Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(12):1089-1093

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis and antimicrobial activity of 3-(substituted phenyl)-1-(7-substituted coumarin-3-yl)prop-2-ene-1-ones

Abida*[1,2], Saleh Alaqel[1], Mohd. Imran[1,2], Said A. El-Feky[1] and S.A. Khan[2]

[1]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Northern Border University, Rafha, Saudi Arabia*
[2]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi*

ABSTRACT

A series of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones was synthesized by the condensation of 5-substituted-3-acetylcoumarins with four chlorosubstituted aromatic aldehydes. The structures of these compounds were elucidated on the basis of IR and, ^{1}H-NMR. These compounds were further evaluated for their antimicrobial activity.

Key words: Coumarin, Chalcone and Antimicrobial activity.

INTRODUCTION

Coumarin derivatives and chalcones have been reported to possess diverse pharmacological activities including antimicrobial activity [1-6]. With a view to achieve better antimicrobial activity, we have synthesized 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones by the condensation of 5-substituted-3-acetylcoumarins with four chlorosubstituted aromatic aldehydes. The chemical structures of the synthesized compounds were confirmed by means of IR and ^{1}H NMR. The synthesized compounds were tested for their antimicrobial activity by cup plate method [7,8].

EXPERIMENTAL SECTION

Melting points were determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC on silica gel plates and spots were visualized by exposure to the iodine vapors. IR (KBr) spectra were recorded on a Perkin Elmer 783 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker model DRX-300 NMR spectrophotometer using TMS as internal reference (δ in ppm).

Synthesis of 7-substituted-3-acetyl coumarin (1a-1c):
A mixture of 5-substituted salicyldehyde (0.02 moles) and ethylacetoacetate (0.03 moles) in 30 ml ethanol was taken in a 100 ml round bottom flask. To this mixture, 3-5 drops of piperidine were added. The reaction mixture was refluxed for 1-2 hr. After completion of reaction, the contents were poured on crushed ice. The solid separated was filtered, dried and recrystallized from ethanol. The purity of compounds was established on the basis of TLC.

Following compounds were prepared by method described above.

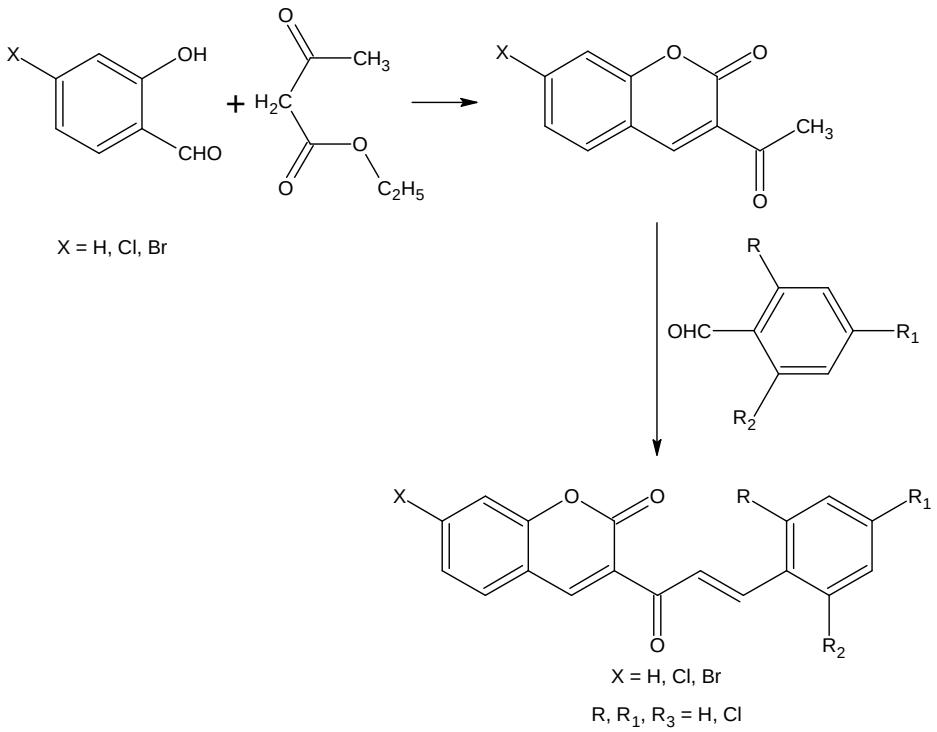
3-Acetylcoumarin: M.P.: 111-113^{0}C; R_f Value (Toluene : Ethyl acetate : Formic acid (T:E:F; 5:4:1): 0.85; %Yield : 80; IR (KBr) cm^{-1}: 1713.40 and 1691.62 (C=O), 1551.78 (C=C); ^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm: 2.58 (s, 3H, CH_3), 7.44 (q, 2H, Ar-H), 7.75 (t, J=8Hz, 1H, Ar-H), 7.95 (d, J=12Hz, 1H, Ar-H), 8.66 (s, 1H, Ar-H).

