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Note

Synthetic procedure for modifying the amine part of carpropamid: Changing 4-chlorophenethylamine to alkyl, alicyclic, and substituted phenylalkylamines

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Compounds of the 4-chlorophenethyl amine part of carpropamid were replaced with alkyl, cycloalkyl and substituted phenylalkyl amines. The amines were obtained from the corresponding ketoximes using a reduction system of sodium borohydride with molybdenum oxide as the additive. © Pesticide Science Society of Japan

Keywords: carpropamid, structural modification, reduction of oxime, amine, cyclopropanecarboxamide.

Introduction

The emergence of fungus resistant to carpropamid (**1**), a melanin biosynthesis inhibitor, was recently reported and the cause was identified as a mutation of the valine residue to methionine in scytalone dehydratase (SDH).[1,2] Carpropamid enters the SDH cavity and forms a tight complex, where the phenyl part binds to the valine residue.[3] Mutation to a more spacious residue is suspected to interfere with the complex formation. In light of the above consideration, we modified the structure of the amine part of carpropamid in the proceeding paper[4] and reported the resistance-busting compounds (Fig. 1). This note describes the preparation procedure for the starting alkyl, cycloalkyl and aralkyl amines, and physical and spectral data of the produced amides that were not reported previously.

Materials and Methods

All melting points (mp) are uncorrected. NMR spectra were obtained with a Varian Gemini 2000 C/H (400 MHz). Chemical shifts were recorded in δ (ppm) and the coupling constant J in Hz. Mass spectra were recorded with a JEOL JMS-700. Isopropylamine, *sec*-butylamine, 4-chloroanilin, 4-chlorobenzylamine, 4-bromo-, 2-chloro-, 3-chloro-, 4-chloro-, 4-fluoro, 4-methyl-, 4-trifluoromethyl-, 2,4-dichloro-, 3,4-dichloro- and 2,4-difluorophenethyamine, 2-(4-chlorophenyl)propyl- and 3-(4-chlorophenyl)propylamine, and 1-methyl-(4-chlorophenyl)ethylamine are commercially available and used without further purification. 1-Methy-4,4,4-trifluoropropylamine[5] and 1-cyclopropylethylamine[6] were prepared according to the reported procedures. 1-Cyclobutylethyl-, 1-cyclopentylethyl- and 1-cyclohexylethylamines are registered in the Chemical Abstract, but the preparative details are not accessible. We prepared these amines from the corresponding acetylcycloalkane oximes[7,8] as well as a new amine, 1-(4-chlorophenyl)propylamine, by slightly modifying the reported procedure (Fig. 2).[9]

Typical reduction procedure: To a mixture of acetylcyclohexane oxime (1.29 g, 0.091 mol) and MoO_3 (1.81 g, 0.126 mol) in 60 ml of methanol in an ice-water bath was added powdered $NaBH_4$ (3.38 g, 0.914 mol) portionwise. An exothermic reaction occurred with vigorous gas evolution about 30 min after the addition. When the exothermic reaction ceased, the cooling bath was set aside and the reaction mixture was stirred at ambient temperature for 5 hr. The mixture was allowed to stand overnight. After separating the supernatant layer by decantation, the rest of the mixture was filtered through a Celite bed with weak suction and the bed washed with methanol. The combined methanol solution was acidified with conc. HCl and the precipitated solid was filtered off. The methanol was distilled off and the residual solid was dissolved in water and, after confirming that the solution was acidic, washed several times with hexane. The aqueous phase was cooled in an ice bath and alkalized to pH 10–12 with solid NaOH, and extracted with ether several times. The combined ether phase was dried over solid KOH. Following the careful distillation of ether, the fraction of 1-cyclohexylethylamine was collected. Yield: 680 mg (59%). Bp. 130–135°C/760 mmHg (34°C/30 mmHg).[10]

1-Cyclobutylethylamine. Yield: 59%. Bp. 128–135/760 mmHg (bp. 135–137°C).[11] *1-Cyclopentylethylamine*. Yield. 16%. Bp. 135–140/760 mmHg (bp. 80–150/740 mmHg).[10] *Cycloheptylethylamine*. Yield. 36%. Bp. 140–145°C (mp. 229–231°C of HCl salt).[12]

