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Short Communication

Synthesis of Carboxylic Acid Derivatives of Dihydrochalcones

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Summary. Reaction of chalcones **1–8** with thioglycolic acid, 3-mercaptopropionic acid or thiosalicylic acid gives dihydrochalcone derivatives **9–23**.

Keywords. Chalcones; Dihydrochalcones; Nucleophilic addition.

Darstellung von Carbonsäurederivaten von Dihydrochalconen (Kurze Mitt.)

Zusammenfassung. Umsetzung der Chalcone **1–8** mit Thioglycolsäure, 3-Mercaptopropionsäure oder Thiosalicylsäure liefert die Dihydrochalconeabkömmlinge **9** bis **23**.

Reaction of chalcones and their heterocyclic analogues with thiols has been investigated by several research groups [1–8]. Substances prepared in this way were found to possess fungicide [4], antiinflammatory [8], and various other activities.

In the course of our studies on the synthesis of pharmacologically active chalcone derivatives the reaction of chalcones **1–8** with thioglycolic acid, 3-mercaptopropionic acid or thiosalicylic acid in hot toluene has been studied; thereby carboxylic acid derivatives of dihydrochalcones **9–23** were obtained (compare formula scheme and Table 1). The structure of these compounds has been elucidated by 1H-NMR spectroscopy by assigning the CH_2 and CH aliphatic signals characteristic for the dihydrochalcone skeleton. ^{1}H-NMR spectral data are summarized in Table 1. All compounds showed antifungal activity: **9**, **13**, and **22** were especially active against *Aspergillus niger, Trichophyton mentagrophytes, Micosporum gypseum*, and *Epidermophyton floccosum* strains.

Experimental Part

The NMR spectra were recorded on a Bruker WP 200 SY spectrometer in $CDCl_3$ (internal standard *TMS*, $\delta = 0.0$ ppm) at room temperature. TLC was performed on Kieselvel 60 F_{254} (Merck) layer using hexane : acetone (7 : 3 *v/v*) as eluant. Starting materials **1–8** were prepared according to known methods [9–12].

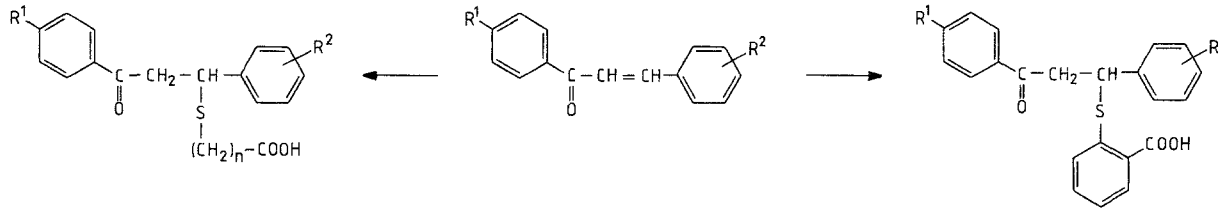
Table 1. Physical constants and ^{1}H-NMR spectral data of compounds **9–23**

