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SYNTHESIS OF NOVEL BENZAMIDE AND ARYLIDENE DERIVATIVES OF 1H-IMIDAZO[4, 5-B]PYRIDINES

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ABSTRACT

The chemistry of benzamides has gained importance in recent times, as most of them showed pronounced bioactive property. Benzamides are identified as important structural unit present in many compounds having potential biological activities, which are extracted from natural sources. For example, molecules, like proteins which play a essential role in almost all biological processes such as enzymatic catalysis, transport/storage (haemoglobin), immune protection (antibodies) and mechanical support (collagen). In amide all the three atoms in the O–C–N chain are reactive which makes them a useful moiety in organic compounds and hence become a key part for medicinal chemists. Some of the naturally occurring amides are Capasaicin Piperine, and Penicillin. Therefore, keeping in view of the varied pharmacological properties of both Imidazo[4,5-b]pyridine and benzamide moiety, a novel series of N-(substituted phenyl)-4-(1H-imidazo[4,5-b]pyridin-2-yl)benzamide derivatives and N-(4-substituted arylidene)-4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines were synthesised for the first time by appropriate synthetic routes and screened for antimicrobial activity.

KEYWORDS: Pencillin, Piperine, Capasaicin, Collagen, Haemoglobin, Analgesic activity.

INTRODUCTION

Benzamides are identified as important structural unit present in many compounds having potential biological activities. The formation of amide bonds are explained by classic reactions like Schotten Baumann, Schmidt and Ugi reactions. The comprehensive medicinal chemistry data base revealed that the carboxamide group appears in more than 25% of known drugs. Benzamides have been reported to possess in vitro antibacterial activity and optimal

antimicrobial activity against Staphylococcus aureus.The fluoro derivatives of dithiobis (benzamide) showed antifungal activity. It is evident from the literature that the benzamide moiety is found as pharmacophore in many therapeutic agents. An interesting observation one could make from a careful survey of the literature is absence of any report on the Imidazo[4,5-b]pyridine derivatives having antimicrobial activity containing N-(4-substitutedphenyl)- benzamides ring at 2nd position. It is also observed that no literature is available on the Imidazo[4,5-b]pyridine derivatives having N-(4-substituted arylidene)aniline moiety at 4th position.

Therefore, keeping in view of the varied pharmacological properties of both Imidazo[4,5-b]pyridine and benzamide moiety it has been considered of prime importance to take-up such synthesis with a view to screen the products for antimicrobial activity. We have synthesized a novel series of Synthesis of N-(substituted phenyl)-4-(1H-imidazo[4,5-b]pyridin-2-yl)benzamide derivatives and N-(4-substituted arylidene)-4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines for the first time by appropriate synthetic routes and screened for antimicrobial activity.

MATERIALS AND METHODS

All melting points were taken in open capillaries on a Veego VMP-1 apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Perkin-Elmer FT IR 240-c spectrometer. The 1H NMR spectra were recorded on Varian-Gemini 200 MHz spectrometer in DMSO-d6 using TMS as an internal standard and mass spectra were recorded on Schimadzu QP 5050A spectrometer.

EXPERIMENTAL SECTION

A. Synthesis of N-(substituted phenyl)-4-(1H-imidazo[4,5-b]pyridin-2- yl) benzamides (IV)

i) Synthesis of 2-(4-chlorophenylcarbamoyl) benzoic acid (III).

A solution of 4-chloro aniline (6.36 g, 50 mmol) in ethyl acetate (80 ml) was gradually added under vigorous stirring to a suspension of phthalic acid anhydride (7.41 g, 50 mmol) in ethyl acetate (100 ml). Stirring was continued for 3–4 h. The reaction was monitored by TLC. The formed product was filtered, washed with ethyl acetate (25 ml), air-dried, and recrystallized from dioxane.

Other compounds (III a-h) in this series were prepared similarly and their characterization data were recorded in Table 1.

ii) Synthesis of N-(4-chlorophenyl)-2-(1H-imidazo[4,5-b]pyridin-2-yl) benzamide (IV).