7-Chloro-3-acetylcoumarin: M.P.: 155-157^{0}C; R_f Value (Benzene:Acetone; 9:1): 0.71; % Yield : 80; IR (KBr) cm^{-1}: 1711.16 and 1693.70 (C=O), 1542.50 (C=C), 1130.38 (C-O-C); ^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm: 2.58 (s, 3H, CH_3), 7.51 (d, J=12Hz, 1H, Ar-H), 7.77 (d, J=12Hz, 1H, Ar-H), 8.09 (s, 1H, Ar-H), 8.61 (s, 1H, Ar-H).

7-Bromo-3-acetylcoumarin: M.P.: 189-191^{0}C; R_f Value (Benzene:Acetone; 9:1): 0.67; % Yield : 80; IR (KBr) cm^{-1}: 1707.93 and 1691.42 (C=O), 1544.66 (C=C), 1143.80 (C-O-C); ^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm: 2.57 (s, 3H, CH_3), 7.43 (d, J=12Hz, 1H, Ar-H), 7.79 (d, J=12Hz, 1H, Ar-H), 8.10 (s, 1H, Ar-H), 8.66 (s, 1H, Ar-H).

Synthesis of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-one (C_1-C_{12}):
Equimolar quantities of 7-substituted-3-acetyl coumarin and different substituted benzaldehydes were refluxed in absolute ethanol using piperidine as catalyst for 8-10 hr. The reaction mixtures were concentrated and poured on to crushed ice. The compounds so obtained were filtered at pump, dried and recrystallized from ethanol to get pure crystalline solids. The purity of the compounds was established on the basis of TLC.

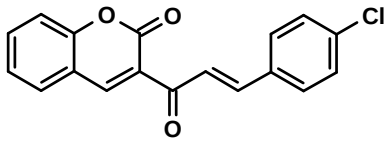
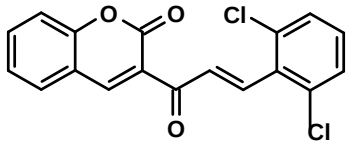
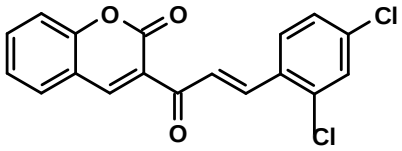
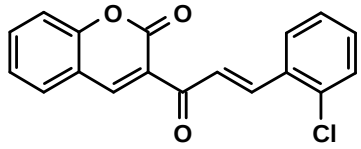
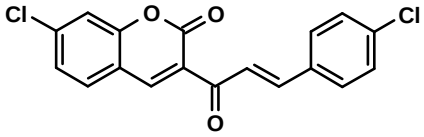
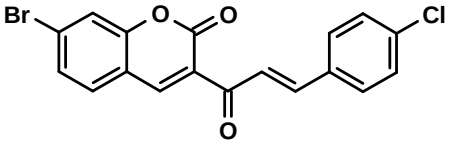
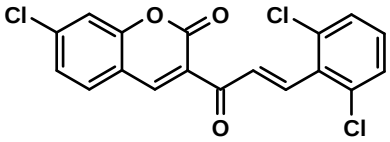
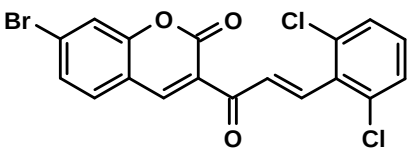
The general scheme for the preparation of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones (C_1 to C_{12}) is provided below.

