A SHORT SYNTHESIS OF POTENTIAL JUVENOIDS BASED ON THE ISOXAZOLE CHEMISTRY

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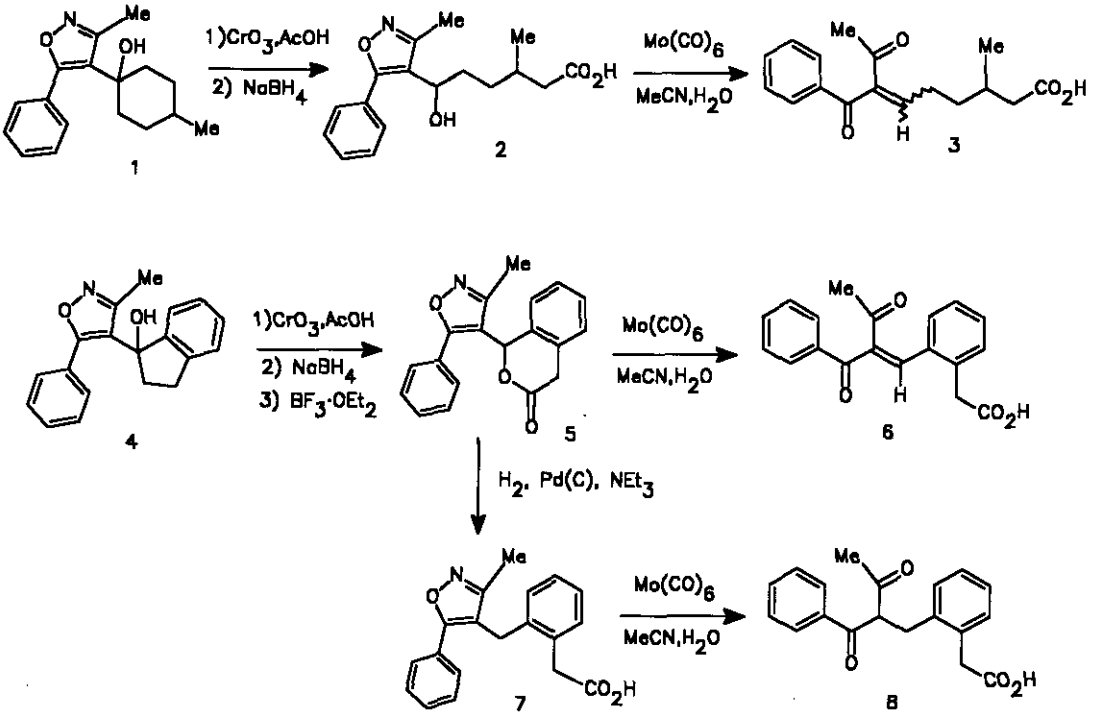
Abstract — 3,4,5-Trisubstituted isoxazoles (**1**) and (**4**) afforded, after chromic oxidation and borohydride reduction, (±)-3-methyl-6-(3-methyl-5-phenylisoxazol-4-yl)-6-hydroxyhexanoic acid (**2**) or (±)-1-(3-methyl-5-phenylisoxazol-4-yl)-3,4-dihydro-1*H*-2-benzopyran-3-ona (**5**) which were reduced to (±)-(Z/E)-3-methyl-7-benzoyl-8-oxonon-6-enoic acid (**3**) and (E)-2-(2-[2-benzoyl-3-oxobut-1-enyl]-phenyl)acetic acid (**6**) with molybdenum hexacarbonyl. Lactone (**5**) afforded a single *E*-diastereoisomer of acid (**6**). Catalytic hydrogenation of **5** afforded selectively isoxazole (**7**) which was reduced with molybdenum hexacarbonyl to 2-(2-[2-benzoyl-3-oxobutyl]phenyl)acetic acid (**8**). Structures of products are related with those of some juvenoids.