2,3-Diaminopyridine (0.001 mmole), 2-(4-chlorophenylcarbamoyl)benzoic acid (III, 0.001m mol)and PPA (10 ml) are heated at 120-1300C for 4 hours. It was then cooled, concentrated and poured into crushed ice and filtered. The solid thus obtained was purified by recrystallization from ethanol.

Other compounds (IV a-h) in this series were prepared similarly and their characterization data were recorded in Table 2.

B. Synthesis of N-(4-substituted arylidene)-4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines (VIII)

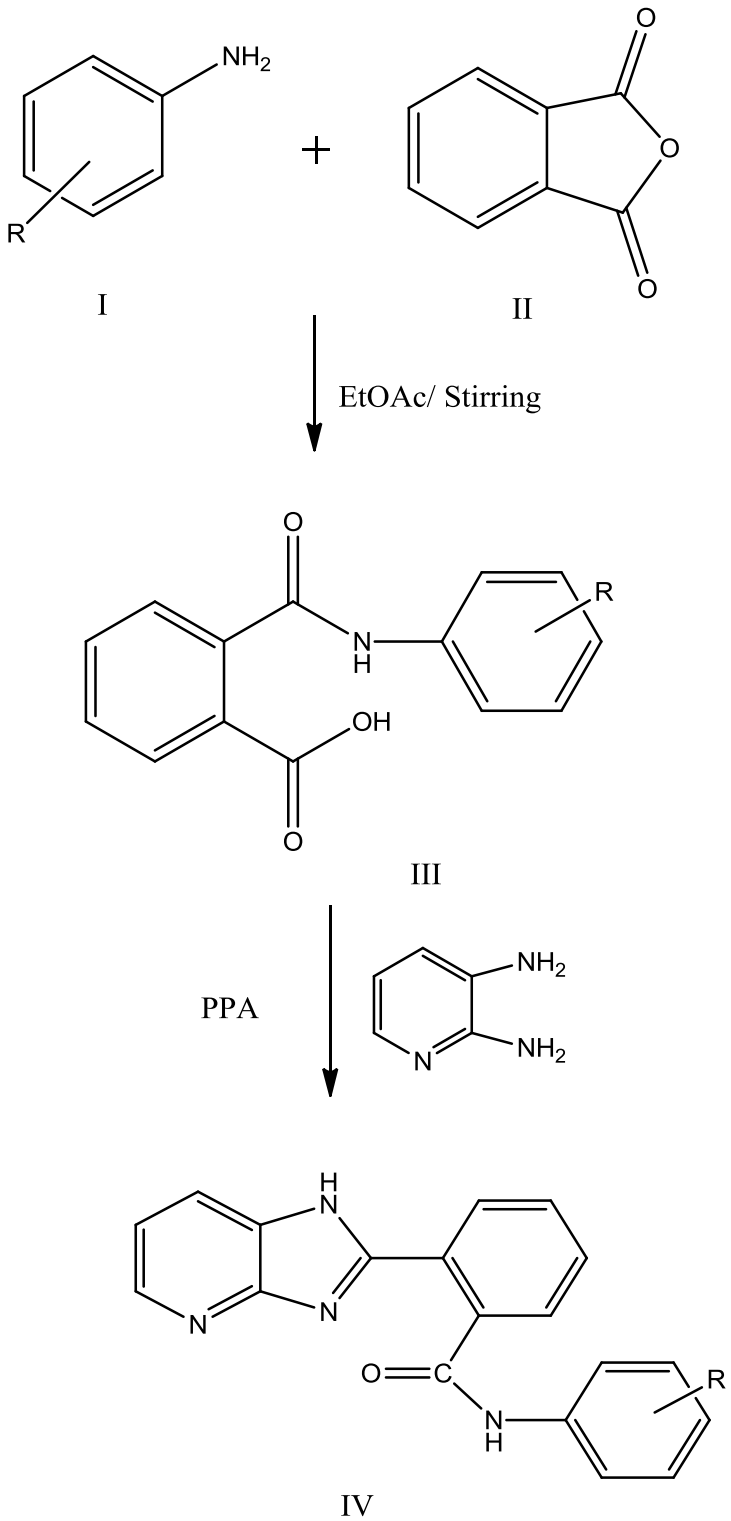
i) Synthesis of 4-(1H-imidazo[4,5-b]pyridin-2-yl)aniline (VII)