1-(4-Chlorophenyl)propylamine. Oxime was prepared by heating a mixture of 4-chlorophenylpropanone (2.40 g, 14 mmol), hydroxylamine·HCl (2.50 g, 39.4 mmol) and dry pyridine (2.5 ml) in dry ethanol (25 ml) for 3 hr at 80°C. After the evaporation of ethanol, the residual liquid was partitioned between water and hexane, and the hexane layer was separated and dried. The hexane was distilled off and the residue that crystallized was rinsed with a small amount of chilled hexane. Yield: 2.34 g (90%). Mp. 67–68°C. IR (KBr) cm^{-1}: 1495, 1090, 972, 920. ^{1}H-NMR δ_H ($CDCl_3$) : 1.16 (3H, t, J=7.4Hz, $CH_2C\underline{H}_3$), 2.80 (2H, q,

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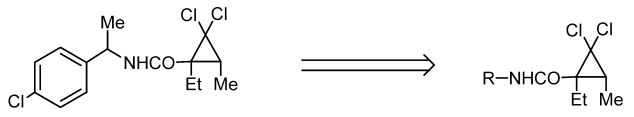

Carpropamid (**1**)

Modified derivatives	R
1) alkyl chain	MeCH(Me)- (**2**) $CH_3CH_2CH(Me)$- (**3**) $CF_3CH_2CH(Me)$- (**4**)
2) cycloalkyl	$(CH_2)_n$–CH(Me)- n= 3 (**5**), 4 (**6**), 5 (**7**), 6 (**8**), 7 (**9**)
3) 4-chlorophenyl	X: – (**10**), CH_2- (**11**), CH_2CH_2- (**12**), $CH_2CH_2CH_2$- (**13**), CH(Et)- (**14**), $CH(Me)CH_2$- (**15**), $CH_2CH(Me)$- (**16**)
4) Substituted phenylethyl	Y, Z: 4-F (**17**), 2,4-F_2 (**18**), 4-CF_3 (**19**), 2-Cl (**20**), 3-Cl (**21**), 2,4-Cl_2 (**22**), 3,4-Cl_2 (**23**), 4-Br (**24**), 4-Me (**25**)

Fig. 1. Modification of the amine part of carpropamid.

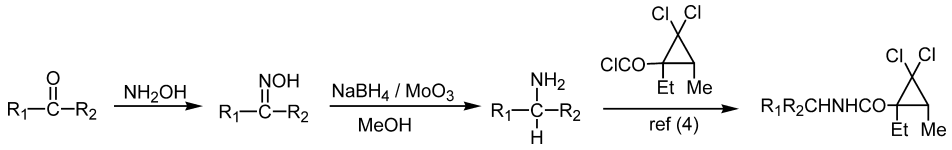

Fig. 2. Synthesis of modified carpropamid.

J=7.4 Hz, CH_2CH_3), 7.35 (2H, d, J=8.6 Hz, Phenyl), 7.54 (2H, d, J=8.6 Hz, Phenyl), 9.51 (1H, bs, OH). EI-MS *m*/*z* (%): 183 (M^+, 100), 166 (63), 138 (78). From oxime (2.20 g, 12 mmol) was obtained 1.06 g of amine in 52% yield by the above reduction procedure. Bp. 72–75/24 mmHg. IR (film) cm^{-1}: 3420. ^{1}H-NMR δ_H ($CDCl_3$): 1.14 (3H, t, J=7.7 Hz, CH_2CH_3), 1.68 (2H, m, CH_2CH_3), 3.80 (1H, t, J=7.0 Hz, CH), 7.24 (2H, d, J=8.2 Hz, Phenyl), 7.28 (2H, d, J=8.2 Hz, Phenyl). EI-MS *m*/*z* (%): 169 (M^+, 3), 166 (71), 153 (42), 138 (100).

The amides were prepared according to the described procedure.[4] The spectral data of the products are as follows:

N-Isopropyl-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**2**). Mp. 99°C. IR (KBr) cm^{-1}: 1645. ^{1}H-NMR δ_H ($CDCl_3$): 1.04 (3H, t, J=7.6 Hz, CH_2CH_3), 1.19–1.21 (9H, overlap, 3-cyclopropyl-CH_3+$CH(CH_3)_2$), 1.55 (1H, m, $CH_{2a}CH_3$), 1.93 (1H, m, $CH_{2b}CH_3$), 2.20 (1H, q, J=6.6 Hz, 3-cyclopropyl-H), 4.15 (1H, m, $CH(CH_3)_2$), 5.55 (1H, bs, NH). EI-MS *m*/*z* (%): 237 (M^+, 16), 222 (100).

