Pak. Jour. of Pharm. Sciences
Vol. 10, No.2, July, 1997, pp.1-12

ACETATES AND BENZOATES OF ALKYL CATECHOLS AND EVALUATION OF THEIR ANTIBACTERIAL ACTIVITY

BINA S. SIDDIQUI, SABIRA BEGUM, QAYYUM ADIL, MURTAZA AKBER, *SADIQA FIRDOUS, **KHURSHEED ALI KHAN, **SHAKEEL AHMED KHAN AND **SYED MOHAMMAD KHALID

H.E.J. Research Institute of Chemistry
**Department of Chemistry, **Department of Microbiology*
University of Karachi, Karachi-75270, Pakistan

ABSTRACT

Potential biologically active alkyl catechol esters were prepared and their antibacterial activity was determined against 12 Gram-positive and 16 Gram-negative bacteria. Esterificalion (acetylation and benzoylation) of mono-, di- and tetra- substituted alkyl calechols afforded the di-acetyl and di-benzovl derivatives in each case. In the primary screening it was observed that the substitution of hydroxyl group in alkyl catechol with an acyl group generally resulted in a decrease of antibacterial activity. A number of acetyl and benzovl derivatives inhibited the growth of *Salmonella typhi.* In case of Gram-positive bacteria only di-O-benzoyl-3,5,6,-tetra-(3-hcsyl) catechol (26) showed a significant activity.

INTRODUCTION

Catechol esters are reported to possess strong bactericidal activity. The phenolic ester of benzoic acid and pytomucic acid showed strong bactericidal activity than the corresponding ester of acetic acid (Kameonos *et al.* 1963). Its mono- and di- acetate derivatives were found to inhibit blood platelet aggregation in human platelet rich plasma (Dupin *et al.,* 1986). The diacetyl catechol was found to be effective against *Psendorrronas* (Wang *et al.,* 1988). It has further been shown that in phenolic compounds the order of biological *properly* is dependent on the number of hydroxyl groups and nature of other substituents. Thus, for example, in the series of 4-n-alkyl resorcinols the gemticidal activity becomes greater as the alkyl group lengthens from ethyl to propyl to butyl and so on (Miller *et al.,* 1918). Trichloroacetate ester of catechol was reported as an effective insecticide (Sen *et al.,* 1949). Chlorosubstituted phenolic compounds such as catechol and its acetoxy derivatives were tested for insecticidal activity on the rice moth Carcya c*ephalo-nica)* and it was observed that replacement of phenolic group by acetoxyl group decreases toxicity to a great extent (Bhargava *et al.,* 1950). Similarly, when the antimutagenic activity of various dihydroxy aromatic antioxidant compounds, pyrocalechol, hydroquinone and 2,6-di-tert-butyl-hydroquinone was studied, it was observed that the most potent antimutagen was 3.5-di-tert-butyl pyrocatechol and that the antimutagenic effect of pyrocatechol and hydroquinones depended upon the position of OH and tort-butyl group (Meyer *et al,* 1982). In another study by Japanese

scientists a catechol ester with 1-aziridinyl phosphoric acid was reported as new anticancer agent (Mamyama *et al,* 1960, Uchida *el al.,* 1957).

Taking into account this back ground, a series of alkyl catechols were prepared and their antibacterial and cytotoxic activity studied (Siddiqui *et al.,* 1993). These studies have been further extended to a series of alkyl catechol esters and form the basis of present communication. Esterification (acetylation and benzoylation) of mono-, di- and tetra-substituted alkyl catechols with acetic anhydride/pyridine and benzoyl chloride/pyridine respectively afforded the di-acetyl and di- bcnzoyl derivatives in each case. Calechol di-acetate and di-benzoate (Vogel *et al.,* 1989) were also prepared for comparison of its activity with alkyl substituted derivatives. Twenty six compounds have been prepared which include the diacetyl and dibenzoyl derivatives of mono-, di- and tetra- 3-heptvl. 2-heptyl, nonyl and benzyl catechol. Compounds 2-13 and 1126 are being reported for the first time. MI the derivatives characterized through spectral studies and their antibacterial activity evaluated.

EXPERIMENTAL

IR and UV spectra were measured on JASCO IRA-1 and Poe-Unicam Sp-800 spectrometers respectively. Mass spectra were recorded on Finnigan MAT-I12. Exact masses of the molecular ions and various fragments were obtained through their peak matching. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a Bruker AM-300 and AM-400 spectrometers operating at 300 and 400 MHz respectively. The chemical shifts are reported in S (ppm) and coupling constants in Hz. Purity of the products was checked on TLC plates of silica gel PF254.

Alkyl catechols were prepared according to the reported method (Siddiqui *et al.,* 1993). In each case, three products (mono-, di- and tetra- substituted alkyl catechols) were obtained Acetylation and betvovlation of these was done as noted below.