An equimolar amounts of pyridine-2,3-diamine(V,1mmol),4-aminobenzoic acid (1mmol) were heated in PPA at 120OC for 4hrs.. The Completion of the response advance was checked by utilizing TLC (10%, ethyl acetate: n-hexane). The reaction mixture was poured into crushed ice and filtered. The product was recrystallized from ethyl alcohol to give the pure product.

ii) Synthesis of N-(4-substituted arylidene)-4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines (VIII)

4-(1H-imidazo[4,5-b]pyridin-2-yl)aniline (VII, 0.01mol) was condensed with 4-chlorobenzaldehyde (0.015mol) by refluxing in 20ml of absolute alcohol containing few drops of acetic acid for 8hrs. The product thus separated was filtered, dried and purified by recrystallization from alcohol.

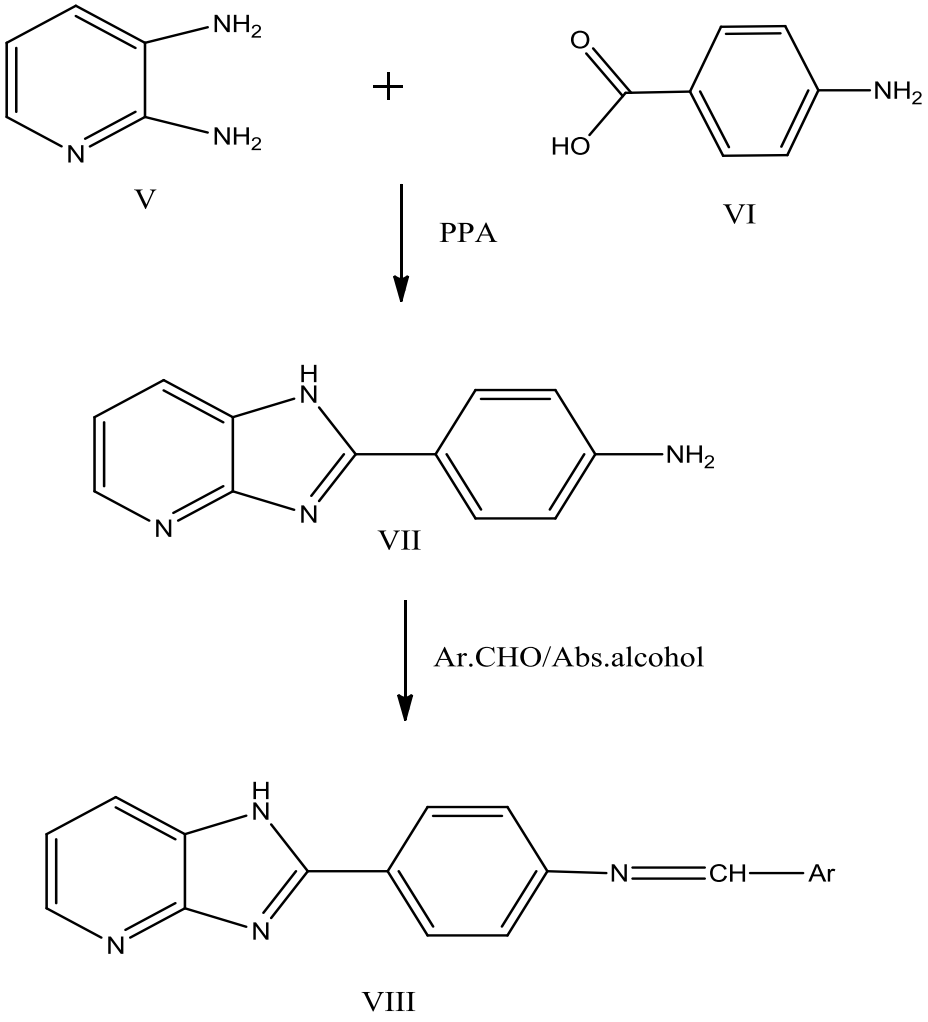
Other compounds (VIII a-h) in this series were prepared similarly and their characterization data were recorded in Table 3.



