SYNTHESIS OF NITROGEN ANALOGS OF PHENVALERATE

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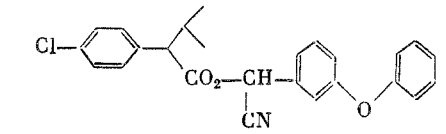
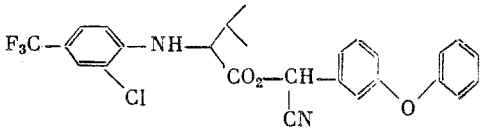
The structural modification of phenvalerate (I) has given a series of new highly efficient insectoacaricides such as fluvalinate (II), which is an α-amino acid derivative [1, 2].



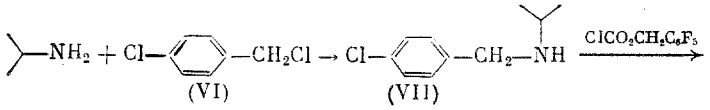
(I)



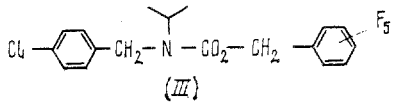
(II)

We have synthesized new phenvalerate analogs having an isopropyl group at the nitrogen atom in the acid fragment of the molecule. In the synthesis of (III), we used N-isopropylarylamine (VII) obtained in 70% yield upon the reaction of p-chlorobenzyl chloride (VI) with isopropylamine.

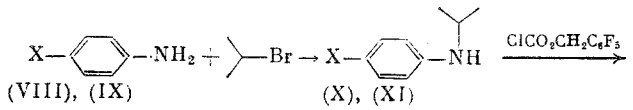
Arylamines (X) and (XI) were obtained by the alkylation of p-chloroaniline (VIII) and aniline (IX) using isopropyl bromide in 95 and 75% yield, respectively. Pentafluorobenzyl chlorocarbonate (XII) was synthesized from pentafluorobenzyl alcohol, which is known as an alcoholic component of pyrethroids [3]. The acylation of amines (VII), (X), and (XI) by chlorocarbonate (XII) in the presence of Na_2CO_3 in acetone leads to pyrethroids (III)-(V) in 70% yield. The PMR spectra of (III)-(V) lack the broad singlet of the i-Pr—NH proton observed in the spectra of amines (VII), (X), and (XI) at 1.23-3.3 ppm, but have signals corresponding to OCH_2 group protons at 5.1-5.2 ppm. The IR spectra of these compounds have bands characteristic for N—C=O (1680 cm^{-1}) and C—F groups (1000-1300 cm^{-1}).



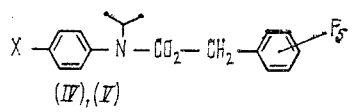
(VI) (VII)



(III)



(VIII), (IX) (X), (XI)



(IV), (V)

X = Cl (IV), (VIII), (X); H (V), (IX), (XI)

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The chemical purity of these products was established by gas-liquid and thin-layer chromatography. Their structures were indicated by IR and PMR spectroscopy and mass spectrometry.

A study of the insecticide activity of (III)-(V) by treatment of the imago of the house fly *(Musca domestica)* by 1% ethanolic solutions using a microvolumetric atomizer showed that these compounds do not possess insecticide activity. However, (V) and the salt obtained from (VII) and MeI display synergism to permethrine and cypermethrine (synergism coefficients of 1.3 and 1.5, respectively).

EXPERIMENTAL

The IR spectra were taken neat on a UR-20 spectrometer. The PMR spectra were taken on a Tesla BS-487 spectrometer at 100 MHz relative to TMS. The mass spectra were obtained on an MKh 1320 mass spectrometer at 70 eV. The temperature of the ionization chamber was 100-180°C. The gas-liquid chromatographic analyses were carried out on a Chrom-5 chromatograph on a 1.2-m column packed with 5% SE-30 on Chromaton N-AW-DMCS. The temperature was raised from 50 to 300°C at 14°C/min and helium was used as the gas carrier. Preparative chromatography was carried out on columns packed with 40/100 μm silica gel manufactured in Czechoslovakia.