Third generation pesticides, based on naturally occurring insect hormones or plant toxins, are emerging as a means for more selective and environmentally benign pest control.[1] Between them, juvenoids are natural or synthetic substances capable of perfectly imitating the effects of insect juvenile hormone.[2] Searching for new economically available syntheses of new potential juvenoids, we have found a simple method to obtain different diketoacids which structures are related with those of some natural[3] and synthetic juvenoids.[4] The method is based on the isoxazole capability to conduct selective oxidation and reduction reactions over conveniently substituted isoxazolic intermediates.[5-8]

Thus, 3,4,5-trisubstituted isoxazoles (**1**) and (**4**) afforded, after chromic oxidation and borohydride reduction, acid (**2**) or lactone (**5**) which were reduced to products(**3**)and(**6**)with molybdenum hexacarbonyl in refluxing acetonitrile-water.[9] In these conditions, acid (**2**) afforded the unsaturated diketo acid (**3**) as a mixture of diastereoisomers, but lactone (**5**) afforded a single *E*-diastereoisomer of acid (**6**), which showed single signals of C=CH group in both ^{1}H and ^{13}C-nmr spectra. Formation of *E*-**6** can be explained by steric hindrance

between phenyl groups in the presumably planar transition state of elimination. The elimination of the hydroxylic function in the C-4 substituent of isoxazole is surprising because it is known[10] that a tertiary hydroxy group bonded to a carbon atom in the 3-position of the isoxazole nucleus is not eliminated in the same conditions. On the other hand, we have not obtained in any case the ß-enamino-ketone which is normally obtained in this kind of reactions,[9,10] probably due to a subsequent hydrolysis catalyzed by the carboxylic acid group, already present or generated in the reaction.



Attempts of opening isoxazole nucleus by catalytic hydrogenation were unsuccessful. Product (**2**) was recuperated unchanged under general hydrogenation conditions for trisubstituted isoxazoles[11] (1% palladium on charcoal as catalyst and triethylamine in ethanol). The same conditions afforded only the lactone hydrogenolysis product (**7**) when started from **5**, allowing a selective hydrogenation of the benzylic lactone group of **5** in the presence of the isoxazole moiety. Product (**7**) was reduced with molybdenum hexacarbonyl in acetonitrile-water, affording the corresponding diketo acid (**8**) in which the double bond of **6** does not exist. The previous hydrogenation of lactone (**5**), followed by reduction of the isoxazole nucleus is then equivalent to a selective reduction of the double bond in **6**. Thus the method allow to obtain different diketo acids in which carbon skeletons are related with some juvenoids, starting from easily available isoxazole derivatives and commercial cyclic ketones, by using a simple procedure.

EXPERIMENTAL

Melting points were obtained in open capillary tubes and are uncorrected. The ir spectra were registered with a Shimadzu IR-408 spectrophotometer in nujol mulls. The ^{1}H- and ^{13}C-nmr spectra were recorded on a Brucker AC200-E spectrometer; chemical shifts are reported in ppm from tetramethylsilane as internal standard, coupling constants in Hz. Methyl, methylene and methine groups, and quaternary carbons, were discriminated in ^{13}C-nmr spectra by DEPT experiments. Mass spectral data were taken with a Hewlett-Packard 5970A capillary glc/mass spectrometer at 75 eV. Elemental analyses were carried out on a Perkin Elmer 240-B apparatus.

General Procedure for the Synthesis of 1 and 4:

A vigorously stirred solution of 3-methyl-5-phenylisoxazol-4-yllithium in ether (225 ml) prepared at -55°C from 4-iodo-3-methyl-5-phenylisoxazole[12] (19.1 g, 67 mmol) and a hexane solution of *n*-butyllithium (1.6 M, 42 ml, 67 mmol) was treated dropwise with the appropriate cyclic ketone (4-methylcyclohexanone or indanone) (67 mmol) dissolved in tetrahydrofuran (40 ml). The mixture was stirred at -55°C for 3 h and then temperature was left to reach room temperature within a period of 5 h. The mixture was then treated with water (250 ml), extracted with ether (5x200 ml) and the combined ethereal portions were dried with magnesium sulfate and evaporated. Separations of products were obtained by using column chromatography (120 cm length, 5 cm diameter) filled with silica gel type 60 (Merck) and benzene as eluent.