General Procedure for Acetylation of Alkyl and Aryl Catechols

Alkyl catechol (15 mg) was dissolved in pyridine (1 ml) to which acetic anhydride (1 ml) was added and the reaction mixture was allowed to stand at room temperature for 24 horns. It was extracted with ethyl acetate and the ethyl acetate layer was washed with water, dried over anhydrous sodium sulphate and freed of the solvent under reduced pressure to afford the respective diacetyl derivatives.

General Procedure for benzoylation of Alkyl and Aryl Catechols

To a solution of alkyl catechols (15 mg) in pyridine (1 ml) benzoyl chloride (I M) was added and the reaction mixture kept at room temperature for 24 hours. The reaction mixture was extracted with ethyl acetate. The ethyl acetate layer was washed successively with dilute sulphuric acid (2M), distilled water, saturated sodium bicarbonate solution and finally with water. The washed ethyl acetate phase was dried over anhydrous sodium sulfate and freed of the solvent under reduced pressure, to furnish the dibenzoates of the alkyl and aryl catechols.

All these derivatives were characterized through spectral data as presented below.

Di-O-acetyl catechol [1]: Yellow needles (MeOH): mp 98°C: UV λ_{max} (MeOH) nm : 203.2 and 261.2; IR ν_{max} ($CHCl_3$): 1750, 1600 and 1260-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.28 (s, 6H. 2xOCO$\underline{CH_3}$). 7.18 (dd. 2H, J=9.68, 2.82 Hz, H-4. H-5) and 7.23 (dd, 2H, J=9.68, 2.82 Hz, H-3, H-6): EIMS *m/z* 194 (M^+) $C_{10}H_{10}O_4$.

Di-O-acetyl-4-henzyl catechol [2]: Brown rods (MeOH): mp 92°C: UV λ_{max} (MeOH) nm: 228.6 and 271.8, 283.0; IR ν_{max} ($CHCl_3$): 1760, 1595 and 1270-1140 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.24 (s, 3H, OCOCH3), 226 (s. 31-1. OCOCH3), 6.96 (d, I H, 1.01 Hz, H-3), 7.03 (dd. 1H, 1=8.92, 2.01 Hz, 1-1-5). 7.08 ((I, 1H.1=8.92 Hz. H-6). 7.17 (dd. 211.1—7.32, 2.74 Hz. 11-3'. H-7'), 7.22 (ddd, 111. 1=8.14, 8.14, 2.74 Hz, H-5') and 7.28 (dd, 2H, 1=8.14, 7.32 Hz, H-4', 1-1-6'); EIMS ma 284 (M^1) C1711I6O4.

Di-O-acetyl-4,5-di-benzyl catechol [3]: Brown needles (EtOH): mp 89°C: UV λ_{max} (MeOH) nm: 213.2 227.8 and 280.4: IR ν_{max} ($CHCl_3$): 1750, 1595 and 1280-1140 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.23 (s 6H, 2xOCO$\underline{CH_3}$), 3.91 (s, 6H, 2xOCO$\underline{CH_3}$). 3-91 (s, 4H, 2xAR-$\underline{CH_2}$) 7.01 (s, 214, H-3, H-6) and 7.10-731 (m, 10H, Ar-CH): EIMS *m/z* 374 (M^+) $C_{24}H_{22}O_4$.

Di-O-acetyl-3,4,6-tetra-benzyl catechol [4]: Yellow needles (MeOH): mp 86°C; UV UV λ_{max} (MeOH) nm: 205.2 and 2612; IR ν_{max} ($CHCl_3$): 1750, 1600 and 1290-1160 cm^{-1} ^{1}H-NMR ($CDCl_3$): δ 2.22 (s, 6H, 2xOCO$\underline{CH_3}$), 3.84 (s, 4H. 2xAr-CH_2), 3.90 (s, 4H, 2xAr-$\underline{CH_2}$) and 7.1-7.34 (m, 20H, Ar-CH): EIMS *m/z* 554 (M^+) $C_{38}H_{34}O_4$.

Di-O-acetyl-4-nonyl catechol [5]: Yellow needles (MeOH): mp 87°C: UV) UV λ_{max} (MeOH) nm: 203.0 and 236.4; IR ν_{max} ($CHCl_3$): 1750, 1595 and 1270-1150 cm^1, ^{1}H-NMR ($CDC1_3$): δ 0.76 (t, 3H, J=7.43 Hz, CH_3), 1.14-1.25 (m, 14H, 7xCH_2). 2.26 (s, 3H, OCO$\underline{CH_3}$), 2.27 (s, 3H, OCO$\underline{CH_3}$), 2.62 (t, 2H, J=8.42 Hz, Ar-$\underline{CH_2}$), 6.92 (d, 1H, J=2.05 Hz, H-3), 7,06 (dd, IH. J=832, 2.05 Hz, H-5) and 7.09 (d, 1H, J=8.32 Hz, H-6), EIMS *m/z* 320 (M^+) $C_{19}H_{28}O_4$.