N-(sec-Butyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**3**). Mp. 111°C. IR (KBr) cm^{-1}: 1645. ^{1}H-NMR δ_H ($CDCl_3$): 0.92–1.01 (6H, overlap), 1.16–1.20 (6H, overlap), 1.55 (3H, overlap, $CHCH_2CH_3$+1-cyclopropyl $CH_{2a}CH_3$), 1.97 (1H, m, 1-cyclopropyl $CH_{2b}CH_3$), 2.21 (1H, q, J=6.6 Hz, 3-cyclopropyl-H,), 3.98 (1H, m, NCH), 5.55 (1H, bs, NH). EI-MS *m*/*z* (%): 251 (M^+, 17), 236 (80), 57 (100).

N-[2-(4,4,4-Trifluoro)butyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**4**). Mp. 122–125°C. IR (KBr) cm^{-1}: 1645. ^{1}H-NMR δ_H ($CDCl_3$): 0.94 (3H, m, CH_2CH_3), 1.20 (3H, m, 3-cyclopropyl-CH_3), 1.36 (3H, m, NCHCH_3), 1.55 (1H, m, $CH_{2a}CH_3$), 1.95 (1H, m, $CH_{2b}CH_3$), 2.21 (1H, q, J=6.6 Hz, 3-cyclopropyl-H), 2.36 (2H, m, CH_2CF_3), 4.40 (1H, m, NHCH), 5.85 (1H, bs, NH). EI-MS *m*/*z* (%): 306 (M^+, 9), 291 (51), 91 (863), 44 (100).

N-(1-Cyclopropylethyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**5**). Mp. 138–140°C. IR (KBr) cm^{-1}: 1640. ^{1}H-NMR δ_H ($CDCl_3$): 0.25–0.56 (4H, m, −CHCH_2CH_2−), 0.85 (1H, m, −CHCH_2CH_2−), 1.00 (3H, m, CH_2CH_3), 1.21 (3H, d, J=6.6 Hz, 3-cyclopropyl-CH_3), 1.25 (3H, m, NCHCH_3), 1.55 (1H, m, $CH_{2a}CH_3$), 1.95 (1H, m, $CH_{2b}CH_3$), 2.19 (1H, q, J=6.6 Hz, 3-cyclopropyl-H), 3.40 (1H, m, NHCH), 5.70 (1H, bs, NH). EI-MS *m*/*z* (%): 263 (M^+, 3), 180 (59), 69 (100).

N-(1-Cyclobutylethyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**6**). Mp. 127–128. IR (KBr) cm^{-1}: 1642. ^{1}H-NMR δ_H ($CDCl_3$): 1.00 (3H, m, CH_2CH_3), 1.21 (3H, d, J=6.6 Hz, 3-cyclopropyl-CH_3), 1.10 (3H, m, NCHCH_3), 1.56 (1H, m, $CH_{2a}CH_3$), 1.80–2.40 (7H, m, cyclobutyl), 1.90 (1H, m, $CH_{2b}CH_3$), 2.21 (1H, q, J=4.8 Hz, 3-cyclopropyl-H), 4.03 (1H, m, NHCH), 5.42 (1H, bs, NH). EI-MS *m*/*z* (%): 277 (M^+, 6), 180 (39), 55 (100).

N-(1-Cyclohexylethyl)-2,2-dichloro-1-ethyl-3-methylcyclo-

propanecarboxamide (**8**). Mp. 117°C. IR (KBr) cm^{-1}: 1640. 1H-NMR δ_H ($CDCl_3$): 0.98–1.82 (21H, overlap, 3-cyclopropyl-$C\underline{H}_3$+cyclohexyl+$NCHC\underline{H}_3$+$C\underline{H}_{2a}CH_3$), 1.95 (1H, m, $C\underline{H}_{2b}CH_3$), 2.20 (1H, m, 3-cyclopropyl-$\underline{H}$), 3.95 (1H, m, $NHC\underline{H}$), 5.55 (1H, bs, $N\underline{H}$). EI-MS *m/z* (%): 305 (M^+, 7), 290 (17), 222 (60), 196 (27), 179 (100).

