Indian Journal of Chemistry
Vol. 46B, November 2007, pp. 1896-1900

Note

Alkaloids of *Sida cordifolia* L.

Ranajit K Sutradhar[a]*, A K M Matior Rahman[b], Mesbah U Ahmad[c] & Koushik Saha[c]

[a]Department of Chemistry, Chittagong University of Engineering and Technology (CUET), Chittagong 4349, Bangladesh

[b]Department of Chemistry, Bangladesh University of Engineering and Technology (BUET), Dhaka 1000, Bangladesh

[c]Department of Chemistry, Jahangirnagar University, Savar, Dhaka, Bangladesh

E mail: rksutradhar2002@yahoo.com

Received 20 November 2006; accepted (revised) 30 August 2007

Four new alkaloids, *viz*; 1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-3-ylamine, 5′-hydroxymethyl-1′-(1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-1-yl)-heptan-1-one, 2-(1′-amino-butyl) indol-3-one and 2′-(3*H*-indol-3-ylmethyl)-butan-1′-ol have been isolated from methanol extract of the aerial parts of *Sida cordifolia* L and characterized using ^{1}H NMR, ^{13}C NMR, COSY, HMBC and mass spectra.

Keywords: *Sida cordifolia* L; Malvaceae; alkaloids.

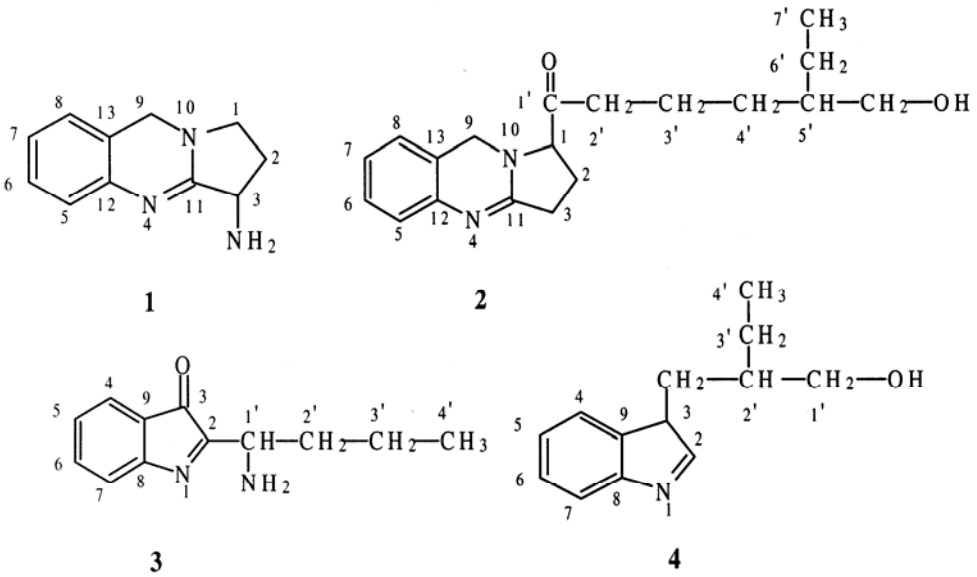
Sida cordifolia L. is an herb belonging to the family Malvaceae. It grows to a height of 3-5 feet and is used as a common herbal drug in the Indian subcontinent. The roots, leaves, stem and seeds of *Sida cordifolia* are used in traditional medicine against chronic dysentery, asthma and gonorrhoea[1,2]. The aqueous extract of the whole plant is specifically used in the treatment of rheumatism[1]. Earlier phytochemical investigations on the roots showed the presence of ephedrine, quinazoline alkaloids, e.g. vasicine, vasicinol, vasicinone, along with *N*-methyl tryptophan[3-6]. We report, herein, the isolation and characterization of four new alkaloids (**1-4**) from the aerial parts of *Sida cordifolia*.