Di-O-acetyl-4,5-di-nonyl catechol [6]: Brown rods (MeOH: Benzene. 1:1): mp 86°C; UV λ_{max} (MeOH) nm: 202.2 and 238.2; IR ν_{max} ($CHCl_3$): 1740, 1590 and 1280-1160 cm^{-1} ^{1}H-NMR ($CDCl_3$): δ (0.86 (t, 3H.J=6.91 Hz, CH_3), 0.91 (t, 3H, J=7.44 Hz, CH_3), 1.12-1.31 (m, 28H, 14xCH_2), 2.17 (s, 6H, 2xOCO$\underline{CH_3}$), 2.310, 2H, J=6.55 Hz, Ar-$\underline{CH_2}$), 2.33 (t, 2H, J=8.42 Hz, Az-$\underline{CH_2}$) and 7.08 (s, 2H, H-6). EIMS *m/z* 446 (M^+) $C_{28}H_{46}O_4$.

Di-O-acetyl-3,4,5,6-tetra-nonyl catechol [7]: Yellow needles (EtOH): mp 84°C; UV λ_{max} (MeOH) nm: 202.2 and 204.6; IR ν_{max} ($CHCl_3$): 1750, 1590 and 1095-1000 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.74-0.88 (m, 12H, 4xCH_3), 105-1.30 (m, 56H, 28xCH_2), 2.18 (s, 6H, 2xOCO$\underline{CH_3}$) and 2.30-2.37 (m, 8H, 4xA $\underline{CH_2}$); EIMS *m/z* 698 (M^+) $C_{46}H_{82}O_4$.

Di-O-acetyl-4-(2-heptyd) catechol [8]: Brown needles (McOH): mp 82°C, UV λ_{max} (MeOH) nm : 205.4 and 238.2. IR ν_{max} ($CHCl_3$): 1750, 1590 and 1260-1170 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 0.76 (t,

3H, J=7.34 Hz, CH_3), 0.82 (d. 3H, J=7.28 Hz. CH_3), 1.12-1.24 (m, 8H, 4xCH_2], 2.26 (s, 6H, 2xOCO$\underline{CH_3}$), 3.28 (m, 1H, Ar-$\underline{CH}$), 6.98 (dd. 1H, J=8.28, 2.02 Hz, H-5), 6.92 (d, 1H, J=2.02 Hz, H-3) and 7,08 (d, 1H, J=8.28 Hz, H-6): EIMS *m/z* 292 (M^+) $C_{I7}H_{24}O_4$.

Di-O-acetyl-45-di-(2-heptyl) catechol [9]: Brown rods (MeOH): mp 79°C; UV λ_{max} (MeOH) (MeOH) nm: 207 and 268; IR ν_{max} ($CHCl_3$): 1740, 1595 and 1265-1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.77-0.90 (m, 12H, 4xCH_3), 1.18-1.32 (m, 16H, 8xCH_2), 2.21 (s, 6H, 2xOCO$\underline{CH_3}$), 3.20-3.31 (m, 2H, Ar-$\underline{CH}$) and 6.98 (s, 2H, H-3. H-6): EIMS *m/z* 390 (M^+) $C_{24}H_{38}O_4$.

Di-O-acetyl-35,6-tetra-(2-heptyl) catechol [10]: Yellow needles (EtOH): mp 88°C; UV λ_{max} (MeOH) nm: 206 and 242.6; IR ν_{max} ($CHCl_3$): 1750, 1595 and 1265-1150 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 0.77-0.92 (m, 24H, 8xCH_3), 1.15-1.35 (m, 32H, I6xCH_2), 2.23 (s, 6H, 2xOCO$\underline{CH_3}$) and 3.26-3.32 (m, 4H, Ar-$\underline{CH}$): EIMS *m/z* 586 (M^+) $C_{38}H_{66}O_4$.

Di-O-acetyl-4-(3-hyexrl) catechol [11]: Brown needles (EtOH): mp 70°C; UV λ_{max} (MeOH) nm : 212.2, 260.6 and 2746: IR ν_{max} ($CHCl_3$). 1750, 1600 and 1270-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.71 (t, 3H, J=7.91 Hz, CH_3), 0.81 (t, 3H, J=7.52 Hz, CH_3), 1.15-1.25 (m, 6H, 3xCH_2), 2.24 (s, 3H. $OCOCH_3$), 2.25 (s, 3H, $OCOCH_3$), 3.33 (m, 1H, Ar-$\underline{CH}$), 6.75 (dd. 1H, J=6.50, 2.04 Hz, H-H), 70 (d, 1H, J=2.04 Hz, H-3) and 7.05 (d, 1H, J=6.50 Hz, H-6); EIMS m/z 278 (M^+) $C_{l6}H_{22}O_4$.

