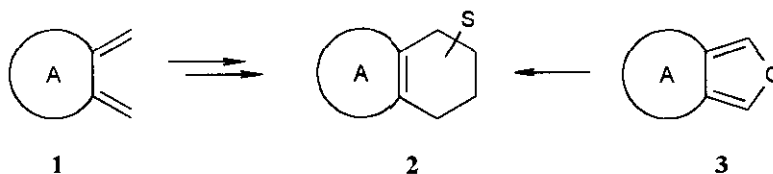


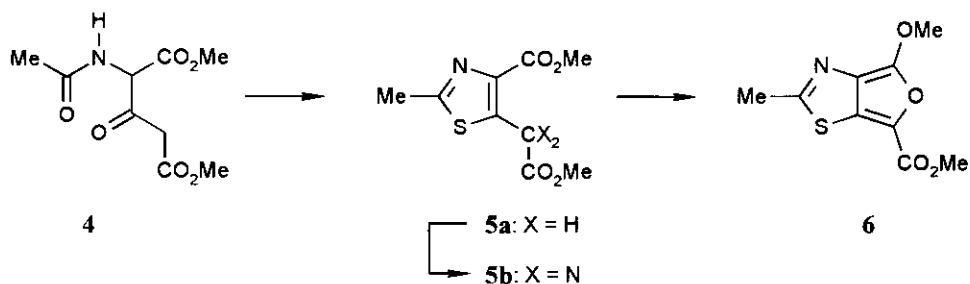
SYNTHESIS AND REACTIONS OF A NOVEL FURO[3,4-*d*]THIAZOLEStephan Reck,^a Christian Näther,^b and Willy Friedrichsen*^a^aInstitut für Organische Chemie der Universität, Otto-Hahn-Platz 4, D-24098 Kiel, Germany^bInstitut für Anorganische Chemie der Universität, Otto-Hahn-Platz 6/7, D-24098 Kiel, Germany

Abstract - The synthesis of a novel furo[3,4-*d*]thiazole (**6**) and some cycloadditions are reported. Density functional theoretical calculations are in accord with the reactivity of this system.

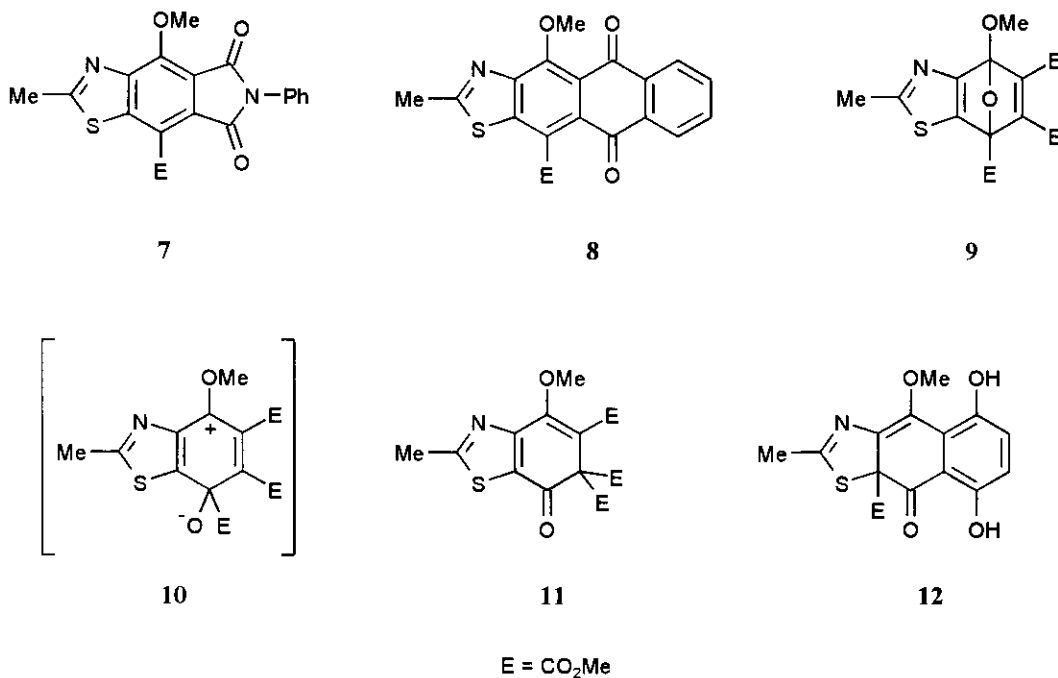
Cycloaddition reactions with *o*-quinodimethane (**1** → **2**, A = benzo)¹ and heteroanalogues thereof² (A = pyridino,³ pyridazino,⁴ quinolino,⁵ quinoxalino,⁶ furo,⁷ thiopheno,⁸ pyrazolo,⁹ thiazolo,¹⁰ isothiazolo,¹¹ oxazolo,¹² indolo¹³) offer an attractive route to polycyclic systems as also do their more stable counterparts **3** (A = benzo,¹⁴ furo,^{14,15} thiopheno,^{14,16} isoxazolo,¹⁴ oxazolo,¹⁷ indolo^{14,18}).