***trans*-4-Methyl-1-(3-methyl-5-phenylisoxazol-4-yl)cyclohexan-1-ol (*trans*-1):**

mp 128-129°C (benzene-hexane); 10.90g (60% yield); ir (Nujol): ῡ 3350, 1625, 1590 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 0.88(3H, d, J=6.0 Hz, C$\underline{H}_3$CH), 1.30(3H, m, 2xC$\underline{H}$eq,C$\underline{H}$CH$_3$), 1.47(2H, m, 2xC$\underline{H}$ax), 1.77(4H, m, 2xC$\underline{H}_2$CHOH), 1.61(1H, s, exch, O$\underline{H}$), 2.46(3H, s, 3-CH$_3$isox), 7.44(m, 5Harom); ^{13}C-nmr ($CDCl_3$): δ 13.16(3-$\underline{C}$H$_3$isox), 22.26($\underline{C}$H$_3$CH), 29.78($\underline{C}$H$_2$CH$\underline{C}$H$_2$), 31.61($\underline{C}$HCH$_3$), 37.90($\underline{C}$H$_2$COH$\underline{C}$H$_2$), 69.49($\underline{C}$OH), 122.43(C4isox), 128.09(C3,C5arom), 129.66(C2,C6arom), 129.75(C4arom), 130.28(C1arom), 158.98(C3isox), 165.29(C5isox); ms: m/z (%): 271(M^+,9), 214[(M-CHOCH$_2$CH$_2$)$^+$,100], 200(10), 157(15), 105(67), 77(60), 55(26), 51(17), 42(17), 41(23); Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.28, H, 7.75, N, 5.17. Found: C, 75.40, H, 7.81, N, 5.03.

***cis*-4-Methyl-1-(3-methyl-5-phenylisoxazol-4-yl)cyclohexan-1-ol (*cis*-1):**

mp 123-124°C (benzene-hexane); 3.26g (18% yield); ir (Nujol): ῡ 3350, 1630, 1590 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 0.83(3H, d, J=6.0 Hz, C$\underline{H}_3$CH), 1.04(2H, m, 2xC$\underline{H}$eqCHCH$_3$), 1.50(2H, m, 2xC$\underline{H}$eqCOH), 1.75(3H, m, 2xC$\underline{H}$axCHCH$_3$, C$\underline{H}$CH$_3$), 1.80(1H, s, exch, O$\underline{H}$), 2.09(2H, m, 2xC$\underline{H}$axCOH), 2.47(3H, s, 3-CH$_3$isox), 7.50(m, 5Harom); ^{13}C-nmr ($CDCl_3$): δ 13.42(3-$\underline{C}$H$_3$isox), 18.70($\underline{C}$H$_3$CH), 28.09($\underline{C}$HCH$_3$), 28.72($\underline{C}$H$_2$CH-$\underline{C}$H$_2$), 34.74($\underline{C}$H$_2$COH$\underline{C}$H$_2$), 70.42($\underline{C}$OH), 120.58(C4isox), 128.21(C3,C5arom), 129.75(C2,C6arom), 129.86 (C4arom), 130.40(C1arom), 159.17(C3isox), 166.67(C5isox); Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.28, H, 7.75,

N, 5.17. Found: C, 75.39, H, 7.83, N, 5.24.