Di-O-acetyl-45-di-(3-hexyl) catechol [12]: Yellow needles (MeOH): mp 67°C; UV λ_{max} (MeOH) nm : 208.6; IR ν_{max} ($CHCl_3$): 1760, 1595 and 1160-1095 cm^{-l}; ^{1}H-NMR ($CDCl_3$): δ 0.75-0.88 (m, 12H, 4xCH_3), 1.15-1.30 (m, 12H, 6xCH_2), 2.25 (s, 6H, 2xOCO$\underline{CH_3}$), 2.26-2.30 (m, 2H, 2xAr-$\underline{CH}$) and 7.02 (s, 2H, H-3, H-6), EIMS *m/z* 362 (M^+) $C_{22}H_{34}O_4$.

Di-O-acetyl-3,4,5,6-tetra-(3-hexyl) catechol [13]: Brown rods (MeOH:Benzene; 1:1): mp 65°C UV λ_{max} (MeOH) nm : 204; IR ν_{max} ($CHCl_3$):1750, 1595 and 1300-1150 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.72-0.89 (m, 24H, 8xCH_3), 1.15-1.35 (m, 24H, 12xCH_2), 2.23 (s, 6H, 2x$OCOH_3$) and 2.26-2 33 (m, 4H, 4xAr-$\underline{CH}$); EIMS *m/z* 530 (M^+) $C_{34}H_{58}O_4$.

Di-O-benzoyl catechol [14]: Yellow needles (MeOH: Benzene; 1:1) mp 102°C; UV λ_{max} (MeOH) nm: 201 and 230.2; IR ν_{max} ($CHCl_3$): 1730, 1595, 1580 and 1260-1160 cm^{-1}: ^{1}H-NMR ($CHCl_3$): δ 7.25-7.69 (m, 8H, Ar) and 8.11-8.18 (m, 6H, Ar); EIMS, *m/z* 318 (M^+) $C_{20}H_{14}O_4$.

Di-O-benzoyl-4-benzyl catechol [15]: Yellow needles (MeOH): mp 99°C: UV λ_{max} (MeOH) nm: 2012 and 272; IR ν_{max} ($CHCl_3$): 1720-1680, 1600, 1580 and 1265-1165 $cm^{1,}$ ^{1}H-NMR ($CDCl_3$): δ 4.05 (s, 2H, Ar-$\underline{CH_2}$), 7.15-7.69 (m. 12H, Ar) and 8.13-8.20 (m, 6H- Ar): EIMS *m/z* 408 (M^+) $C_{27}H_{20}O_4$.

Di-O-benzoyl-4-5-di-benzyl catechol [16]: Yellow rods (EtOH) nip 97°C; UV λ_{max} (MeOH) nm: 202.2 and 272: IR ν_{max} ($CHCl_3$) 1720-1680, 1600, 1580 and 1265-1165 cm^{-1}: ^{1}H-NMR ($CDCl_3$): δ 4.0 (s, 4H, 2xAr-$\underline{CH_2}$), 7.25-7.69 (m, 16H, Ar) and 8.12-8.16 (m, 6H, Ar): EIMS *m/z* 498 (M^+) $C_{34}H_{26}O_4$.

Di-O-benzoyl-3,4,5,6-tetra-benzyl catechol [17]: Yellow needles (EtOH): mp 96°C; UV λ_{max} (MeOH) nm: 204.6 and 268.6: IR ν_{max} ($CHCl_3$): 1720-1690, 1590, 1580 and 1265-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 3.92 (s, 4H, 2xAr-$\underline{CH_2}$), 4.07 (s, 4H, 2xAr-$\underline{CH_2}$), 7.18-7.20 (m, 24H, Ar) and 8.10-8.16 (m, 6H. Ar); EIMS *m/z* 678 (M^+) $C_{48}H_{38}O_4$.

Di-O-benzoyl-4-nonyl catechol [18]: Brown rods (MeOH): mp 88°C: UV λ_{max} (MeOH) nm: 201.8 and 240: IR ν_{max} ($CHCl_3$): 1720, 1595, 1580 and 1270-1160 cm^{-1}; ^{1}H-NMR ($CHCl_3$) d 0.84 (t, 3H, J=8.15 Hz, CH_3), 125-1.39 (m, 14H, 7xCH_2), 2.37 (t, 2H, J=6.81 Hz, Ar-$\underline{CH_2}$), 7.24-7.71 (m, 7H, Ar) and 8.12-8.17 (m, 6H. Ar). EIMS *m/z* 444 ($M^{+\cdot}$) $C_{29}H_{32}O_4$.

Di-O-benzoyl-4,5-di-nonyl catechol [19]: Yellow needles (EtOH): mp 87°C: UV λ_{max} (MeOH) nm: 212.6 and 274.6; IR ν_{max} ($CHCl_3$): 1720-1700, 1590-1580 and 1270-1160 $cm^{-1;}$ ^{1}H-NMR ($CDCl_3$): δ 0.87 (t, 3H, J=7.31 Hz, CH_3), 0.91 (t, 3H, J=6.93 Hz, CH_3), 1.23-1.41 (m, 28H, 14xCH_2), 2.34-2.37 (m, 4H, 2xAR-$\underline{CH_2}$), 7.24-7.70 (m, 6H. Ar) and 8.10-8.17 (m, 6H, Ar): EIMS *m/z* 570 (M^+) $C_{38}H_{50}O_4$.