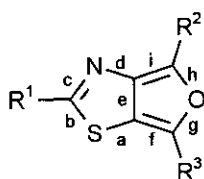
Recent work on a 2,3-dimethylenethiazole (**1**, A = thiazolo)¹⁰ prompts us to report our preliminary results on the synthesis and reactions of a furo[3,4-*d*]thiazole (**6**). The starting material (**4**) is available by reductive acylation of the known¹⁹ dimethyl α -nitrosoacetonedicarboxylic acid.²⁰ Treatment of **4** with phosphorus pentasulfide²¹ yields thiazole (**5a**).²² Diazo group transfer (*Regitz* reaction)²³ with 4-azidosulfonylbenzoic acid and DBU in acetonitrile gives **5b**,²⁴ which was subjected to the conditions of a *Hamaguchi-Ibata* reaction²⁵ ($\text{Rh}_2(\text{OAc})_4$, 1,2-dichloroethane, reflux). Furo[3,4-*d*]thiazole (**6**) was obtained as a crystalline compound,²⁶ which could be stored for several weeks without significant decomposition. Up to now furo[3,4-*d*]thiazoles seem not to have been reported in the literature.



In line with expectations **6** reacts with electron poor dienophiles like *N*-phenylmaleimide and 1,4-naphthoquinone to give **7**²⁷ and **8**,²⁸ respectively. On treatment of **6** with dimethyl acetylenedicarboxylate (DMAD) compound (**11**) was obtained. This type of reaction is well known for other *c*-annulated furans.^{14,29} Probably **9** is formed in the primary reaction step. Ring opening (to **10**) with subsequent migration of an ester group gives **11**.³⁰ Surprisingly the reaction of **6** with *p*-benzoquinone proceeds in a similar manner. Compound (**12**) was obtained as red crystals with mp 140 °C.³¹ The structure of **12** was determined unequivocally by an X-Ray investigation.³²



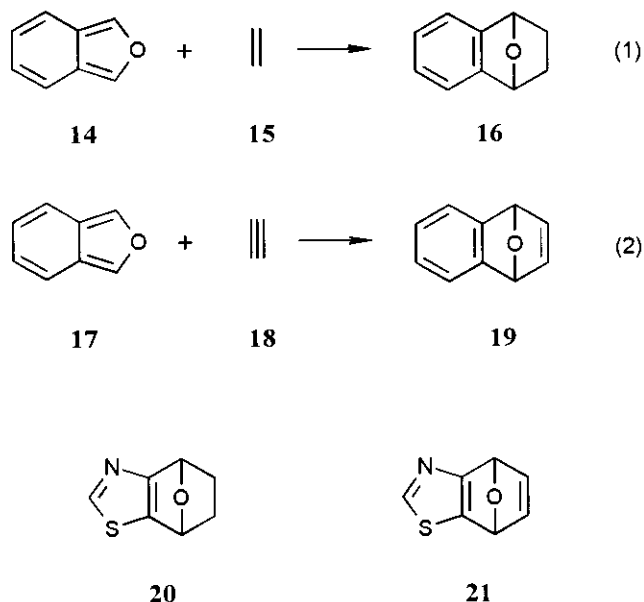
Although the exact geometry of furo[3,4-*d*]thiazoles is unknown, density functional theoretical methods (DFT)³³ have been proven to be of considerable value in the prediction of geometric and energetic data of organic compounds.³⁴ According to these calculations³⁵ the furo[3,4-*d*]thiazole is entirely planar. Bond lengths for both **6** and the parent compound (**13**) are given in Scheme 2.