(±)-1-(3-Methyl-5-phenylisoxazol-4-yl)indan-1-ol (4):

mp 142-143°C (benzene-hexane); 14.60g (75% yield); ir (Nujol): ũ 3400, 1625, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.10(3H, s, 3-C<u>H</u>$_3$isox), 2.45(2H, t, J=5.0 Hz, C<u>H</u>$_2$COH), 2.70(1H, s, exch, OH), 3.00(2H, m, J=5.0 Hz, C<u>H</u>$_2$C$_6$H$_4$), 7.20(m, 9Harom); ms: m/z (%): 273[(M-H_2O)$^+$,25], 231(31), 203(66), 202(64), 77($C_6H_5^+$,100); Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.35, H, 5.84, N, 4.81. Found: C, 78.21, H, 5.93, N, 4.90.

General Procedure for the Synthesis of 2 and 5:

Chromic Oxidation of Compounds (1) and (4): A vigorously stirred solution of the isoxazole derivative (20 mmol) dissolved in glacial acetic acid (150 ml) was heated at 30°C for 1 h with chromium trioxide (12 g, 120 mmol). After working up, the acid residue was purified by column chromatography (silica gel 60G Merck, chloroform/methanol 10/1 as eluent) and crystallized in benzene-hexane when it is a solid.

(±)-3-Methyl-6-(3-methyl-5-phenylisoxazol-4-yl)-6-oxohexanoic acid:

Oil, 4.99g (83% yield), ir (Neat): ũ 3200, 1700, 1610, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 0.85(3H, d, J=6.0 Hz, C<u>H</u>$_3$CH), 1.70(3H, m, C<u>H</u>$_2$C<u>H</u>), 2.20(2H, m, C<u>H</u>$_2$CO_2<u>H</u>), 2.45(3H, s, C<u>H</u>$_3$isox), 2.50(2H, m, C<u>H</u>$_2$CO), 7.50 (br, s, 5Harom), 9.10(1H, br, s, exch, CO_2<u>H</u>); ms: m/z (%): 301(M^+,1), 214[(M-$CH_3CHCH_2CO_2H$)$^+$, 100], 105(82), 77(31); Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.77, H, 6.31, N, 4.65. Found: C, 67.61, H, 6.43, N, 4.72.

2-(2-[3-Methyl-5-phenylisoxazol-4-ylcarbonyl]phenyl)acetic acid:

mp 152-153°C (benzene-hexane); 5.57g (87% yield); ir (Nujol): ũ 3500, 1700, 1655, 1610, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.30(3H, s, C<u>H</u>$_3$isox), 4.20(2H, s, C<u>H</u>$_2$), 7.35(m, 7Harom), 7.70(m, 2Harom), 7.75(1H, br, s, exch, CO_2<u>H</u>); ms: m/z (%): 321(M^+,1), 235(25), 105($C_6H_5CO^+$, 100), 77(65); Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.03, H, 4.67, N, 4.36. Found: C, 71.15, H, 4.58, N, 4.43.

Reduction of ketoacids to 2 and 5:

The corresponding keto acid (12.5 mmol) dissolved in aqueous NaOH (0.5 N, 30 ml) was treated overnight with $NaBH_4$ (0.95 g, 25 mmol) dissolved in aqueous NaOH (2 N, 20 ml) at room temperature. Then, solution was acidified with aqueous 2 N HCl, extracted with ether (4x250 ml), the combined extracts were dried ($MgSO_4$) and evaporated. Products were purified by crystallization or by column chromatography (chloroform/methanol 9/1 as eluent) in case of oil (**2**). Lactone (**5**) was obtained by refluxing crude acid with boron trifluoride etherate (48% w/w, 3 ml) in dry benzene (50 ml) for 1 h. Water produced was removed by distillation in a Dean-Stark unit. After working up, lactone (**5**) was crystallized in benzene-hexane from the residue.