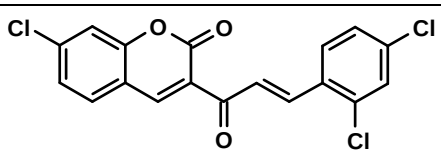
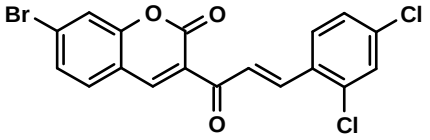
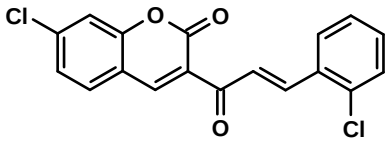
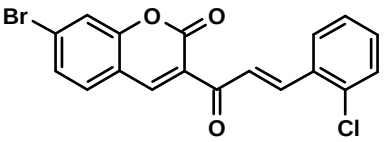


Scheme 1

The characterization data of 3-substitutedphenyl-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones (C_1-C_{12}) is provided in Table-I.

TABLE-I: Characterization data of 3-substitutedphenyl-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones (C_1-C_{12})

Compound	Chemical Structure	Characterization data
C_1		**Chemical Name:** 3-(4-chlorophenyl)-1-(coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 165-167 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.73; **% Yield :** 70%; **IR (KBr) cm^{-1}:** 1712.28 and 1693.84 (C=O), 1546.60 (C=C), 1137.40 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 6.97 (d, J=12Hz, 1H, =CH-CO-), 7.28 (t, J=8Hz, 2H, Ar-H), 7.45 (m, 6H, Ar-H), 7.75 (d, J=12Hz, 1H, -CH=CH-CO-), 8.24 (s, 1H, Ar-H).
C_2		**Chemical Name:** 3-(2,6-dichlorophenyl)-1-(coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 186-188 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.78; **% Yield:** 75%; **IR (KBr) cm^{-1}:** 1713.51 and 1692.45 (C=O), 1543.55 (C=C), 1132.20 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 7.04 (t, J=8Hz, 1H, Ar-H), 7.15 (d, J=12Hz, 1H, =CH-CO-), 7.26 (m, 4H, Ar-H), 7.44 (d, J=12Hz, 1H, Ar-H), 7.50 (t, J=8Hz, 1H, Ar-H), 8.02 (d, J=12Hz, 1H, -CH=CH-CO-), 8.20 (s, 1H, Ar-H).
C_3		**Chemical Name:** 3-(2,4-dichlorophenyl)-1-(coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 163-165 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.71; **% Yield**: 70%; **IR (KBr) cm^{-1}:** 1711.44 and 1692.02 (C=O), 1544.35 (C=C), 1135.63 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 7.04 (d, J=12Hz, 2H, Ar-H, =CH-CO-), 7.19 (d, J=12Hz, 1H, Ar-H), 7.27 (t, J=8Hz, 2H, Ar-H), 7.44 (d, J=12Hz, 1H, Ar-H), 7.51 (t, J=8Hz, 1H, Ar-H), 7.73 (s, 1H, Ar-H), 7.96 (d, J=12Hz, 1H, -CH=CH-CO-), 8.21 (s, 1H, Ar-H).
C_4		**Chemical Name:** 3-(2-chlorophenyl)-1-(coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 158-160 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.73; **% Yield:** 70%; **IR (KBr) cm^{-1}:** 1710.05 and 1692.04 (C=O), 1544.52 (C=C), 1140.10 (C-O-C).
C_5		**Chemical Name:** 3-(4-chlorophenyl)-1-(7-chlorocoumarin-3-yl)prop-2-ene-1-one; **M.P.:** 190-192 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.69; **% Yield:** 75%; **IR (KBr) cm^{-1}:** 1712.10 and 1693.08 (C=O), 1543.55 (C=C), 1134.06 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 6.98 (d, J=12Hz, 1H, =CH-CO-), 7.17 (d, J=12Hz, 1H, Ar-H), 7.36 (d, J=12Hz, 1H, Ar-H), 7.41 (d, J=12Hz, 3H, Ar-H), 7.49 (d, J=12Hz, 2H, Ar-H), 7.85 (d, J=12Hz, 1H, -CH=CH-CO-), 8.10 (s, 1H, Ar-H).
C_6		**Chemical Name:** 3-(4-chlorophenyl)-1-(7-bromocoumarin-3-yl)prop-2-ene-1-one; **M.P.:** 154-156 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.68; **% Yield:** 80%; **IR (KBr) cm^{-1}:** 1708.94 and 1694.02 (C=O), 1544.50 (C=C), 1132.06 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 6.99 (d, J=12Hz, 1H, =CH-CO), 7.28 (d, J=12Hz, 1H, Ar-H), 7.38 (m, 3H, Ar-H), 7.49 (d, J=12Hz, 2H, Ar-H), 7.84 (d, J=12Hz, 2H, Ar-H, -CH=CH-CO-), 8.17 (s, 1H, Ar-H).
C_7		**Chemical Name:** 3-(2,6-dichlorophenyl)-1-(7-chloro coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 177-179 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.76; **% Yield :** 75%; **IR (KBr) cm^{-1}:** 1707.88 and 1691.72 (C=O), 1543.50 (C=C), 1132.04 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 7.03 (d, J=12Hz, 1H, =CH-CO-), 7.15 (m, 2H, Ar-H), 7.24 (d, J=12Hz, 2H, Ar-H), 7.34 (d, J=12Hz, 1H, Ar-H), 7.39 (s, 1H, Ar-H), 8.02 (d, J=12Hz, 1H, -CH=CH-CO-), 8.14 (s, 1H, Ar-H).
C_8		**Chemical Name:** 3-(2,6-dichlorophenyl)-1-(7-bromo coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 194-196 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.63; **% Yield:** 70%; **IR (KBr) cm^{-1}:** 1712.08 and 1693.28 (C=O), 1546.12 (C=C), 1132.40 (C-O-C); **^{1}H NMR ($CDCl_3$, DMSO-d_6) δ ppm:** 6.99 (d, J=12Hz, 1H, =CH-CO-), 7.15 (t, J=8Hz, 1H, Ar-H), 7.25 (d, J=12Hz, 3H, Ar-H), 7.38 (d, J=12Hz, 1H, Ar-H), 7.71 (s, 1H, Ar-H), 8.01 (d, J=12Hz, 1H, -CH=CH-CO-), 8.15 (s, 1H, Ar-H).