Compound	M.p. °C	Yield %	Molecular formula[a]	^{1}H-NMR δ (ppm)
9	137–138[b]	75.0	$C_{17}H_{16}O_3S$	3.10 (dd, 2H), 3.60 (d, 2H), 4.80 (t, 1H), 7.28–7.96 (m, 10 aromatic protons), 11.15 (s, 1H)
10	105–106	73.9	$C_{17}H_{15}ClO_3S$	3.25 (dd, 2H), 3.68 (d, 2H), 5.26 (t, 1H), 7.16–9.97 (m, 9 aromatic protons), 10.03 (s, 1H)
11	145–146	89.8	$C_{17}H_{15}ClO_3S$	3.08 (dd, 2H), 3.57 (d, 2H), 4.75 (t, 1H), 7.27–7.92 (m, 9 aromatoc protons)
12	121–122	75.7	$C_{17}H_{14}Cl_2O_3S$	3.10 (dd, 2H), 3.60 (d, 2H), 4.70 (t, 1H), 7.26–8.90 (m, 8 aromatic protons)
13	147–148	79.5	$C_{17}H_{14}Cl_2O_3S$	3.60 (d, 2H), 3.90 (dd, 1H), 4.30 (dd, 1H), 5.72 (t, 1H), 7.20–8.30 (m, 8 aromatic protons)
14	128–129	68.1	$C_{17}H_{15}ClO_3S$	3.08 (dd, 2H), 3.58 (d, 2H), 4.78 (t, 1H), 7.25–7.87 (m, 9 aromatic protons), 10.86 (s, 1H)
15	134–135	78.7	$C_{17}H_{15}BrO_3S$	3.08 (dd, 2H), 3.56 (d, 2H), 4.77 (t, 1H), 7.25–7.80 (m, 9 aromatic protons), 9.72 (s, 1H)
16	161–162	77.3	$C_{18}H_{18}O_3S$	2.55 (dd, 4H), 3.52 (d, 2H), 4.58 (t, 1H), 7.28–7.93 (m, 10 aromatic protons)
17	113–114	60.5	$C_{18}H_{17}ClO_3S$	2.65 (dd, 4H), 3.54 (d, 2H), 5.15 (t, 1H), 7.12–7.95 (m, 9 aromatic protons), 10.94 (s, 1H)
18	131–132	83.0	$C_{18}H_{17}ClO_3S$	2.58 (dd, 4H), 3.52 (d, 2H), 4.57 (t, 1H), 7.26–7.94 (m, 9 aromatic protons), 10.57 (s, 1H)
19	102–103	67.9	$C_{18}H_{16}Cl_2O_3S$	2.64 (dd, 4H), 3.56 (dd, 2H), 5.08 (t, 1H), 7.14–7.92 (m, 8 aromatic protons)
20	132–133	58.4	$C_{18}H_{16}Cl_2O_3S$	1.48 (dd, 2H), 1.66 (dd, 2H), 2.50 (dd, 1H), 2.77 (dd, 1H), 4.26 (t, 1H), 5.82–6.70 (m, 8 aromatic protons)
21	166–167	68.4	$C_{22}H_{18}O_3S$	3.70 (dd, 2H), 5.18 (dd, 1H), 7.20–8.10 (m, 14 aromatic protons)
22	139–140	61.0	$C_{22}H_{17}ClO_3S$	3.64 (dd, 2H), 5.80 (dd, 1H), 7.10–8.10 (m, 13 aromatic protons)
23	159–160	65.5	$C_{22}H_{17}ClO_3S$	3.62 (dd, 2H), 5.18 (dd, 1H), 7.20–8.12 (m, 13 aromatic protons)

[a] Elemental analyses (C, H, S) were in good agreement with the calculated values
[b] Ref. [2] m.p. 126 °C

General Procedure for the Preparation of Compounds **9–23**

A mixture of compounds **1–8** (20.0 mmol), mercaptocarboxylic acid (30.0 mmol), and toluene (100.0 ml) was refluxed for 6 h, the solvent evaporated in vacuum and the residue crystallized from benzene to afford substances **9–23**. For properties see Table 1.



9–20 1–8 21–23

1: $R^1 = R^2 = H$
2: $R^1 = H$, $R^2 = 2\text{-Cl}$
3: $R^1 = H$, $R^2 = 4\text{-Cl}$
4: $R^1 = H$, $R^2 = 2,4\text{-Cl}_2$
5: $R^1 = H$, $R^2 = 3,4\text{-Cl}_2$
6: $R^1 = H$, $R^2 = 2,6\text{-Cl}_2$
7: $R^1 = Cl$, $R^2 = H$
8: $R^1 = Br$, $R^2 = H$
9: $R^1 =$, $R^2 = H$
10: $R^1 = H$, $R^2 = 2\text{-Cl}$, $n = 1$
11: $R^1 = H$, $R^2 = 4\text{-Cl}$, $n = 1$
12: $R^1 = H$, $R^2 = 3,4\text{-Cl}_2$, $n = 1$
13: $R^1 = H$, $R^2 = 2,6\text{-Cl}_2$, $n = 1$
14: $R^1 = Cl$, $R^2 = H$, $n = 1$
15: $R^1 = Br$, $R^2 = H$, $n = 1$
16: $R^1 = R^2 = H$, $n = 2$
17: $R^1 = H$, $R^2 = 2\text{-Cl}$, $n = 2$
18: $R^1 = H$, $R^2 = 4\text{-Cl}$, $n = 2$
19: $R^1 = H$, $R^2 = 2,4\text{-Cl}_2$, $n = 2$
20: $R^1 = H$, $R^2 = 2,6\text{-Cl}_2$, $n = 2$
21: $R^1 = R^2 = H$
22: $R^1 = H$, $R^2 = 2\text{-Cl}$
23: $R^1 = Cl$, $R^2 = H$

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