Results and Discussion

The dried powder (5.5 kg) of the aerial parts of *Sida cordifolia* was successively extracted with $CHCl_3$ and MeOH respectively. The acid-base separation of the methanol extract (30 g) led to the isolation of a crude alkaloidal material 4.2 g (ref. 7). Alkaloid **1** (0.005%) and **2** (0.007%) were separated by preparative TLC technique using solvent system (1:1:1) MeOH:EtOAc:$CHCl_3$. Alkaloid 3 (0.008%) and 4 (0.007%) were also separated from the alkaloidal material using same technique eluting with (1:1:1) EtOAc:$CHCl_3$:*n*-hexane.

Alkaloid **1** gave positive reactions with Mayer's and Dragendorff reagents for an alkaloid[8] and was shown to be a quinazoline alkaloid[9] (λ_{max} MeOH 293 and 232 nm). The IR spectrum of **1** showed intense absorptions at 3450 cm^{-1} (N-H) and 1635 cm^{-1} (C=N). The HREIMS of **1** showed a molecular ion peak (M^+) at *m/z* 187.2456 corresponding to the molecular formula $C_{11}H_{13}N_3$ (Calcd. for $C_{11}H_{13}N_3$, 187.2460). Although the number of carbon atoms (**Table I**) in **1** is eleven, like that in vasicine ($C_{11}H_{12}N_2O$, *m/z* 188), the nitrogen content is different ($C_{11}H_{13}N_3$). If a NH_2 group is substituted for the OH group of vasicine, the observed molecular formula for **1** is satisfied. The structure thus obtained for **1** was confirmed by the ^{1}H NMR, ^{13}C NMR, COSY, HMBC and mass spectra. Two multiplets centred at δ 3.30 and 3.40 in the ^{1}H NMR spectrum are attributed to two NH_2 protons. The position of the NH_2 group at C-3 was confirmed from the HMBC correlations of NH_2 protons to C-11 (δ 164.46) and C-2 (δ 30.49). Protons attached to C-2 and C-1 appeared as multiplets centred at δ1.98 (H-2) and 2.38 (H-1) respectively, whereas a methine proton at C-3 and two methylene protons at C-9 appeared as an overlapping multiplet[9] at δ 4.60. The four aromatic protons appeared as a 3H multiplet centred at δ 6.97 and a 1H triplet (J = 7.4 Hz, H-5) centred at δ 7.13. The important H-H and H-C correlations are presented in **Figure 1**. Alkaloid **1** is thus characterized as 1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-3-ylamine.

Alkaloid **2** also possesses a quinazoline nucleus; UV λ_{max} MeOH 237 and 288 nm[9]. The IR spectrum of **2** showed the presence of O-H (3400 cm^{-1}) and C=O (1701 cm^{-1}) functions. The alkaloid, $C_{19}H_{26}N_2O_2$ (M^+, *m/z* 314.4288) showed nineteen ^{13}C signals (**Table I**) and was a different alkaloid from those isolated earlier from *Sida cordifolia*[3-6]. However, its ^{1}H NMR and ^{13}C NMR spectra are quite similar to those of **1**. Alkaloid **2** showed four 1H absorptions in the aromatic region at δ 7.03 (d, J = 7.6 Hz, H-8), 7.26 (t, J = 7.6 Hz, H-6), 7.10 (t, J = 7.4 Hz, H-7) and 8.30 (d, J = 8.4 Hz, H-5) and the ^{13}C NMR spectrum confirmed the presence of six aromatic carbon atoms (**Table I**). Methylene proton absorptions as an AB system at δ 4.92 (d, J = 14.8 Hz, H-9) and 5.03 (d, J = 14.8 Hz, H-9) along with two sets of methylene proton



1 **2** **3** **4**

Table I — ^{13}C NMR data of the alkaloids **1, 2, 3** and **4** (100 MHz, CD_3OD)

