaction time	product	yield (%)
2a	CH_3	CH_3	7 d	DA EN	44 32
2b			7 d	DA EN	44 34
2c			24 h	DA EN	39,5 34,5
2d		CH_3	14 d RT/ 8 h Reflux	DA EN	4 (fraction 1, 9e) 6,2 (fraction 2, 9d) -



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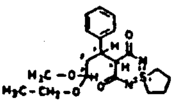
Domino KN/DA reactions have further been carried out intermolecular on a three component basis in methanol employing 2a-d, aromatic aldehydes and ethylvinylether as dienophile to give corresponding heterocycles of type 12 in addition to solvolysis products, for example 13.



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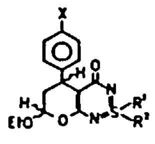

12 trans > cis

X	R^1	R^2	yield%
H	CH_3	CH_3	36
Cl	"	"	28
O_2N	"	"	49
H	$(CH_2)_4$		9
Cl	"		24
O_2N	"		36

References

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