SCHEME – I

R = a) –H b) -4HCl c)-4 NO2 d) 2,4-tribromo e) 2,4,6-trinitro

f) 2-chloro-4-nitro g) 2,4,6-trichloro h) 2-Cl



SCHEME – II

R = a) Phenyl b) Salicyl c) Veratralyl d) Anisalyl e) 4-hydroxyphenyl

f) 4-dimethylaminophenyl g) 4-chlorophenyl h) 2,4,6-trinitrophenyl

SPECTRAL DATA

IR Spectrum data of compound IIId

The IR Spectrum (KBr) of the compound exhibited characteristic absorption bands (cm-1) at: 3364 (N-H), 3152 (O-H), 1683 (C=O), 1665 (C=O), 1615 (C=C, Ar), 1195(C-N), 765(C-Cl).

1 H NMR Spectrum data of compound IIId

1H NMR Spectrum (DMSO-d6) has been found to exhibit characteristic proton signals (□, ppm) at: 13.3 (s, 1H, OH), 10.3(s, 1H, NH), 8.3 (d, 1H, Ar-H), 7.8 (t, 2H,Ar-H),7.5 (d, 1H, ArH), 7.3 (d, 2H, ArH), 7.0(d,2H, ArH).

IR Spectrum data of compound IVd

The IR Spectrum (KBr) of the compound exhibited characteristic absorption bands (cm-1) at: 3350 (N-H), 3146 (NH), 1672 (C=O), 1528 (C=C, Ar), 1342(C-N), 669(C-Cl).

1 H NMR Spectrum data of compound IVd

1H NMR Spectrum (DMSO-d6) has been found to exhibit characteristic proton signals (□, ppm) at: 13.6 (s, 1H, NH (pyridine ring)), 10.1 (s, 1H, NH (amido group)), 8.4 (d, 1H,Ar-H),8.2 (d, 2H, ArH), 7.9 (d, 2H, ArH), 7.7 (d, 1H, ArH), 7.4(d, 2H, ArH), 7.2 (t, 1H, ArH), 6.9(d, 2H, ArH).

Mass Spectrum data of compound IVd

ESI-MS: m/z 349 [M+H]+.

IR Spectrum data of compound VII

The IR Spectrum (KBr) of the compound exhibited characteristic absorption bands (cm-1) at. 3400, 3485 (NH2), 3214 (N-H), 3012 (C-H, Aromatic), 1644 (C=N), 1462 (C=C, Ar).

1 H NMR Spectrum data of compound VII

1H NMR Spectrum (DMSO-d6) has been found to exhibit characteristic proton signals (□, ppm) at: 13.6 (s, 1H, NH), 8.6 (d, 1H, Ar-H, Pyiridine ring), 8.0(d, 2H, ArH), 7.5 (d, 1H,ArH, Pyridine ring), 7.2 (t, 1H,Ar-H, Pyridine ring),6.9 (d,2H, ArH), 5.4 (s, 2H, NH2).

IR Spectrum data of compound VIIIg:The IR Spectrum (KBr) of the compound exhibited characteristic absorption bands (cm-1) at: 3412 (N-H), 3016 (C-H, Aromatic), 1654 (C=N), 1424 (C=C, Ar),.

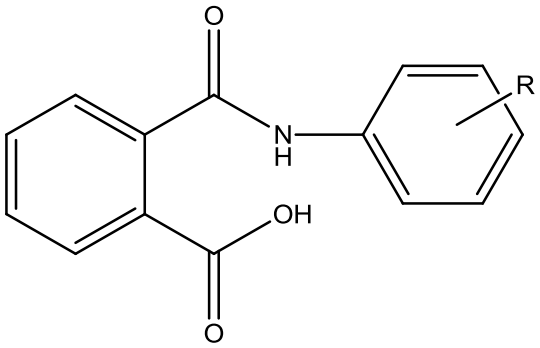
1 H NMR Spectrum data of compound VIIIg

1H NMR Spectrum (DMSO-d6) has been found to exhibit characteristic proton signals (□, ppm) at: 13.4 (s, 1H, NH), 8.7 (s, 1H, CH), 8.2 (d, 1H, Ar-H, Pyiridine ring), 7.8 (m, 5H,ArH), 7.2 (t, 2H,Ar-H, Pyridine ring), 6.7 (d,2H, ArH), 6.4 (d, 1H, ArH).