a	1.732	(1.748)	f	1.372	(1.360)
b	1.822	(1.800)	g	1.402	(1.371)
c	1.290	(1.287)	h	1.348	(1.363)
d	1.379	(1.386)	i	1.381	(1.367)
e	1.428	(1.443)			

Scheme 2. Calculated bond lengths (in Å) for **6** ($R^1 = \text{Me}$, $R^2 = \text{OMe}$, $R^3 = \text{CO}_2\text{Me}$) and **13** ($R^1 = R^2 = R^3 = \text{H}$; values in parentheses) ($E(\mathbf{6})$: -1102.18038 a. u.; $E(\mathbf{13})$: -720.45081 a. u.).

Although quantitative investigations are still lacking the furo[3,4-*d*]thiazole (**6**) seems to be less reactive in Diels-Alder reactions than the corresponding benzo[*c*]furan. DFT calculations for the model reactions (1) and (2) and the corresponding reactions of **13** with ethene (to **20**) and acetylene (to **21**) revealed the following results (Table 1).



Scheme 3

(a) Furo[3,4-*d*]thiazole (**13**) is *less reactive* than benzo[*c*]furan (**14**) (both with ethene and acetylene); (b) In strongly related reactions (to **16/20** and **19/21**, respectively) the heats of reaction can serve as a measure of reactivity.

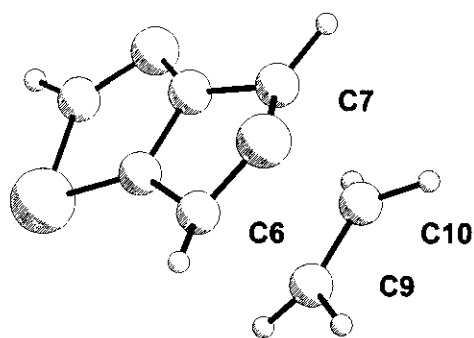
Table 1: Heats of reaction (ΔE) and transition state energies ($\Delta E(\text{ts})$) (values in kcal/mol)^a

Compound	ΔE	$\Delta E(\text{ts})$
16	-29.8 ^b	15.4
19	-34.4 ^c	17.8
20	-19.6 ^d	19.7
21	-21.6 ^e	21.9

^aB3LYP/6-31G*. ^bFor reaction (1). ^cFor reaction (2). ^dFor the reaction of 13 with ethene (to 20). ^eFor the reaction of 13 with acetylene (to 21).

The transition states of 20 and 21 are shown in Figure 1 and Figure 2. In line with expectations the transition states are nearly symmetrical with slightly pyramidalized (bent) reaction centers.

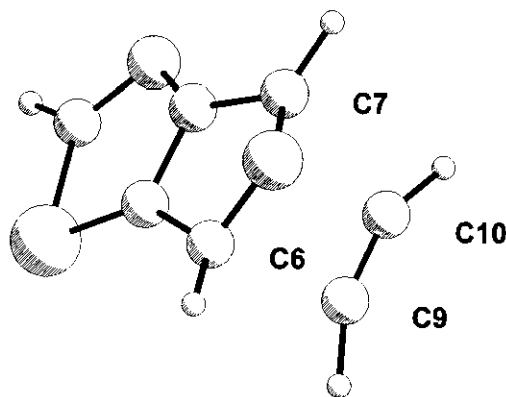
Figure 1: Transition state geometry of 20.