Carbon	**1**	**2**	**3**	**4**
1	47.74	87.25		
2	30.49	29.71	161.81	145.88
3	72.40	30.06	162.57	77.23
4			127.14	129.42
5	129.35	127.66	127.99	118.31
6	125.70	123.79	127.99	116.15
7	124.05	124.28	135.68	129.21
8	120.68	119.68	150.42	135.01
9	49.63	44.25	121.86	132.92
11	164.46	157.66		
12	142.99	134.78		
13	120.68	134.34		
1′		201.91	73.23	64.53
2′		31.94	44.58	50.12
3′		24.76	31.06	29.37
4′		22.70	14.42	20.78
5′		52.70		
6′		29.37		
7′		14.12		
CH_2(OH)		68.02		
CH_2				29.71

absorptions at δ 2.04, m (H-2) and 2.47, m (H-3), confirmed the presence of a quinazoline nucleus[9]. Of the eight methylene carbons in **2** (**Table I**) three were assigned to the quinazoline nucleus and the other five to the side chain. The downfield shift of the methine proton at δ 5.26 (t, *J* = 6.4 Hz, H-1), as compared to that in **1,** showed that the linkage of the side chain is through a C=O group attached to C-1. That linkage was confirmed by the HMBC correlation peaks observed between H-1 proton (δ 5.26) to C-9 (δ 44.25) and C-2′ (δ 31.94). The important correlations between H-H and H-C are presented in **Figure 1**. The nature of the side chain was established from the ^{1}H NMR and ^{13}C NMR spectra. The doublet at δ 3.63 (CH_2-OH) and the triplet at δ 2.59 (H-2′) showed the presence of methylene protons attached to a hydroxyl group and another set attached to C=O group respectively. Three other sets of methylene protons appeared at δ 1.28 as singlet and three methyl protons appeared at δ 0.88 (H-7′) as a triplet in the ^{1}H NMR spectrum. Alkaloid **2** is thus 5′-hydroxymethyl-1′-(1,2,3,9-tetrahydro-pyrrolo [2,1-*b*]quinazolin-1-yl)-heptan-1-one.

Alkaloid **3** proved to be an indolenine alkaloid (λ_{max} 230, 267, 302 nm)[10]. The IR spectrum of **3** showed the presence of N-H (3408 cm^{-1}) and C=O (1684 cm^{-1} α, β unsaturated) functions. The HREIMS of **3** showed the molecular ion peak at *m/z* 202.2568 corresponding to a molecular formula $C_{12}H_{14}N_2O$ (Calcd. $C_{12}H_{14}N_2O$, *m/z* 202.2574) and the ^{13}C NMR spectral analysis confirmed the presence of twelve carbon atoms in the molecule (**Table I**). The molecular mass of 3 (*m/z* 202.2568) is identical to that of vasicinone ($C_{11}H_{10}N_2O_2$, *m/z* 202)[4], but the spectral data clearly indicated it to be an indolenine alkaloid rather than quinazoline alkaloid. The ^{1}H NMR spectrum of **3** showed four absorptions in the aromatic region each for one proton at δ 7.53 (t, *J* = 7.4 Hz, H-5), 7.75 (d, *J* = 8.0 Hz, H-4), 7.82 (t, *J* =7.2 Hz, H-6) and 8.24 (d, *J* =7.6 Hz, H-7) of the indolenine nucleus. The ^{13}C NMR spectrum of **3** confirmed the presence of six aromatic carbons in the