(±)-3-Methyl-6-(3-methyl-5-phenylisoxazol-4-yl)-6-hydroxyhexanoic acid (2):

Oil; 3.40g (90% yield); ir (Neat): ũ 3400, 1715, 1660 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 0.90(3H, d, J=6.0 Hz,

$C\underline{H}_3CH$), 1.29(2H, m, $C\underline{H}_2CHCH_3$), 1.50(1H, m, $C\underline{H}CH_3$), 1.95(2H, m, $C\underline{H}_2CHOH$), 2.03(1H, s, exch, $CHO\underline{H}$), 2.16(2H, m, $C\underline{H}_2CO_2H$), 2.35(3H, s, $C\underline{H}_3$isox), 4.83(1H, t, J=6.0 Hz, $C\underline{H}OH$), 6.70(1H, br, s, exch, CO_2H), 7.40(m, 3Harom), 7.60(m, 2Harom); ^{13}C-nmr ($CDCl_3$): δ 11.43($\underline{C}H_3$isox), 19.62($\underline{C}H_3CH$), 29.68, 29.73($\underline{C}HCH_3$, 2 diastereomers), 32.73($\underline{C}H_2CHCH_3$), 33.40($\underline{C}H_2CHOH$), 41.28($\underline{C}H_2CO_2H$), 65.42, 65.70 ($\underline{C}HOH$, 2 diastereomers), 116.64(C4isox), 127.78(C1phenyl), 127.94(C3,C5phenyl), 128.80((C2, C6phenyl), 130.04(C4phenyl), 159.86(C3isox), 166.06(C5isox), 178.16($\underline{C}O_2H$); Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31, H, 6.98, N, 4.62. Found: C, 66.93, H, 6.89, N, 4.54.

(±)-1-(3-Methyl-5-phenylisoxazol-4-yl)-3,4-dihydro-1*H*-2-benzopyran-3-ona (5):

mp 201 °C (benzene-hexane); 3.50g (92% yield); ir (Nujol): ῡ 1750, 1640 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.10(3H, s, $C\underline{H}_3$isox), 3.84(2H, d, J=3.0 Hz, $C\underline{H}_2CO$), 6.55(1H, s, $C\underline{H}OCO$), 7.01(d, J=7.0 Hz, 1Harom), 7.35(m, 3Harom), 7.53(m, 5Harom); ^{13}C-nmr ($CDCl_3$): δ 11.18($\underline{C}H_3$isox), 36.57 ($\underline{C}H_2CO_2$), 73.65($\underline{C}HOCO$), 109.65(C4isox), 126.94(C1phenyl), 127.77(C3,C5phenyl), 129.11(C2,C6phenyl), 130.67(C4phenyl), 124.67, 127.57, 127.87, 129.64(C4,C5,C6,C7[2-benzopyran]), 131.23, 132.66(C9,C10[2-benzopyran]), 160.24(C3-isox), 168.72(C5isox), 169.60($\underline{C}OO$); Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74, H, 4.95, N, 4.59. Found: C, 74.83, H, 5.02, N, 4.52.

Synthesis of 7:

Lactone (**5**) (4.1 mmol), dissolved in a mixture of ethyl acetate (25 ml), triethylamine (25 ml) and dimethylformamide (10 ml), was hydrogenated (3 atm) in a Chas. W. Cook hydrogenator for 1 h at 50 °C, using 1% palladium on charcoal (1 g) as catalyst. Then catalyst was filtered and the solution was washed with water (20 ml). The organic layer was separated and the aqueous layer was extracted with ether (300ml). The combined extracts were dried ($MgSO_4$), filtered and evaporated, affording **7** as a sticky solid.

