5-ACETYLLINDAN ARYLOXYACETOHYDRRAZONE DERIVATIVES: SYNTHESIS AND ANTITUBERCULOSIS ACTIVITY

5-ASETLINDAN ARİLOXİASETOHYDRAZON TÜREVLERİ: SENTEZLERİ VE ANTITUBERKÜLOZ ETKİLERİ

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Some 5-aceyllindan ariloxyceto hydrzone derivatives were synthesized by reacting 5-aceyllindan with ariloxyceto hydrzone derivatives in butanol. The structure of the compounds obtained were performed by using IR, 1H NMR, Mass (FAB+) spectroscopy and elemental analysis results. The antituberculosis activity was examined by TAACF.

**Keywords**: 5-Acetyllindan; Aryloxyaceto hydrzone; Antituberculous Activity

Bazı 5-aceyllindan ariloxiseto hydrzone türevleri, 5-aceyllindan ve ariloxiseto hydrzone türevlerinin bitanolu içinde reaksiyonu ile sentezlendi. Bileşiklerin yapılıarı, IR, 1H NMR, Mass (FAB +) spektroskopisi ve elemental analiz sonuçları kullanılarak aydınlatıldı. Antitüberkülöz etki TAACF tarafından denendi.

**Anahtar kelimeler**: 5-Acetyllindan; Ariloxiseto hydrzone, Antitüberköloz Aktivite

Introduction

It is well known that hydrazide/hydrazone derivatives show diverse biological activities (tuberculostatic(1-3), antibacterial and antifungal activities(4-6), monoamine oxidase inhibitor activity (7,8)).

In this work, we have synthesized some new 5-acetyllindan ariloxyceto hydrzone derivatives by reacting 5-acetyllindan with ariloxyceto hydrzones. (Figure)

The antituberculosis activities of the compounds were examined by TAACF (Tuberculosis Antimicrobial Acquisition and Coordinating Facility), Southern Research Institute, GWL Hansen’s Disease Center, Colorado State University.

Materials and Methods

Melting points were determined by using a Gallenkamp apparatus and are uncorrected. Spectroscopic data were recorded by the following instruments: IR: Shimadzu IR-435 Spectrofotometer; 1H-NMR: Bruker 250 MHz Spectrometer; MS: Fast atom bombardment mass spectra (FAB-MS) were obtained by VG Quattro Mass Spectrometer. Microanalytical data were obtained by Microanalytical Section of Service Central (CNRS, Ecole Normale Chimie de Montpellier, France).

**General Procedure for the Synthesis of the Compounds 5-Acetyllindan(I)**

This compound was prepared according to the method reported in literature(9,10).

5-Aryloxyaceto hydrzones(2)

These compounds were prepared according to the previously reported method(1,11,12).

5-Acetyllindan ariloxyceto hydrzone derivatives(3a-n)

A mixture of 5-acetyllindan (0.005 mol) and an appropriate ariloxyceto hydrzone or α-aryloxy propio hydrzone (0.005 mol) in butanol was refluxed for 5h. The solid separated upon cooling was filtered, dried and recrystallized (Table 1).

**The Spectral Data Of The Compounds**

3a: IR(KBr, cm⁻¹): 3205 (N-H), 1686 (C=O), 1665, 1560 (C=N, C=C), 1260 (C=O-C)

**Microanalytical Data**: Anal. Calcd. for C₁₉H₂₀N₂O₂ (308.38): C, 74.00; H, 6.54; N, 9.08. Found: C, 73.87; H, 6.23; N, 9.00

3b: IR (KBr, cm⁻¹): 3195 (N-H), 1690 (C=O), 1670, 1575 (C=N, C=C), 1250 (C=O-C)

**Microanalytical Data**: Anal. Calcd. for C₁₉H₂₀N₂O₂ (308.38): C, 74.00; H, 6.54; N, 9.08. Found: C, 73.87; H, 6.23; N, 9.00

3I-1NMR (250 MHz) (DMSO -d₆, δ ppm): 1.95-2.10 (2H, m, protons C₂ of indan), 2.20 and 2.25 (3H, two s, CH₃) 2.80-2.95 (4H, m, protons C₁ and C₃ of indan), 4.75 and 5.15 (2H, two s, COCH₃), 6.85-7.05 (3H, m, protons C₃,C₄ and C₅ of phenyl), 7.25-7.35 (3H, m, protons C₄, C₆, C₇ of indan), 7.55, 7.70 (2H, d(J=7.86 Hz), protons C₂ and C₆ of phenyl), 10.50 (1H, br, NH).