Di-O-benzoyl-3,4,5,6-tetra-nonyl catechol [20]: Yellow needles (MeOH): mp 94°C: UV λ_{max} (MeOH) nm: 213.8 and 268.6: IR ν_{max} ($CHCl_3$): 1720-1695, 1595, 1580 and 1265-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.87-0.91 (m, 12H. 4xCH_3), 1.21-1.45 (m, 56H, 28xCH_2), 2.31-2.37 (m, 8H, 4xAR-$\underline{CH}$2), 7.22-7.69 (m, 4H, Ar) and 8.10-8.17 (m, 6H, Ar): EIMS *m/z* 822 ($M^{+\cdot}$) $C_{56}H_{86}O_4$.

Di-O-benzoyl-4-(2-heptyl) catechol [21]: Yellow needles (MeOH): mp 92°C: UV λ_{max} (MeOH) nm: 233.6 and 280.6; IR ν_{max} ($CHCl_3$): 1720-1690, 1590, 1580 and 1265-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.82 (t, 3H, J=8.23 Hz, CH_3), 0.88 (d, 3H, J-7.52 Hz, CH_3). 1.21-141 (m, 8H, 4xCH_2), 3.31 (m, 1H, Ar-$\underline{CH}$), 6.678-7.69 (m, 7H, Ar) and 8.10.8.17 (m, 6H, Ar); EIMS *m/z* 416 ($M^{+\cdot}$) $C_{27}H_{18}O_4$.

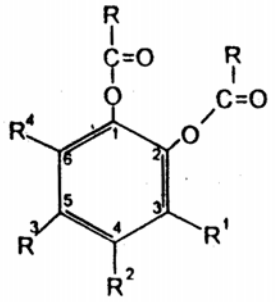
Di-O-Benzyol-4,5-di-(2-heplyl) catechol [22]: Yellow needles (MeOH): mp 89°C; UV λ_{max} (MeOH) nm 230.2 and 281.2; IR ν_{max} ($CHCl_3$): 1720-1690, 1600, 1580 and 1270, 1160 cm^{l}; 1H-NMR ($CDCl_3$); δ 0.79-0.91 (m, 12H, 4xCH_3), 1.25-145 (m, 16H, 8xCH_2), 2.32-2.40 (m, 2H, 2xAr-$\underline{CH}$), 7.21-7.69 (m, 614, Ar) and 8.09-8.17 (m, 6H, Ar); EIMS *m/z* 514 (M^+) $C_{34}H_{42}O_4$.

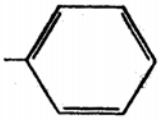
Di-O-benzoyl-3,4,5,6-tetra-(2-heptyl) catechol [23]: Yellow needles (EtOH): mp 87°C: UV λ_{max} (MeOH) mn: 202 and 272.6; IR ν_{max} ($CHCl_3$): 1720, 15950, 1580 and 1270-1160 cm^{-1}; ^{1}H-NMR ($CHCl_3$): δ 0.79-0.92 (m, 24H,8xCH_3), 1.20-1.41 (m, 32H, 16xCH_2), 2.31-2.42 (m 4H, 4xAr-$\underline{CH}$), 7 33-7.96 (m,4H. Ar) and 8.10-8.17 (m, 6H, Ar); EIMS *m/z* 710 (M^+) $C_{48}H_{70}O_4$.

Di-O-benzoyl-4-(3-hexyl) catechol [24]: Yellow needles (MeOH: Benzene; 1:1): mp 89°C; UV λ_{max} (MeOH) nm: 200.8 and 277.4: IR ν_{max} ($CHCl_3$). 1720, 1590, 1580 and 1275-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.77 (t. 3H, J=7.3 Hz CH_3), 0.87 (t, 3H, J=7.45 Hz, CH_3), l.24-1.40 (m, 6H, 3xCH_2). 3.32 (m, 1H. Ar-$\underline{CH}$), 677-7.70 (m, 7H, Ar) and 8.10-8.17 (m, 6H, Ar); EIMS *m/z* 402 (M^+) $C_{26}H_{26}O_4$.

Di-O-benzoyl-4,5-di-(3-hexyl) catechnl [25]: Yellow needles (MeOH): mp 87°C: UV λ_{max} (MeOH) nm: 201.24 and 277.2: IR ν_{max} ($CHCl_3$): 1720, 1595, 1580 and 1265-1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.91 (m, 12H4xCH_3), 1.23-1.42 (m, 12H, 6xCH_2),2.33-2.39 (m, 2H, 2.xAr-CH), 7.15-7.69 (m, 6H, Ar) and 8.10-8.17 (m, 6H. Ar); EIMS *m/z* 486 (M^+) $C_{32}H_{38}O_4$.