N-Isopropyl-p-chlorobenzylamine (VII). A mixture of 16.1 g (0.10 mole) p-chlorobenzyl chloride (VI), 75 ml isopropylamine, 10.1 g (0.12 mole) $NaHCO_3$, and 10 ml glycerin was heated at reflux for 5 h and cooled to 20°C. The solidified mass was dissolved in 10% aq. KOH and extracted with three 100-ml portions of ether. The ethereal extract was washed with water and dried over solid KOH. The solvent was removed and the residue was distilled to give 13.5 g (70%) (VII), bp 71-72°C (1 mm), n_D^{20} 1.5190. IR spectrum (ν, cm^{-1}): 670, 690-710, 820, 850, 1100-1220, 1375-1395, 1500, 1580, 1600, 3300-3350. PMR spectrum in $CDCl_3$ (δ, ppm): 1.07 d (6H, $(C\underline{H}_3)_2CH$, J = 6.5 Hz), 1.23 bs (1H, N<u>H</u>), 2.80 sept (1H, $(CH_3)_2C\underline{H}$, J = 6.3 Hz), 3.70 s (2H, $C\underline{H}_2$), 6.73-7.58 m (4H, arom.).

Mixing amine (VII) and MeI at 5°C gave $[ClC_6H_4CH_2NHCH(CH_3)_2]\cdot CH_3I$ as a viscous yellow salt. IR spectrum (ν, cm^{-1}): 820, 1030, 1100, 1380, 1470, 1500, 1600, 2670-2740, 2860-2980, 3300-3500. Found, %: C 45.47; H 5.54; N 4.80. $C_{11}H_{16}IN$. Calculated, %: C 45.66; H 5.57; N 4.83.

N-Isopropyl-p-chloroaniline (X). A mixture of 2.5 g (0.02 mole) p-chloroaniline and 1.5 ml (0.016 mole) isopropyl bromide was heated for 2 h [4] and cooled to 20°C. The solidified mass was dissolved in 20% aq. KOH and extracted with ether. The ethereal extracts were combined, washed with water, and dried over solid KOH. Removal of the solvent gave 2.6 g (95%) (X) with 90% purity as indicated by gas-liquid chromatography. The product was purified on a silica gel column with 10:1 hexane–ether as the eluent, n_D^{20} 1.5180. IR spectrum (ν, cm^{-1}): 690-710, 820, 850, 1100-1220, 1375-1395, 1500, 1580, 3300-3350. PMR spectrum in $CDCl_3$ at 60 MHz (δ, ppm): 1.08 d [6H, $(C\underline{H}_3)_2CH$, J = 6.5 Hz], 3.3 br.s (1H, N<u>H</u>), 3.46 sept [1H, $(CH_3)_2C\underline{H}$, J = 6.3 Hz], 6.26-6.50 m (2H, arom.), 6.92-7.13 m (2H, arom.).

N-Isopropylaniline (XI) was obtained by analogy to (X) by the alkylation of aniline using isopropyl bromide. The yield of (XI) was 75%. IR spectrum (ν, cm^{-1}): 820, 850, 1100-1220, 1375-1395, 1500, 1580, 3300-3350. PMR spectrum in $CDCl_3$ at 60 MHz (δ, ppm): 1.10 d [6H, $(C\underline{H}_3)_2CH$, J = 6.5 Hz], 3.12 br.s (1H, N<u>H</u>), 3.5 sept [1H, $(CH_3)_2C\underline{H}$, J = 6.3 Hz], 6.25-6.55 m (3H, arom.), 6.83-7.08 m (2H, arom.).

Pentafluorobenzyl Chlorocarbonate (XII). A cooled solution of 20 g (0.1 mole) pentafluorobenzyl alcohol in 30 ml ether was added with stirring to 60-65 g phosgene condensed at −70°C in a three-necked flask equipped with a thermometer and condenser and cooled to −70°C with a dry ice–acetone bath. The mixture was maintained for 2 h at 0°C. The flask contents were warmed to 20°C. Excess phosgene evaporated. Then, the solvent was evaporated to give 26.6 g (100%) (XII), which did not require purification.