2-(2-[3-Methyl-5-phenylisoxazol-4-ylmethyl]phenyl)acetic acid (7):

Sticky solid; 1.05g (84% yield); ir (Nujol): ῡ 3300, 1720, 1650 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.05(3H, s, $C\underline{H}_3$isox), 3.69(2H, s, $C_6H_4C\underline{H}_2$isox), 3.91(2H, s, $C\underline{H}_2CO_2H$), 6.90(m, 1Harom), 7.19(m, 3Harom), 7.32(m, 3Harom), 7.51(m, 2Harom), 9.82(1H, br, s, exch, $CO_2\underline{H}$); ^{13}C-nmr ($CDCl_3$): δ 10.00($\underline{C}H_3$isox), 25.84($C_6H_4\underline{C}H_2$isox),38.83($\underline{C}H_2CO_2H$),110.90(C4isox),126.59(C3,C5phenyl*mono*)127.72(C1phenyl*mono*), 128.78(C2,C6phenyl*mono*), 130.86(C4phenyl*mono*), 126.93, 127.42, 127.97, 129.62(C2,C5phenyl*orthodi*), 132.32, 136.51 (C1,C2phenyl*orthodi*), 161.31 (C3isox), 165.94(C5isox), 177.01($\underline{C}O_2H$); Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25, H, 5.58, N, 4.56. Found: C, 73.31, H, 5.49, N, 4.63.

General Procedure for the Synthesis of 3, 6 and 8:

Molybdenum hexacarbonyl (0.18 g, 0.68 mmol) was added to a solution of hydroxy acid (**2**), lactone (**5**) or acid (**7**) (1 mmol) dissolved in a mixture of acetonitrile (15 ml) and water (5 ml) and the mixture was refluxed for 3 h under N_2 atmosphere. Then solvent was evaporated and the acid purified by dry chromatography (chloroform/methanol 10/1 as eluent).

(±)-(Z/E)-3-Methyl-7-benzoyl-8-oxonon-6-enoic acid (3):

Oil; 0.147g (51% yield); ir (Neat): ῡ 3300, 1700, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 0.99(3H, d, J=6.0 Hz, $C\underline{H}_3CH$), 1.25(2H, m, $C\underline{H}_2CHCH_3$), 1.62(1H, m, $C\underline{H}CH_3$), 2.11(2H, m, $C\underline{H}_2CH=CH$), 2.22(2H, m, $C\underline{H}_2CO_2H$), 2.35(3H, s, $C\underline{H}_3CO$), 7.46(m, 3Harom + $\underline{H}C=C$), 7.85(m, 2Harom) 8.52(1H, br, s, exch, $CO_2\underline{H}$); ^{13}C-nmr ($CDCl_3$): δ 19.46($\underline{C}H_3CH$), 29.52($\underline{C}HCH_3$), 29.75($\underline{C}H_3CO$), 29.87($\underline{C}H_2CHCH_3$), 31.17 ($C\underline{H}_2CH=C$), 41.34($\underline{C}H_2CO_2H$), 128.33, 128.80, 130.00((C2-C6phenyl), 136.50(C1phenyl), 133.50, 134.00 ($\underline{C}=CH$, 2 isomers), 142.55($C=\underline{C}H$), 178.64($\underline{C}O_2H$), 196.55, 196.75($\underline{C}OC_6H_5$, 2 isomers), 202.25 ($\underline{C}OCH_3$); Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81, H, 6.99. Found: C, 69.56, H, 6.54.

(E)-2-(2-[2-Benzoyl-3-oxobut-1-enyl]phenyl)acetic acid (6):

Sticky solid; 0.246g (80% yield); ir (Nujol): ῡ 3300, 1700, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.54(3H, s, $C\underline{H}_3CO$), 3.61(2H, s, $C\underline{H}_2CO_2H$), 7.03(m, 2Harom), 7.25(m, 2Harom), 7.56(m, 3Harom), 7.83(m, 2Harom), 8.37(1H, s, $C=C\underline{H}$); ^{13}C-nmr ($CDCl_3$): δ 26.77($\underline{C}H_3CO$), 43.12($\underline{C}H_2CO_2H$), 126.11, 128.10, 129.93, 134.02(C3-C6phenyl*orthodi*), 135.94, 140.14(C1,C2phenyl*orthodi*), 128.68(C3,C5phenyl*mono*), 129.16(C2, C6phenyl*mono*), 131.23(C4phenyl*mono*), 138.64(C1phenyl*mono*), 132.70($\underline{C}=CH$), 141.95($C=\underline{C}H$), 176.44($\underline{C}O_2H$), 197.52($C_6H_5\underline{C}O$), 198.28($CH_3\underline{C}O$); Anal. Calcd for $C_{19}H_{16}O_4$: C, 74.01, H, 5.23. Found: C, 73.12, H, 5.16.