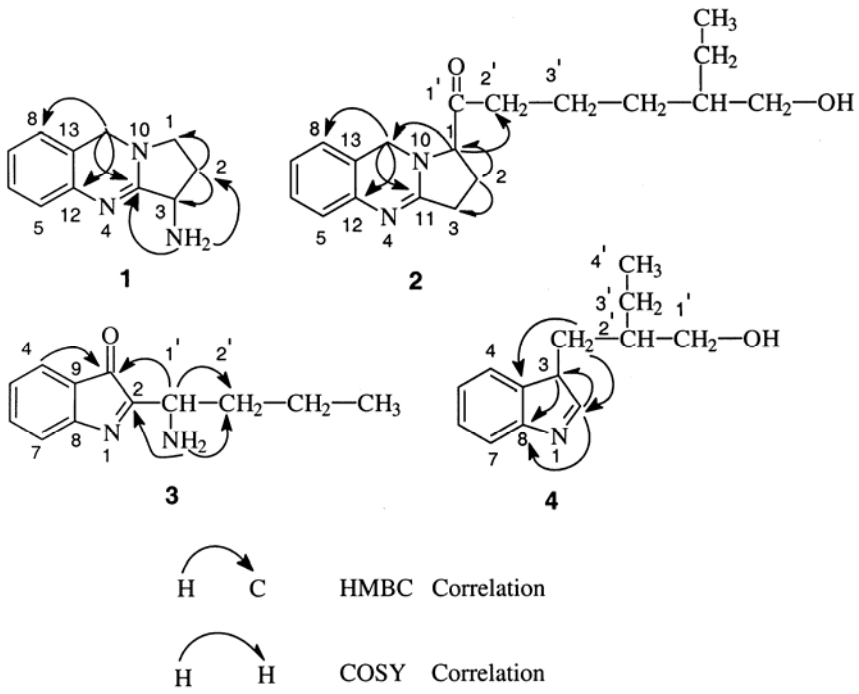


Figure 1 — Important HMBC and COSY correlations of alkaloids **1**, **2**, **3** and **4**.

molecule and also showed the presence of two methylene carbons and one methyl carbon in **3** (**Table I),** which suggested that an aliphatic side chain is attached to the indolenine nucleus. The structure for **3** was corroborated by the ^{1}H NMR, ^{13}C NMR, COSY, HMBC and mass spectra. The two protons attached to N appeared as 1H multiplets at δ 4.01 and 4.26, respectively, for their proximity to the indolenine nucleus. The protons of the two methylene groups and the methyl group of the side chain appeared as multiplets at δ 2.15 (H-2′), 1.59 (H-3′) and a triplet at δ 0.93 (H-4′), respectively. A methine proton attached to the carbon bearing the NH_2 group appeared at δ 5.11 (t, *J* = 7.2 Hz, H-1′). The position of the NH_2 group at C-1′ was confirmed by the HMBC correlations of NH_2 protons to C-2′(δ 44.58) and C-2 (δ 161.87). The important H-C correlations are seen from the HMBC spectrum in **Figure 1**. Alkaloid **3** is therefore 2-(1′-amino-butyl)-indol-3-one.

Alkaloid **4** is also an indolenine alkaloid (λ_{max} MeOH 243, 280 and 306 nm)[10]. The IR spectrum of **4** showed a broad absorption (3540 cm^{-1}) for O-H and a M^+ at *m/z* 203.2846 in its HREIMS for $C_{13}H_{17}NO$ (calcd. for $C_{13}H_{17}NO$, *m/z* 203.2850). The presence of thirteen carbon atoms in the molecule was confirmed by the ^{13}C NMR spectrum (**Table I**). The four aromatic protons of the indolenine nucleus appeared at δ 6.65 (d, *J* = 7.2 Hz, H-4), 6.73 (t, *J* = 7.1 Hz, H-6), 7.05 (d, *J* = 7.2 Hz, H-7) and 7.07 (t, *J* = 7.6 Hz, H-5). The ^{13}C NMR spectrum (**Table I**) supported the presence of an aromatic ring in **4**. Proton attached to C=N appeared at δ 5.33 (d, *J* = 7.2 Hz, H-2). The presence of a side chain attached to the indolenine nucleus is on the basis of the absorptions for three methylene carbons and one methyl carbon in the ^{13}C NMR spectrum. The side chain is attached to the carbon bearing the proton, which appeared as a multiplet at δ 4.29 (H-3). Structure for **4** is proposed on the basis of ^{1}H NMR, ^{13}C NMR, COSY, HMBC and mass spectra. Two methylene protons attached to hydroxyl group appeared at δ 3.62 (d, *J* = 7.2 Hz, H-1′) and other four methylene protons appeared at δ 1.24 as singlet. The triplet at δ 0.85 and the multiplet at δ 2.07 are due to the terminal methyl group and H-2′ protons respectively. The linkage of the side chain at C-3 was confirmed by the HMBC correlations from CH_2 protons (δ 1.24) to C-2 (δ 145.88) and C-9 (δ 132.92). The important H-H and H-C correlations are seen from the COSY and HMBC spectra in **Figure 1**. Thus the alkaloid **4** is 2′-(3*H*-indol-3-ylmethyl)-butan-1′-ol.