Pentafluorobenzyl(N,N-isopropyl-p-chlorobenzyl)carbamate (III). A solution of 1.22 g (11 mmoles) Na_2CO_3 in 13 ml water was added to 2.0 g (11 mmoles) (VII) dissolved in 100 ml acetone. Then, 3.1 g chlorocarbonate (XII) was added with vigorous stirring at 20°C and stirred for an additional 5 h. The solvent was removed. The residue was extracted with three 50-ml portions of CH_2Cl_2 and dried over 4-Å molecular sieves. Removal of the solvent gave 3.36 g (75%) (III) as a viscous, light yellow liquid, R_f 0.35 (Silufol, 4:1 hexane–ether as eluent). IR spectrum (ν, cm^{-1}): 1000-1300 (C–F), 1375-1390, 1680 (N–C=O). PMR

spectrum in $CDCl_3$ at 100 MHz (δ, ppm): 1.11 d [6H, $(C\underline{H}_3)_2CH$, J = 6.8 Hz], 4.34 s + sept [3H, $C\underline{H}_2N$, $(C\underline{H}_3)_2C\underline{H}$], 5.236 s (2H, $OC\underline{H}_2$), 7.195-7.28 m (4H, arom.). Mass spectrum, m/z: 407 (M^+), 226 ($M - CH_2C_6F_5$)$^+$, 184, 181 ($CH_2C_6F_5$)$^+$. Found, %: C 53.16; H 3.77; Cl 8.77; N 3.17. $C_{18}H_{15}ClF_5NO_2$. Calculated, %: C 53.02; H 3.71; Cl 8.70; N 3.43.

Pentafluorobenzyl(N,N-isopropyl-p-chlorophenyl)carbamate (IV) was obtained by analogy to (III) by the acylation of (X) using chlorocarbonate (XII). Carbamate (IV) was obtained in 78% yield as a white, crystalline powder, mp 127-128°C, R_f 0.32 (Silufol, 4:1 hexane–ether as the eluent). IR spectrum (ν, cm^{-1}): 1000-1300 (C–F), 1375-1390, 1680 (N–C=O). PMR spectrum in $CDCl_3$ at 100 MHz (δ, ppm): 1.095 d [6H, $(C\underline{H}_3)_2CH$, J = 6.8 Hz], 4.558 sept [1H, $(CH_3)_2C\underline{H}$), 5.161 s (2H, $OC\underline{H}_2$), 6.956-7.437 m (4H, arom). Mass spectrum, m/z: 393 (M^+), 181 ($CH_2C_6F_5$)$^+$, 168 [$ClC_6H_4NC_3H_7$]$^+$, 125, 99, [$C_3H_7NCO_2$]$^+$. Found, %: C 51.90; H 3.38; Cl 9.17; N 3.45. $C_{17}H_{13}ClF_5NO_2$. Calculated, %: C 51.85; H 3.33; Cl 9.02; N 3.55.

Pentafluorobenzyl-N-isopropylanilate (V) was obtained by analogy to (III) by the acylation of (XI) by chlorocarbonate (XII). Product (V) was obtained in 70% yield as a white crystalline powder, mp 80-81°C, R_f 0.34 (Silufol, 4:1 hexane–ether). IR spectrum (ν, cm^{-1}): 1000-1300 (C–F), 1375-1390, 1680 (N–C=O). PMR spectrum in $(CD_3)_2CO$ at 60 MHz (δ, ppm): 1.04 d [6H, $(C\underline{H}_3)_2CH$, J = 6.8 Hz], 4.43 sept [1H, $(CH_3)_2C\underline{H}$], 5.13 s (2H, $OC\underline{H}_2$), 6.97-7.38 m (5H, arom.). Mass spectrum, m/z: 359 (M^+), 344 ($M_1 - CH_3$)$^+$, 317 ($M_1 - C_3H_6$)$^+$, 300 ($M_1 - 59$), 273, 181 ($C_6F_5CH_2$)$^+$, 134 [$PhN(C_3H_7)$]$^+$, 119. Found, %: C 56.72; H 3.94; N 3.84. $C_{17}H_{14}F_5NO_2$. Calculated, %: C 56.83; H 3.93; N 3.90.

CONCLUSIONS

Syntheses were reported for new nitrogen analogs of phenvalerate, which possess a synergistic effect to pyrethroids.

LITERATURE CITED

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