C_9		**Chemical Name:** 3-(2,4-dichlorophenyl)-1-(7-chloro coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 173-175 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.72; **% Yield :** 75%; **IR (KBr) cm^{-1}:** 1707.06 and 1693.42 (C=O), 1545.04 (C=C), 1133.02 (C-O-C).
C_{10}		**Chemical Name:** 3-(2,4-dichlorophenyl)-1-(7-bromo coumarin-3-yl)prop-2-ene-1-one; **M.P.:** 162-164 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.69; **% Yield :** 70%; **IR (KBr) cm^{-1}:** 1711.64 and 1693.40 (C=O), 1543.55 (C=C), 1132.08 (C-O-C).
C_{11}		**Chemical Name:** 3-(2-chlorophenyl)-1-(7-chlorocoumarin-3-yl)prop-2-ene-1-one; **M.P.:** 185-187 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.77; **% Yield :** 75%; **IR (KBr) cm^{-1}:** 1708.92 and 1691.18 (C=O), 1546.05 (C=C), 1132.04 (C-O-C).
C_{12}		**Chemical Name:** 3-(2-chlorophenyl)-1-(7-bromocoumarin-3-yl)prop-2-ene-1-one; **M.P.:** 193-195 ^{0}C; **R_f Value (Benzene: Acetone; 9:1):** 0.70; **% Yield :** 80%; **IR (KBr) cm^{-1}:** 1710.84 and 1694.70 (C=O), 1545.38 (C=C), 1132.52 (C-O-C).

Antimicrobial activity

The *in vitro* antimicrobial activity was carried out against 24 hr old cultures of five bacteria and one fungus. The bacteria used were *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Salmonella typhi*. The fungus used was *Candida albicans*. Pure cultures of microorganisms were procured from the cultures maintained at department of pathology, Majeedia Hospital, Hamdard Nagar, New Delhi-110062. The antimicrobial activity was performed by cup plate method [7,8]. Nutrient agar and Sabouraud agar media were used for antibacterial and antifungal activity respectively. The compounds were tested at concentration of 50 µg/ml in dimethylformamide using Amikacin and Fluconazole as standard for antibacterial and antifungal activity respectively. Inhibition was recorded by measuring the diameter of the inhibition zone after 24 hr for bacteria and 48 hr for fungus. Each experiment was repeated thrice and average of the three independent determinations was recorded. Antimicrobial activity of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones is provided in Table-II.