N-(1-Cycloheptylethyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**9**). Mp. 143–144°C. IR (KBr) cm^{-1}: 1645. ^{1}H-NMR δ_H ($CDCl_3$): 0.96–1.71 (23H, overlap, 3-cyclopropyl-$C\underline{H}_3$+cycloheptyl+$NCHC\underline{H}_3$+$C\underline{H}_{2a}CH_3$), 1.93 (1H, m, $C\underline{H}_{2b}CH_3$), 2.20 (1H, m, 3-cyclopropyl-$\underline{H}$), 4.00 (1H, m, $NHC\underline{H}$), 5.56 (1H, bs, $N\underline{H}$). EI-MS *m/z* (%): 319 (M^+, 3), 222 (58), 179 (81), 55 (100).

N-(4-Chlorophenyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**10**). Mp. 144°C. IR (KBr) cm^{-1}: 1665. ^{1}H-NMR δ_H ($CDCl_3$): 1.04 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 1.24 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.63 (1H, m, $C\underline{H}_{2a}CH_3$), 2.12 (1H, m, $C\underline{H}_{2b}CH_3$), 2.29 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$), 7.28 (2H, d, J=8.8 Hz, *ortho* $\underline{H}$ to CH_2), 7.52 (2H, d, J=8.8 Hz, *meta* $\underline{H}$), 8.22 (1H, bs, $N\underline{H}$). EI-MS *m/z* (%): 305 (M^+, 42), 79 (100).

N-(4-Chlorobenzyl)-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**11**). Mp. 130–131°C. IR (KBr) cm^{-1}: 1650. ^{1}H-NMR δ_H ($CDCl_3$): 0.96 (3H, t, J=7.7 Hz, $CH_2C\underline{H}_3$), 1.21 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.57 (1H, m, $C\underline{H}_{2a}CH_3$), 1.95 (1H, m, $C\underline{H}_{2b}CH_3$), 2.29 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$), 4.48 (2H, d, J=5.9 Hz, benzyl), 6.13 (1H, bs, $N\underline{H}$), 7.25 (2H, d, J=8.6 Hz, *ortho* $\underline{H}$), 7.30 (2H, d, J=8.6 Hz, *meta* $\underline{H}$). EI-MS *m/z* (%): 319 (M^+, 2), 125 (100).

N-[3-(4-Chlorophenyl)propyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**13**). Liquid. IR (film) cm^{-1}: 1640. ^{1}H-NMR δ_H ($CDCl_3$): 0.96 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 1.13 (3H, d, J=6.3 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.53 (1H, m, $C\underline{H}_{2a}CH_3$), 1.86 (3H, overlap, $C\underline{H}_{2b}CH_3$+$CH_2C\underline{H}_2CH_2$), 2.16 (1H, q, J=6.3 Hz, 3-cyclopropyl-$\underline{H}$), 2.66 (2H, m, $NCH_2CH_2C\underline{H}_2$), 3.33 (2H, m, $NC\underline{H}_2CH_2CH_2$), 5.74 (1H, bs, $N\underline{H}$), 7.11 (2H, d, J=8.0 Hz, *ortho* $\underline{H}$), 7.33 (2H, d, J=8.0 Hz, *meta* $\underline{H}$). EI-MS *m/z* (%): 347 (M^+, 9), 79 (100).

N-[1-(4-Chlorophenyl)propyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**14**). Mp. 155–157°C. IR (KBr) cm^{-1}: 1640. ^{1}H-NMR δ_H ($CDCl_3$): 0.81 (3H, t, J=7.5 Hz, $CHCH_2C\underline{H}_3$), 0.93 (3H, t, J=7.0 Hz, 1-cyclopropyl-$CH_2C\underline{H}_3$), 1.19 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.52 (1H, m, $C\underline{H}_{2a}CH_3$), 1.80–2.00 (3H, overlap, $C\underline{H}_{2b}CH_3$+$CHC\underline{H}_2CH_3$), 2.18 (1H, m, 3-cyclopropyl-$\underline{H}$), 4.89 (1H, m, $NHC\underline{H}CH_2$), 5.84 (1H, d, J=7.7 Hz, $N\underline{H}$), 7.26 (2H, d, J=8.0 Hz, *ortho* $\underline{H}$), 7.31 (2H, d, J=8.0 Hz, *meta* $\underline{H}$). EI-MS *m/z* (%): 347 (M^+, 2), 126 (100).