2-(2-[2-Benzoyl-3-oxobutyl]phenyl)acetic acid (8):

Sticky solid; 0.248g (80% yield); ir (Nujol): ῡ 3300, 1700, 1600 cm^{-1}; ^{1}H-nmr ($CDCl_3$): δ 2.10(3H, s, $C\underline{H}_3CO$), 3.20(2H, d, J=6.0 Hz, $C\underline{H}_2CO_2H$), 3.60(2H, m, $CH_2C_6H_4$), 4.85(1H, m, $OCC\underline{H}CO$), 7.00(m, 4Harom), 7.30(m, 3Harom), 7.75(m, 2Harom), 8.89(1H, br, s, exch, $COO\underline{H}$); ^{13}C-nmr ($CDCl_3$): δ 28.81($\underline{C}H_3CO$), 31.29($CH\underline{C}H_2C_6H_4$), 38.10($\underline{C}H_2CO_2H$), 62.84($OC\underline{C}HCO$) 126.78, 127.17, 129.63, 133.49(C3-C6phenyl*orthodi*), 132.16, 136.18(C1,C2phenyl*orthodi*), 128.56(C3,C5phenyl*mono*), 128.69(C2, C5phenyl*mono*), 130.66 (C4phenyl*mono*), 136.90(C1phenyl*mono*), 175.69($\underline{C}O_2H$), 195.83($C_6H_5\underline{C}O$), 203.15($CH_3\underline{C}O$); Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.53, H, 5.85. Found: C, 72.12, H, 5.94.

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REFERENCES

1. W. Sirremberg, '*Chemistry of Pesticides*', ed. by K. H. Büchel, Wiley, New York, 1983, p. 185.
2. Z. Wimmer and M. Romanuk, *Coll. Czech. Chem. Comm.*, 1989, **54**, 2302.
3. W. S. Bowers, H. M. Fales, M. J. Thomson, and E. C. Uebel, *Science*, 1966, **154**, 1020.
4. Z. Wimmer and M. Romanuk, *Coll. Czech. Chem. Comm.*, 1981, **46**, 2573.
5. T. Antequera, V. Ramos, and T. Torroba, *Heterocycles*, 1986, **24**, 3203.
6. T. Antequera, C. Polo, V. Ramos, and T. Torroba, *An. Quim. C*, 1988, **84**, 329.
7. C. Polo, V. Ramos, T. Torroba, R. Bossio, S. Marcaccini, and R. Pepino, *Heterocycles*, 1990, **31**, 811.
8. C. Polo, V. Ramos, T. Torroba, R. Bossio, S. Marcaccini, and R. Pepino, *Heterocycles*, 1991, **32**, 1757.
9. M. Nitta and T. Kobayashi, *J. Chem. Soc., Chem. Commun.*, 1982, 877.
10. P. G. Baraldi, A. Barco, S. Benetti, M. Guarneri, S. Manfredini, G. P. Pollini, and D. Simoni, *Tetrahedron Lett.*, 1985, **26**, 5319.
11. P. G. Baraldi, A. Barco, S. Benetti, G. P. Pollini, and D. Simoni, *Synthesis*, 1987, 857, and references cited therein.
12. N. K. Kochetkov, S. D. Sokolov, and N. M. Vagurtova, *Zhur. Obsh. Khim.*, 1961, **31**, 2326.

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