Di-O-benzoyl-3-,4,5,6-tetra-(3-hexyl) catechol [26]: Yellow needles (EtOH): mp 84°C; UV λ_{max} (MeOH) nm: 200.8 and 277.2; IR ν_{max} ($CHCl_3$); 1720, 1600, 1580 and 1275-1160 cm^{-1}; ^{1}H-NMR ($CHCl_3$): δ 0.78-092 (m, 241-1, 8xCH_3), 1.20-1.42 (m, 24H, 12xCH_2), 3.32-3.51 (m, 4H, 4xAr-CH), 7.30-7.70 (m, 4H, Ar) and 8.10-8.16 (m, 6H, Ar); EIMS *m/z* 654 (M^+) $C_{44}H_{62}O_4$.

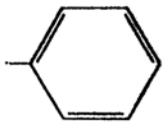


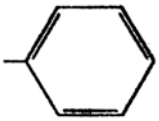
1	$R=CH_3$	$R^1=R^2=R^3=R^4=H$	
2	$R=CH_3$	$R^1=R^3=R^4=H$	$R^2=$ 
3	$R=CH_3$	$R^1=R^4$	$R^2=R^3=$ 
4	$R=CH_3$	$R^1=R^2=R^3=R^4=$ 	
5	$R=CH_3$	$R^1=R^3=R^4=H$	$R^2= -CH_2-(CH_2)_7-CH_3$
6	$R=CH_3$	$R^1=R^4=H$	$R^2=R^3= -CH_2-(CH_2)_7-CH_3$
7	$R=CH_3$	$R^1=R^2=R^3=R^4= -CH_2-(CH_2)_7-CH_3$	
8	$R=CH_3$	$R^1=R^3=R^4=H$	$R^2= -CH-(CH_2)_4-CH_3$ CH_3
9	$R=CH_3$	$R^1=R^4=H$	$R^2=R^3= -CH-(CH_2)_4-CH_3$ CH_3
10	$R=CH_3$	$R^1=R^2=R^3=R^4= -CH-(CH_2)_4-CH_3$ CH_3	
11	$R=CH_3$	$R^1=R^3=R^4=H$	$R^2= -CH-(CH_2)_2-CH_3$ CH_2-CH_3

12 $R=CH_3$ $R^1=R^4=H$ $R^2=R^3=$ -CH-$(CH_2)_2$-CH_3 (CH_2-CH_3)

13 $R=CH_3$ $R^1=R^2=R^3=R^4=$ -CH-$(CH_2)_2$-CH_3 (CH_2-CH_3)

14 $R=C_6H_5$ $R^1=R^2=R^3=R^4=H$

15 $R=C_6H_5$ $R^1=R^3=R^4=H$ $R^2=$ -CH_2- 

16 $R=C_6H_5$ $R^1=R^4=H$ $R^2=R^3=$ -CH_2- 

17 $R=C_6H_5$ $R^1=R^2=R^3=R^4=$ -CH_2- 

18 $R=C_6H_5$ $R^1=R^3=R^4=H$ $R^2=$ -CH_2-$(CH_2)_7$-CH_3

19 $R=C_6H_5$ $R^1=R^4=H$ $R^2=R^3=$ -CH_2-$(CH_2)_7$-CH_3

20 $R=C_6H_5$ $R^1=R^2=R^3=R^4=$ -CH_2-$(CH_2)_7$-CH_3

21 $R=C_6H_5$ $R^1=R^3=R^4=H$ $R^2=$ -CH-$(CH_2)_4$-CH_3 (CH_3)

22 $R=C_6H_5$ $R^1=R^4=H$ $R^2=R^3=$ -CH-$(CH_2)_4$-CH_3 (CH_3)

23 $R=C_6H_5$ $R^1=R^2=R^3=R^4=$ -CH-$(CH_2)_4$-CH_3 (CH_3)

24 $R=C_6H_5$ $R^1=R^3=R^4=H$ $R^2=$ -CH-$(CH_2)_2$-CH_3 (CH_2-CH_3)

25 $R=C_6H_5$ $R^1=R^4=H$ $R^2=R^3=$ -CH-$(CH_2)_2$-CH_3 (CH_2-CH_3)

26 $R=C_6H_5$ $R^1=R^2=R^3=R^4=$ -CH-$(CH_2)_2$-CH_3 (CH_2-CH_3)

CHEMICAL RESULTS AND DISCUSSION

The IR spectrum of the acetyl derivatives (2-13) showed strong absorptions in the region 1760-1740 cm^{-1} indicating the presence of ester carbonyl function in the molecule. This was further supported by the presence of broad absorption in the region 1300-1000 cm^{-1} corresponding to (C=O) stretchings. Sharp absorptions in the region 1600-1590 cm^{-1} were due to aromatic (C=C) bonds. In each case the mass spectrum afforded the molecular ion M^+ peaks showing the acetylation of alkyl catechols.