Mass Spectrum data of compound VIIIg

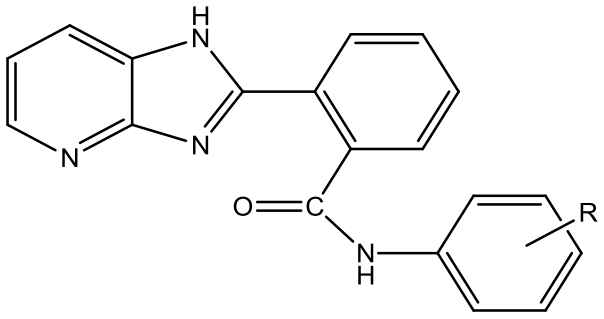
ESI-MS: m/z 333 [M+H]+

Table 1: Physical data of 2-(substituted phenylcarbamoyl) benzoic acid (III)



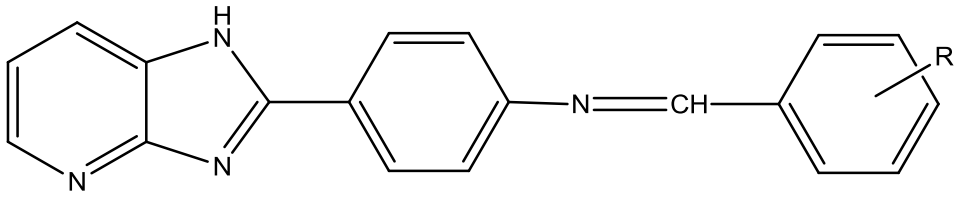
S.No	Compound	R	Chemical Formula	M.P(0C)	Yield (%)	Elemental Analysis Found (Calc %)		
						C	H	N
1	III a	H	C14H11NO3	242-244	66	69.77 (69.79)	4.62 (4.60)	5.84 (5.81)
2	III b	-4 Cl	C14H10NClO3	254-256	65	61.00 (60.99)	3.68 (3.66)	5.04 (5.08)
3	III c	-4 NO2	C14H10N2O5	260-262	66	58.77 (58.74)	3.50 (3.52)	9.83 (9.79)
4	III d	2,4,6-tribromo	C14H8Br3NO3	302-304	58	35.14 (35.18)	1.65 (1.69)	2.95 (2.93)
5	III e	2,3,6-trinitro	C14H8N4O9	309-311	65	44.73 (44.69)	2.10 (2.14)	14.88 (14.89)
6	III f	2,4-dichloro	C14H9Cl2NO3	280-282	58	54.20 (54.22)	2.95 (2.93)	4.55 (4.52)
7	III g	2,4,6 trichloro	C14H8Cl3NO3	320-322	58	48.85 (48.80)	2.40 (2.34)	4.08 (4.06)
8	III h	-2-Cl	C14H10NClO3	288-290	65	60.95 (60.99)	3.62 (3.66)	5.06 (5.08)

Table 2: Physical data of N-(substituted phenyl)-4-(1H-imidazo[4,5-b]pyridin-2-yl)benzamide(IV).



S.No	Compound	R	Chemical Formula	M.P(0C)	Yield (%)	Elemental Analysis Found (Calc %)		
						C	H	N
1	IV a	H	C19H14N4O	230-232	58	72.58 (72.60)	4.48 (4.49)	17.80 (17.82)
2	IV b	4-Cl	C19H13ClNO	260-262	54	65.45 (65.43)	3.78 (3.76)	16.02 (16.06)
3	IV c	4-NO2	C19H13N5O3	280-282	55	63.55 (63.51)	3.64 (3.65)	19.45 (19.49)
4	IV d	2,4,6-tribromo	C19H11Br3N4O	321-323	52	41.40 (41.41)	2.02 (2.01)	10.11 (10.17)
5	IV e	2,4,6-trinitro	C19H11N7O7	290-292	54	50.74 (50.79)	2.44 (2.47)	21.85 (21.82)
6	IV f	2,4-dichloro	C19H12Cl2N4O	312-314	58	59.58 (59.55)	3.10 (3.16)	14.66 (14.62)
7	IV g	2,4,6-trichloro	C19H11Cl3N4O	302-304	54	54.63 (54.64)	2.64 (2.65)	13.44 (13.41)
8	IV h	2-Cl	C19H13ClN4O	270-272	54	65.47 (65.43)	3.74 (3.76)	16.04 (16.06)

Table 3: Physical data of N-(4-substitutedbenzylidene)-4-(1H-imidazo[4,5- b] pyridin-2-yl) anilines (VIII).