C(7)-C(10): 2.19 Å

C(6)-C(9): 2.22 Å

Figure 2: Transition state geometry of 21.



C(7)-C(10): 2.21 Å

C(6)-C(9): 2.23 Å

The results shown in Scheme 2 and Table 1 underline the validity and reliability of DFT calculations also reported by other authors^{14c,37,38,39} in theoretical studies of ground and transition states of organic molecules (reactions).

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27. Colorless crystals; yield 33%; mp 141 °C; IR (KBr) ν 1763, 1721, 1693, 1570, 1504 cm^{-1} ; UV (MeCN) λ log(ϵ) 214 (4.078), 232 (4.044, sh); ^1H NMR (CDCl_3) δ 2.90 (s, 3H), 4.04 (s, 3H), 7.38-7.54 (m, 5H); ^{13}C NMR (CDCl_3) δ 20.41 (q), 51.18 (q), 63.44 (q), 116.58 (s), 116.96 (s), 126.92 (s), 127.78 (d), 128.24 (d), 129.07 (d), 131.61 (s), 144.89 (s), 148.23 (s), 153.00 (s), 164.17 (s), 164.48 (s), 165.39 (s), 171.10 (s); MS (70 eV) m/z 382 (78, M^+), 353 (16), 322 (100); HRMS calcd

for $C_{19}H_{14}N_2O_5S$: 382.06235, found: 382.06285.

28. Yellow needles; yield 27%; mp 175 °C; IR (KBr) ν 1724, 1666, 1592, 1560, 1297 cm^{-1} ; UV (MeCN) λ log(ϵ) 251 (4.609), 272 (4.690) 372 (3.812); 1H NMR ($CDCl_3$) δ 2.92 (s, 3H), 4.07 (s, 3H), 4.42 (s, 3H), 7.72-7.83 (m, 2H), 8.17-8.20 (m, 1H), 8.26-8.29 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.63 (q), 53.34 (q), 63.15 (q), 122.26 (s), 123.82 (s), 126.80 (d), 127.21 (d), 128.75 (s), 132.83 (s), 133.56 (d), 134.49 (d), 134.91 (s), 141.62 (s), 150.29 (s), 155.22 (s), 168.75 (s), 170.77 (s), 181.86 (s), 182.42 (s); MS (70 eV) m/z 367 (100, M^+), 338 (93), 306 (11), 279 (12); HRMS calcd for $C_{19}H_{13}NO_5S$: 367.05145, found: 367.05135.
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31. IR (KBr) ν 3380, 1742, 1660, 1641, 1575 cm^{-1} ; UV (MeCN) λ log(ϵ) 235 (4.277), 262 (4.113, sh), 328 (3.812), 455 (3.687); 1H NMR ($CDCl_3$) δ 2.41 (s, 3H), 3.70 (s, 3H), 4.29 (s, 3H), 6.86 (d, 1H), 7.10 (d, 1H), 8.72 (s, 1H, exchange with D_2O), 11.01 (s, 1H, exchange with D_2O); ^{13}C NMR ($CDCl_3$) δ 21.06 (q), 54.59 (q), 62.52 (q), 109.70 (s), 116.10 (s), 120.88 (d), 129.70 (d), 135.83 (s), 143.25 (s), 148.70 (s), 156.41 (s), 167.00 (s), 167.17 (s), 194.60 (s); MS (70eV) m/z 335 (10, M^+), 320 (14), 276 (100), 261 (36).
32. Space group: monoclinic, $P2_1/n$. Cell dimensions: $a = 8.2815$ (8) Å, $b = 14.540$ (2) Å, $c = 12.277$ (3) Å, $\alpha = 90.00^\circ$, $\beta = 94.35$ (1) $^\circ$, $\gamma = 90.00^\circ$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 101141. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. (fax: +44-(0)1223-336033 or email: deposit@ccdc.cam.ac.uk).
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