Table-II: Antimicrobial activity of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones

Compound	*E. coli*	*S. aureus*	*B. subtilis*	*P. aeruginosa*	*S. Typhi*	*C. albicans*	*Average of % activity against all microbes*
C_1	70.13	62.66	62.15	77.88	51.55	53.77	63.02
C_2	68.74	75.50	55.18	61.46	88.90	72.55	70.38
C_3	66.82	63.45	48.33	44.26	82.33	92.74	66.32
C_4	75.33	88.33	27.77	54.27	56.44	51.42	58.92
C_5	72.66	85.88	44.75	78.52	52.50	77.14	68.57
C_6	58.44	78.50	83.90	64.50	72.75	79.18	72.87
C_7	76.90	90.50	71.85	34.33	83.66	92.64	74.98
C_8	89.74	57.25	87.75	67.65	56.33	70.11	71.47
C_9	67.66	67.75	70.50	81.44	42.65	76.32	67.72
C_{10}	88.40	54.73	77.33	58.55	75.70	77.24	71.99
C_{11}	84.58	79.66	87.65	70.55	77.33	58.27	76.34
C_{12}	76.74	80.33	56.75	46.50	89.50	66.42	69.37
Control	-	-	-	-	-	-	-
Standard	100.00	100.00	100.00	100.00	100.00	100.00	-

*No zone of inhibition for dimethylformamide. Zone of inhibition of Amikacin (100%) = 24mm (E. coli), 32mm (S. aureus), 28mm (B. subtilis), 28mm (P. aeruginosa), 38mm (S. typhi). Zone of inhibition of Fluconazole (100%) = 28mm (C. albicans). n = 5, *P < 0.05, **P < 0.01, ***P < 0.001*

RESULTS AND DISCUSSION

Antimicrobial activity of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones reveals that compounds C_8 and C_{10} showed highest activity against *E. coli*. Compound C_{11} also displayed appreciable activity while other compounds presented moderate activity against *E. coli*. Compound C_7 showed highest activity against *S. aureus*. Compounds C_4 and C_5 presented appreciable activity while other compounds displayed moderate activity against *S. aureus*. Compounds C_8 and C_{11} showed highest activity against *B.subtilis*. Compound C_6 also displayed appreciable activity while other compounds presented moderate activity against *B.subtilis*. Compounds C_9 showed highest activity against *P. aeruginosa* while other compounds presented moderate activity against *P. aeruginosa*. Compounds C_2 and C_{12} showed highest activity against *S. typhi*. Compounds C_3 and C_7 also displayed appreciable activity while other compounds presented moderate activity against *S. typhi*. Compounds C_3 and C_7 showed highest activity against *C. albicans* while other compounds presented moderate activity against *C. albicans*. The antimicrobial activity of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones also reveals that compound C_1 showed moderate actvivity against all microorganisms. The average of % activity of 3-(substitutedphenyl)-1-(7-substitutedcoumarin-3-yl)prop-2-ene-1-ones against all microorganisms reveals that compound C_{11} displayed highest activity, but less than standard drug, against all microorganisms while compound C_4 displayed least activity against all microorganisms. None of the tested compounds showed comparable activity with respect to standard drugs.

Acknowledgements
The authors are thankful to Jamia Hamdard (Hamdard University) for providing facilities to carry out this research work.

REFERENCES

[1] M. Imran, S.A. Khan, *Asian J. Chem.*, **2004**, 16: 543-545.
[2] P.K. Monga, D. Sharma, A. Dubey, *J. Chem. Pharm. Res.*, **2012**, 4(1):822-850.
[3] M. V. Girgaonkar, S. G. Shirodkar, *J. Chem. Pharm. Res.*, **2012**, 4(1):260-264.
[4] M. R. Ahmad, V. G. Sastry, N. Bano, S. Anwer, G. Kumaraswamy, *J. Chem. Pharm. Res.*, **2011**, 3(5):710-717.
[5] C.K. RamaGanesh, D.B. Yadav, K.B. Venkatesh, *Indian J. Chem.*, **2010**, 49B: 1151-1154.
[6] Y. R. Prasad, A. L. Rao, R. Rambabu, *Eur. J. Chem.*, **2008** ,5(3): 461-466.
[7] M. J. Pelczar, E.C.S. Chain, N.R. Krieg, Microbiology, 5nd Edition, Tata McGraw-Hill, New York, **1993**, 488-538.
[8] A.L. Barry, Procedure and Theoretical Consideration for testing anti microbial agents in Agar media, 5th edition William wilkins Baltimore, **1991**, 180-195.