N-[2-(4-Chlorophenyl)propyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**15**). Mp. 84–87°C. IR (KBr) cm^{-1}: 1625. ^{1}H-NMR δ_H ($CDCl_3$): 0.80–1.18 (9H, overlap, cyclopropyl-$CH_2C\underline{H}_3$+3-cyclopropyl-$C\underline{H}_3$+$C\underline{H}_3CHCH_2$), 1.49 (1H, m, $C\underline{H}_{2a}CH_3$), 1.80 (1H, m, 3-cyclopropyl-$\underline{H}$), 2.13 (1H, m, $C\underline{H}_{2b}CH_3$), 2.95–3.03 (1H, m, $C\underline{H}(CH_3)CH_2$), 3.3–3.7 (2H, m, $CH(CH_3)C\underline{H}_2$), 5.74 (1H, m, $N\underline{H}$), 7.15–7.31 (4H, m, phenyl ring). EI-MS *m/z* (%): 347 (M^+, 8), 152 (100).

N-[2-(4-Chlorophenyl)-1-methylethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**16**). Mp. 112–115°C. IR (KBr) cm^{-1}: 1635. ^{1}H-NMR δ_H ($CDCl_3$): 0.71–0.91 (3H, m, 1-cyclopropyl-$CH_2C\underline{H}_3$), 1.12–1.18 (6H, overlap, 3-cyclopropyl-CH_3+$CH_2CHC\underline{H}_3$), 1.46 (1H, m, $C\underline{H}_{2a}CH_3$), 1.71–2.11 (1H, m, 3-cyclopropyl-$\underline{H}$), 2.14 (1H, m, $C\underline{H}_{2b}CH_3$), 2.58–2.94 (2H, m, $CH_2CHC\underline{H}_3$), 4.31 (1H, m, $CH_2C\underline{H}NH$), 5.53–5.62 (1H, m, $N\underline{H}$), 7.11–7.26 (4H, m, phenyl ring). EI-MS *m/z* (%): 347 (M^+, 1), 179 (100).

N-[2-(4-Fluorophenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**17**). Mp. 123°C. IR (KBr) cm^{-1}: 1635. ^{1}H-NMR δ_H ($CDCl_3$): 0.90 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 1.19 (3H, d, J=6.3 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.52 (1H, m, $C\underline{H}_{2a}CH_3$), 1.85 (1H, m, $C\underline{H}_{2b}CH_3$), 2.18 (1H, q, J=6.3 Hz, 3-cyclopropyl-$\underline{H}$), 2.85 (2H, m, $NCH_2C\underline{H}_2$), 3.58 (2H, m, $NC\underline{H}_2CH_2$), 5.82 (1H, bs, $N\underline{H}$), 7.15 (2H, dd, J=8.6/8.6_{H-F} Hz, *meta* $\underline{H}$ to CH_2,), 7.28 (2H, dd, J=8.6/5.2_{H-F} Hz, *ortho* $\underline{H}$ to CH_2). EI-MS *m/z* (%): 317 (M^+, 28), 122 (100).

N-[2-(2-Chlorophenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**20**). Mp. 140–142°C. IR (KBr) cm^{-1}: 1640. ^{1}H-NMR δ_H ($CDCl_3$): 0.90 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 1.19 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.52 (1H, m, $C\underline{H}_{2a}CH_3$), 1.90 (1H, m, $C\underline{H}_{2b}CH_3$), 2.19 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$), 3.01 (2H, t, J=7.1 Hz, $NCH_2C\underline{H}_2$), 3.66 (2H, m, $NC\underline{H}_2CH_2$), 5.97 (1H, bs, $N\underline{H}$), 7.16–7.37 (4H, m, benzene ring). EI-MS *m/z* (%): 333 (M^+, 36), 139 (100).