The ^{1}H-NMR spectra of the alkyl acetyl catechols (mono-, di-, and tetra-) showed a similar pattern in the region below 4 ppm. The methyl and methylene protons were observed in the range of S 0.71-0.92 and 8 1.05-1.35 respectively. In case of di- and tetra- alkyl catechols both the acetoxyl methyls appeared as a six- proton singlet whereas, in the mono acetyl derivatives of the mono- alkyl di-acetyl catechols two singlets were observed in this region for the two acetoxy group Ar-CH2 and Ar-CH protons were observed in the region of δ 2.3-2.47 and 2.6-2.68 respectively.

In case of benzyl catechol a singlet of Ar-CH_2 protons was also observed in the region of S 3.84-3.96. The dibenzoates produced a strong absorption in the range of 1720-1680 cm^{-1} for the carbonyl groups of the ester functions. Two absorptions at 1600 and 1580 cm^{-1} were due to the aromatic (C=C) bonds and C-O stretching vibrations were noted in the region 1275-1160 cm^{-1}.

The mass spectra of the dibenzoates confirmed the presence of two ester groups in each case. The upfield region of the ^{1}H-NMR spectra of the dibenzoates showed a similar pattern as that of the diacetates. However, the downfield region presented a complex picture since the catechol ring protons and the benzoyl ring protons both appeared in the region of δ 7.10-8.2.

BIOLOGICAL RESULTS AND DISCUSSION

Antibacterial Activity:

Compounds (**1-26**) were evaluated for their antibacterial activity against 12 Gram-positive and 16 Gram-negative bacteria and the primary screening results showed that acylation generally resulted in a decrease of antibacterial activity. Both the acetyl (**1-5, 7, 8, 10-13**) and benzoyl derivatives (**14-16**, **18-21** and **23**) inhibited the growth of Grain-negative bacterium Salmonella lyphi whereas the rest were unaffected. In case of the Gram-positive bacteria, growth of a few organisms was inhibited by the acetyl derivatives (Table-1) while the benzoyl derivatives were almost inactive except the di-O-benzoyl-3-hexyl catechol (**26**) which was most active among the compounds tested against Gram-positive organisms and showed significant activity against eight out of 12 Gram-positive organisms (Table-1).

Table 1
Screening of Catechol and its Derivatives (1-13) for anti-bacterial Activity
in vitro (zone of inhibition in millimeters)

Compound Number	1	2	3	4	5	6	7	8	9	10	11	12	13
GRAM NEGATIVE													
Salmonella typhi	14	12	10	12	10	7	15	13	7	18	14	13	15
Salmonella typhi Para A	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonella typhi Para B	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonella typhimurium	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonela gallinarium	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonela pullorum	0	0	0	0	0	0	0	0	0	0	0	0	0
Shigella dysenteriae	0	0	0	0	0	0	0	0	0	0	0	0	0
Shigella flexnerii	0	7	10	9	0	0	9	7	0	9	0	7	15
Shigella sonnei	0	0	0	0	0	0	0	0	0	0	0	0	0
Escherichia coli	0	8	0	9	8	0	8	0	0	8	7	0	0
Enterobacter cloacae	0	0	0	0	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	0	0	0	0	0	0	0	0	0	0	0	0	0
Pseudomonas pseudemallii	0	0	0	0	0	0	0	0	0	0	0	0	0
Pseudomonas aeruginosa	0	0	0	0	0	0	0	0	0	0	0	0	0
Proteus mirabilis	0	0	0	0	0	0	0	0	0	0	0	0	0
Aeromonas hydrophila	8	8	8	0	0	10	11	0	9	8	9	0	10
GRAM POSITIVE													
Corynebacterium hoffmanii	7	0	0	9	0	0	9	0	8	8	7	8	9
Corynebacterium xerosis	0	0	8	7	7	0	9	9	0	9	0	7	8
Streptococcus agalactiae	0	8	10	9	0	0	12	0	0	13	7	9	10
Streptococcus faecalis	0	0	0	0	0	0	0	0	0	0	0	0	0
Staphylococcus aureus	0	7	9	0	8	9	10	9	0	11	0	0	9
Staphylococcus epidermidis	0	0	7	0	0	0	8	7	0	9	0	0	8
Bacillus subtilis	0	10	10	12	7	0	8	12	7	13	8	8	12
Bacillus anthracis	7	12	13	10	12	7	13	15	7	17	10	9	10
Listeria monocytogenes	0	0	0	0	0	0	9	0	8	8	0	0	8
Listeria ivanovii	0	0	0	0	0	0	0	0	0	0	0	0	0
Lactobacilli acidophilus	0	8	12	9	8	0	14	7	0	11	8	10	12
Micrococcus luteus	0	0	8	7	8	0	0	0	0	0	0	0	10

continue on next page

Screening of Catechol and its Derivatives (14-26) for anti-bacterial Activity *in vitro* (zone of inhibition in millimeters)