S.No	Compound	R	Chemical Formula	M.P(0C)	Yield (%)	Elemental Analysis Found (Calc %)		
						C	H	N
1	VIII a	H	C19H14N4	215-217	75	76.44 (76.49)	4.75 (4.73)	18.77 (18.78)
2	VIII b	-2-OH	C19H14N4O	256-258	70	72.64 (72.60)	4.51 (4.49)	17.44 (17.82)
3	VIII c	2,3-(OCH3)	C21H18N4O2	287-289	71	70.40 (70.38)	5.01 (5.06)	15.68 (15.63)
4	VIII d	4 –OCH3	C20H16N4O	228-230	75	73.11 (73.15)	4.88 (4.91)	17.02 (17.06)
5	VIII e	4-OH	C19H14N4O	236-238	66	72.65 (72.60)	4.43 (4.49)	17.84 (17.82)
6	VIII f	4-N(CH3)2	C21H19N5	245-247	61	73.89 (73.88)	5.65 (5.61)	20.54 (20.51)
7	VIII g	4 -Cl	C19H13ClN4	260-262	60	68.52 (68.57)	3.96 (3.94)	16.88 (16.84)
8	VIII h	2,4,6-(NO2)3	C19H11N7O6	280-282	60	52.61 (52.66)	2.57 (2.56)	22.66 (22.63)

RESULTS AND DISCUSSION

A series of various anilines(I) were treated with phthalic anhydride(II) in ethyl acetate under vigorous stirring to get 2-(4-substituted phenylcarbamoyl)benzoic acids(III) upon recrystallization from dioxane. These 2-(4-substituted phenylcarbamoyl)benzoic acids(III) on heating with 2,3-diamino pyridine in PPA afforded the targeted compounds N-(substituted phenyl)-4-(1H-imidazo[4,5-b]pyridin-2-yl)benzamide(IV). Scheme-I (Table-1 and Table-2) Sixteen new compounds have been synthesised in Scheme-I

4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines (VII) were obtained by treatment of 2,3-diamino-pyridine (V) with 4-aminobenzoic acid in PPA under reflux condition. Finally the compound 4-(1H-imidazo[4,5-b]pyridin-2-yl)anilines (VII) on reaction with various aromatic aldehydes in absolute alcohol afforded the targetted compounds N-(4-substituted arylidene)-4-(1H-imidazo[4,5-b]pyridin- 2-yl)anilines (VIII) Scheme-II (Table-3)

Eight new compounds has been synthesised in Scheme-II

The structures of all the above compounds have been established on the basis of analytical and spectral data.

REFERENCES

1. Ji XY, Wang H Q, Hao L H, He WY, Gao RM, Li Y P, Li YH, Jiang J D, Li Z R, Molecules, 2013; 18(3): 3630-40.
2. Ashraf M S, Pathak D P, Inter.J.of Pharma-frontier, 2012; 2: 1.
3. Bindu BM, Ravinder MA, David B, Naga MN, Ramalingum R, Swetha D, Inter. Jour. Pharm.Pharme Sci, 2009; 1: 156-16.
4. Nagalakshmi G, Maity T K, Maiti BC , Int.J.Chem.Tech.Research, 2013; 5,5, 2057-67.
5. Yan F, Hu Y, Dil B, He PL,Sun G, J Pharm Pharmaceut Sci, 2012; 15,2, 208-20.
6. Bowman W R, Heaney H, Smith PHG, Arkinov, 2003; 434-42.
7. Lavanya P, Veena V K, Vasu K, Suresh M, Jhansi Rani V, Venkata Rao C J. Chem. Pharm. Res, 2010; 2,3, 25-32.
8. Venkatesh P, Pandeya SN, Inter. Jour. Of Chem Tech. Resea, 2009; 1,3: 733-41.