N-[2-(3-Chlorophenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**21**). Mp. 111–112°C. IR (KBr) cm^{-1}: 1630. ^{1}H-NMR δ_H ($CDCl_3$): 0.91 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$), 1.19 (3H, d, J=6.7 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.52 (1H, m, $C\underline{H}_{2a}CH_3$), 1.87 (1H, m, $C\underline{H}_{2b}CH_3$), 2.19 (1H, m, 3-cyclopropyl-$\underline{H}$), 2.84 (2H, m, $NCH_2C\underline{H}_2$), 3.59 (2H, m, $NC\underline{H}_2CH_2$), 5.88 (1H, bs, $N\underline{H}$), 7.10–7.29 (4H, m, benzene ring). EI-MS *m/z* (%): 333 (M^+, 74), 179 (100).

N-[2-(3,4-Dichlorophenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**23**). Mp. 110°C. IR (KBr) cm^{-1}: 1630. ^{1}H-NMR δ_H ($CDCl_3$): 0.92 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$), 1.20 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.53 (m, 1H, $C\underline{H}_{2a}CH_3$), 1.87 (1H, m, $C\underline{H}_{2b}CH_3$), 2.18 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$), 2.84 (2H, m, $NCH_2C\underline{H}_2$), 3.58 (2H, m, $NC\underline{H}_2CH_2$), 5.90 (1H, bs, $N\underline{H}$), 7.06 (1H, m, benzene ring), 7.32 (m, 1H, benzene ring), 7.37 (1H, m, benzene ring). EI-MS *m/z* (%): 367 (M^+, 44), 172 (100).

N-[2-(4-Bromophenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**24**). Mp. 144–146°C. IR (KBr) cm^{-1}: 1630. ^{1}H-NMR δ_H ($CDCl_3$): 0.90 (3H, t, J=7.6 Hz, $CH_2C\underline{H}_3$), 1.19 (3H, d, J=6.6 Hz, 3-cyclopropyl-$C\underline{H}_3$), 1.52 (1H, m, $C\underline{H}_{2a}CH_3$), 1.84 (1H, m, $C\underline{H}_{2b}CH_3$), 2.18 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$,), 2.84 (2H, m, $NCH_2C\underline{H}_2$), 3.58 (2H, m, $NC\underline{H}_2CH_2$), 5.79 (1H, bs, $N\underline{H}$), 7.11 (2H, d, J=8.1 Hz, *ortho* $\underline{H}$), 7.43 (2H, d, J=8.1 Hz, *meta* $\underline{H}$). EI-MS *m/z* (%): 379 (M^+, 34), 182 (100).

N-[2-(4-Methylphenyl)ethyl]-2,2-dichloro-1-ethyl-3-methylcyclopropanecarboxamide (**25**). Mp. 118–119°C. IR (KBr) cm^{-1}: 1640. ^{1}H-NMR δ_H ($CDCl_3$): 0.90 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$),

1.18 (3H, d, J=6.6 Hz, 3-cyclopropyl-C$\underline{H}_3$), 1.50 (1H, m, C$\underline{H}_{2a}$CH$_3$), 1.85 (1H, m, C$\underline{H}_{2b}$CH$_3$), 2.18 (1H, q, J=6.6 Hz, 3-cyclopropyl-$\underline{H}$), 2.33 (3H, s, tolyl), 2.81 (2H, m, NCH$_2$C$\underline{H}_2$), 3.58 (2H, m, NC$\underline{H}_2$CH$_2$), 5.85 (1H, bs, N$\underline{H}$), 7.12 (4H, bs, benzene ring). EI-MS m/z (%): 313 (M^+, 13), 144 (100).

Results and Discussion

Alkyl amines can be prepared in various ways.[13] The reduction of the corresponding oximes is a representative route and seemed suitable for the present secondary alkyl amines because the starting ketones are readily accessible. Lithium aluminum hydride is often used for this transformation, but it is sometimes difficult to separate from the concomitant rearranged products in the case of phenylketone oximes.[14] Sodium borohydride does not reduce oximes under ambient conditions; however, the reactivity enhancement has been elaborated by adding Lewis acids like $TiCl_4$,[15] $CoCl_2$,[16] $ZrCl_4$,[17] $FeCl_3$,[18] $NiCl_2$,[9] or MoO_3.[9] Among the above additives, Ipaktschi's procedure using MoO_3 gave the best results for the present oximes. The last step to the final amides proceeded smoothly according to the reported protocol,[4] and the structures were confirmed by IR, NMR and MS spectra.

This note showed that the sequence from the ketone *via* oxime to α-alkyl amine is a suitable scheme for the necessary derivatives of modified carpropamid.

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