Microanalytical Data: Anal. Calcd. for C₁₉H₂₀N₂O₂ (308.38): C, 74.00; H, 6.54; N, 9.08. Found: C, 73.87; H, 6.23; N, 9.00

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(J=8.92 Hz) protons C₃ and C₅ of phenyl), 7.20-7.40
(3H, m, protons C₄, C₆, C₇ of indan), 7.60 (2H, d (J=7.20 Hz), protons, C₂ and C₆ of phenyl), 10.70 (1H, br, NH)

**MASS (FAB) M+1:** m/z: 343

**Microanalytical Data:** Anal. Calcd. for C₁₉H₁₀Cl₂N₂O₂
(342.82): C, 66.56; H, 5.58; N, 8.17. Found: C, 66.23; H, 5.07; N, 8.02

3c: IR (KBr, cm⁻¹); 3189 (N-H), 1686 (C=O), 1667, 1570 (C=N, C=C), 1270- (C-O-C)

**¹H-NMR (250 MHz) (DMSO-d₆, δ, ppm):** 1.90-2.10
(2H, m, protons C₂ of indan), 2.25 2.30 (6H, two s, two CH₃), 2.80-2.95 (4H, m, protons C₁ and C₃ of indan), 4.70 and 5.10 (2H, two s, COCH₂), 6.75 6.90 (2H, two d (J=8.41 Hz and J=8.46 Hz), protons C₄ and C₅ of phenyl), 7.00-7.25 (3H, m, protons C₄, C₆ and C₇ of indan), 7.50, 7.70 (2H, two d (J=7.85 Hz and 8.02 Hz), protons C₂ and C₆ of phenyl), 10.70 (1H, br, NH)

**MASS (FAB) M+1:** m/z: 323

**Microanalytical Data:** Anal. Calcd. for C₂₀H₂₂N₂O₂
(322.40): C, 74.51; H, 6.87; N, 8.69. Found: C, 74.22; H, 6.88; N, 8.47

3d: IR (KBr, cm⁻¹); 3198 (N-H), 1691 (C=O), 1673, 1580 (C=N, C=C), 1285 (C-O-C)

**¹H-NMR (250 MHz) (DMSO-d₆, δ, ppm):** 1.95-2.15
(2H, m, protons C₂ of indan), 2.25 and 2.30 (3H, two s, CH₃), 2.80-2.95 (4H, m, protons C₁ and C₃ of indan), 4.70 and 5.40 (2H, two s, COCH₂), 7.00-7.40 (3H, m, protons C₄, C₆, C₇ of indan), 7.55 (2H, d (J=7.53 Hz), protons C₂ and C₆ of phenyl), 8.15, 8.30 (2H, two d (J=8.19 and 8.02 Hz) protons C₁ and C₅ of phenyl), 9.50 and 10.60 (1H, two s, NH) **MASS (FAB) M+1:** m/z: 354

**Microanalytical Data:** Anal. Calcd. for C₁₉H₁₀N₃O
(353.38): C, 64.57; H, 5.42; N, 11.89. Found: C, 64.55;
Table 1. Some Characteristics of Compounds

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H, 5.27; N, 11.92
3e: IR (KBr, cm⁻¹): 3172 (N-H), 1689 (C=O), 1665, 1569 (C=N, C=C), 1280 (C-O-C)

¹H-NMR (250 MHz) (DMSO-d₆ δ ppm): 1.90-2.05 (2H, m, protons C₂ of indan), 2.15, 2.20, 2.25 (9H, tree s, tree CH₃), 2.83-2.95 (4H, m, protons C₁ and C₃ of indan), 4.40 and 4.75 (2H, two s, COCH₂), 6.80-7.65 (6H, m, aromatic protons), 10.30 and 10.65 (1H, two s, NH)

MASS (FAB) M+1: m/z: 337

Microanalytical Data: Anal. Calcd. for C₂₁H₂₆N₂O₂ (336.43): C, 74.97; H, 7.19; N, 8.32. Found: C, 74.90; H, 7.00; N, 8.57
3f: IR (KBr, cm⁻¹); 3165 (N-H), 1679 (C=O), 1665, 1575 (C≡N, C≡C), 1250 (C-O-C)

1H-NMR (250 MHz) DMSO-d₆  δ ppm): 1.55 (3H, d (J=6.61 Hz), CH₃-C-O), 1.95-2.05 (2H, m, protons C₂ of indan), 2.20, 2.25 (3H, two s, CH₃), 2.70-2.95 (4H, t, protons C₁ and C₂ of indan), 5.10 and 5.70 (1H, two q(J=6.54 and 6.55 Hz) COCH), 6.80-7.05 (3H, m, protons C₃, C₅, and C₇ of phenyl), 7.20-7.45 (3H, m, protons C₆, C₆, C₇ of indan), 7.55 and 7.65 (2H, two d(J=6.88 Hz and J=7.85 Hz), protons C₂ and C₇ of phenyl), 10.60 (1H, br, NH)

MASS (FAB) M⁺: m/z: 323

Microanalytical Data: Anal. Calcd. for C₂₀H₂₁N₂O₂ (367.39); C, 65.38; H, 5.76; N, 11.43. Found: C, 65.73; H, 5.52; N, 11.80