Compound Number	14	15	16	17	18	19	20	21	22	23	24	25	26
GRAM NEGATIVE													
Salmonella typhi	17	12	16	7	20	10	13	20	9	11	0	0	0
Salmonella typhi Para A	0	0	7	7	8	0	0	9	0	7	0	0	0
Salmonella typhi Para B	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonella typhimurium	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonella gallinarium	0	0	0	0	0	0	0	0	0	0	0	0	0
Salmonella pullorum	0	0	0	0	0	0	0	0	0	0	0	0	0
Shigella dysenteriae	0	7	8	9	8	9	7	8	9	7	0	0	0
Shigella flexneri	0	0	0	0	0	0	0	0	0	0	0	0	0
Shigella sonnei	0	7	0	0	0	0	7	0	0	0	0	0	0
Escherichia coli	0	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter cloacae	0	0	0	0	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	0	0	0	0	0	0	0	0	0	0	0	0	0
Pseudomonas pseudemallii	0	0	0	7	0	0	0	0	0	7	0	0	0
Pseudomonas aeroginosa	0	0	0	7	0	0	0	0	0	7	0	0	0
Proteus mirabilis	0	0	0	0	0	0	0	0	0	0	0	0	0
Aeromonas hydrophila	0	0	0	0	0	0	0	0	0	0	0	0	0
GRAM POSITIVE													
Corynebacterium hoffmanii	7	7	7	7	9	7	8	7	7	7	0	0	0
Corynebacterium xerosis	0	0	0	0	0	0	0	0	0	0	0	0	0
Streptococcus agalactiae	0	0	0	0	0	0	0	0	0	0	0	0	0
Streptococcus faecalis	0	0	0	0	0	0	0	0	0	0	0	0	16
Staphylococcus aureus	0	0	0	0	0	0	0	0	0	0	0	0	20
Staphylococcus epidermidis	0	8	7	7	7	8	8	7	7	8	7	8	30
Bacillus subtilis	0	0	0	0	0	0	0	0	0	0	0	0	28
Bacillus anthracis	0	0	9	8	8	8	0	9	0	0	0	12	30
Listeria monocytogenes	0	0	0	0	0	0	0	0	0	0	0	0	30
Listeria ivanovii	0	0	0	0	0	0	0	0	0	0	0	0	30
Lactobacilli acidophilus	8	7	7	8	7	0	7	7	10	9	0	0	0
Micrococcus luteus	0	0	0	0	0	0	0	0	0	0	12	30	30

REFERENCES

Bhargava, P.M., Sen, A.B. (1950). Search for insecticides. Chemical constitution and insecticidal activity. *J. Sci. Food Ag.* **1**: 178-182.

Dupin, J.P., Gravier, D., Casadebaig, F., Biosscau, M.R., Bernard, H. (1986). Acetoxy benzene derivatives in vitro antiaggregant activity. *Farmaco, Ed. Sc*. **41**: 934-941.

Kameonov, N.A., Starkov, A.V., Batekovskaya, Z.P., Saveleva, A.R. (1963). Effect of the nature of chemical substance on bactericidal activity. *Tr. Tsentr. Nauchi. –Issled. Dezinfektsion Inst.* **16**: 56-61.

Maruvama, M., Uchida, M. (1960). Mode of action of RC4. n new anticancer agent containing the ethlenimino ring. *Gann.* **51**: 187-199. Ref. Cheer. Abstr.

Meyer, B.N., Ferrigni, R.R., Putnam, J.E., Jacobsen, L.B., Nichols, D.E.; McLaughlin, J.L. (1982). Brine shrimp: A convenient general bioassay for active plant constituents. *Planta Medica* **45**: 31-34.

Miller, E., Hartung, W.H., Rock, H.J, Crossley, F.S. (1938). Antiseptics: Alkyl catechol. *J. Am. Chem. Soc.* **60**: 7-10.

Sen, A.B., Bhargava, P.M. (1949). Search for insecticides. *J. Indian Chem. Soc.* **26**: 243-244.

Siddiqui, B.S., Adil, Q., Begum, S., Siddigni, S. Khan, K.A., Khan, S.A., Khalid, S.M. (1993). Synthesis of alkyl catechols and evaluation of their antibacterial and cytotoxic activity. *Pak J. Pharm. Sci.* **6**: 53-69.

Uchida, M., Takagi, H. (1960). Antitumor substances. *Takamine Kenkyusho Nempo,* **9***:* 113-122. Ref. Chem. Abstr.

Vogel, I. (1989). Practical Organic Chemistry (5th Edition). 642.

Wang, J.X., Zhang, L., Zhu, L., Gong. R. (1988). Extraction of pyrocatechol from leaves of Sally *babylonic* and preparation of diacetyl pyrocatechol. *Yaoxue tongbao.* **23**: 15-16. Ref. Chem. Abstr.