3k: IR (KBr, cm⁻¹); 3272 (N-H), 1677 (C=O), 1655, 1583 (C≡N, C≡C), 1250 (C-O-C)

1H-NMR (250 MHz) DMSO-d₆  δ ppm): 1.50-2.15 (3H, m, CH₃-C-O), 1.95-2.05 (2H, m, protons C₂ of indan), 2.25, 2.30 (3H, two s, CH₃), 2.80-2.95 (4H, m, protons C₁ and C₂ of indan), 5.20 and 5.90 (1H, two q(J=6.53 and 6.50 Hz) COCH), 7.20-7.90 (7H, m, aromatic protons), 9.50 and 10.70 (1H, two s, NH)

MASS (FAB) M⁺: m/z: 368

Microanalytical Data: Anal. Calcd. for C₂₀H₂₁N₂O₄ (367.39); C, 65.38; H, 5.76; N, 11.43. Found: C, 65.02; H, 5.57; N, 11.09

3l: IR (KBr, cm⁻¹); 3226 (N-H), 1679 (C=O), 1670, 1573 (C≡N, C≡C), 1280 (C-O-C)

1H-NMR (250 MHz) DMSO-d₆  δ ppm): 1.60 (3H, two s, CH₂-C-O), 1.90-2.05 (2H, m, protons C₂ of indan), 2.25, 2.30 (3H, two s, CH₃), 2.80-2.95 (4H, m, protons C₁ and C₂ of indan), 5.20 and 5.90 (1H, two q(J=6.53 and 6.50 Hz) COCH), 6.95-7.25 (3H, m, protons C₄, C₆, C₇ of indan), 7.50 and 7.60 (2H, two d(J=10.99 Hz and J=7.92 Hz), protons C₂ and C₆ of phenyl), 8.15, 8.25 (2H, two d(J=6.96 Hz and J=7.02 Hz), protons C₃ and C₅ of phenyl), 10.80 (1H, br, NH)

MASS (FAB) M⁺: m/z: 368

Microanalytical Data: Anal. Calcd. for C₂₀H₂₁N₂O₄ (367.39); C, 65.38; H, 5.76; N, 11.43. Found: C, 65.27; H, 5.87; N, 11.72

3m: IR (KBr, cm⁻¹); 3207 (N-H), 1696 (C=O), 1664, 1598 (C≡N, C≡C), 1270 (C-O-C)

1H-NMR (250 MHz) DMSO-d₆  δ ppm): 1.50 (3H, d(J=6.65 Hz), CH₃-C-O), 1.95-2.10 (2H, m, protons C₂ of indan), 2.20, 2.35 (6H, m, two CH₃), 2.80-2.95 (4H, t, protons C₁ and C₂ of indan), 4.95 and 5.60 (1H, two q(J=6.55 and 6.51 Hz) COCH), 6.70, 6.85 (2H, two d(J=8.52 Hz and J=8.50 Hz), protons C₃ and C₅ of phenyl), 7.00 and 7.25 (2H, m, protons C₄, C₆, C₇ of indan), 7.55, 7.65 (2H, two d(J=9.27 Hz and J=8.90 Hz), protons C₂ and C₆ of phenyl), 10.50 and 10.70 (1H, two s, NH)

MASS (FAB) M⁺: m/z: 337

Microanalytical Data: Anal. Calcd. for C₂₁H₂₄N₂O₅ (336.43); C, 74.97; H, 7.19; N, 8.32. Found: C, 75.32; H, 6.98; N, 8.43
Antituberculosis Activity

Primary screening was conducted at 12.5 μg/ml against Mycobacterium tuberculosis H37 Rv in BACTEC 12 B medium. Antituberculosis activities of the compounds were examined by TAACF according to the BACTEC 460 radiometric system (13, 14).

Results and Discussion

In the present work, 14 new 5-acetylindan aryloxyacetohydrazide derivatives were synthesized by reacting 5-acetylindan with aryloxyacetohydrazides.

The structure of the compounds were elucidated by IR, 1H-NMR, MASS spectra and elemental analyses. In the IR spectra of all the compounds N-H and C=O bands were observed at about 3450-3200 cm⁻¹ and 1680 cm⁻¹, respectively. The 1H-NMR spectra of all the compounds gave the peaks characteristic for protons C1, C2, C3 of indan. We observed paired peaks for protons of CH3-C=N, COCH2, COCH and NH, corresponding to trans(E) and cis(Z) forms of the compounds. For each compound, the intensities of these paired peaks differed from others, due to the variable amounts of E and Z, which are usually unequal.

A low antituberculosis activity (MIC=12.5 μg/ml) was observed only for compounds 3a, 3b, 3d in the range 23.35 and 26% respectively. Rifampicin showed inhibition values (at 0.25 μg/ml) in the range 98%.

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References


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