Experimental Section

The UV and IR spectra were recorded on a Shimadzu UV-visible spectrophotometer, Model UV 1601 PC and Shimadzu FTIR Model 8400,

respectively. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker BPX-200 spectrometer operating at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR spectra. The chemical shift values are reported as parts per million (ppm) relative to tetramethylsilane. The mass spectra were obtained on a JEOL JMDS-300 instrument. Preparative thin layer chromatography (PTLC) was performed on alumina pre-coated aluminum sheets. The plates were developed in different solvent systems by ascending method. Compounds were detected by UV light.

Plant material. The aerial parts of *Sida cordifolia* were collected from the hilly region of the district of Chittagong situated in the south-eastern region of Bangladesh. For the experimental purpose only the matured, sound, fresh and flowering plants were collected during the month of November 2002. The plant was identified in Bangladesh National Herbarium (BNH) by Mrs. Bushra Begum and a voucher specimen (Herbarium accession No. 31238) was deposited at BNH.

Extraction and isolation. The plant materials were chopped into small pieces, dried at room temperature and ground into powder. The dried powder (5.5 kg) of *Sida cordifolia* was successively extracted with $CHCl_3$ (3 × 72 h) and MeOH (3 × 72 h) respectively. Both of the extracts gave deep green residue ($CHCl_3$ 100 g; MeOH 150g) on removal of the solvent under reduced pressure at a temperature < 40˚C. The methanol extract (30 g) was acidified (*p*H 2) with 2 *M* HCl and the final volume was adjusted to 400 mL. The aqueous acidic solution was then extracted with EtOAc (3 × 300 mL) to remove neutral components. After removal of neutral components (15 g) the aqueous layer was then made alkaline (*p*H 9) with 30% NH_4OH solution and repeatedly extracted with EtOAc (3 × 300 mL). The combined extracts were washed with water, dried, and evaporated under reduced pressure to yield the crude alkaloid 4.2 g (0.38%) as a solid brown mass[7]. The alkaloidal material proved to be a mixture of at least four alkaloids by TLC. Two alkaloids **1** (55 mg) and **2** (77 mg) were separated using preparative TLC technique with (1:1:1) MeOH:EtOAc:$CHCl_3$ as a developing solvent system. Alkaloids **3** (90 mg) and **4** (82 mg) were separated from the alkaloidal material by prep-TLC eluting with (1:1:1) EtOAc:$CHCl_3$: *n*-hexane as the developing solvent. Alkaloids **1** and **2** were purified by repeated crystallization using EtOH:EtOAc (1:1) solvent system and the alkaloids **3** and **4** were also purified as in **1** and **2** using EtOAc:$CHCl_3$ (1:1) as solvent system.

Alkaloid 1. Brown amorphous powder, m.p. 165-166˚C. UV λ_{max} (MeOH) nm: 232, 293; IR (KBr): 3450 (N-H) and 1635 (C=N) cm^{-1}; ^{1}H NMR (CD_3OD): δ 1.98 (2H, m, H-2), 2.3 (2H, m, H-1), 3.30(1H, m, NH_2), 3.40 (1H, m, NH_2), 4.60 (1H, m, H-3), 4.60 (2H, m, H-9), 6.97 (3H, m, H-6,7,8) and 7.13 (1H, t, *J* = 7.4 Hz, H-5); ^{13}C NMR data: **Table I**; EIMS 70 eV: *m/z* (rel. int) 187 (100) [M^+], 171 (15), 159 (16), 131 (18), 104 (10) etc; HREIMS 70 eV: *m/z* 187.2456 [M^+] (calcd. for $C_{11}H_{13}N_3$, *m/z* 187.2460).

Alkaloid 2. Brown amorphous powder, m.p. 178-179˚C. UV λ_{max} (MeOH) nm: 273 and 288; IR (KBr): 3400 (O-H), 1701 (C=O) cm^{-1}; ^{1}H NMR (CD_3OD): δ 0.88 (3H, t, H-7′), 1.28 (3 × 2H, s, H-3′,4′,6′), 2.07 (2H, m, H-2), 2.32 (H, m, H-5′), 2.47 (2H, m, H-3), 2.59 (2H, t, H-2′), 3.63 (2H,d, CH_2OH), 4.92(1H, d, *J* = 14.8 Hz, H-9), 5.03 (1H, d, *J* = 14.8 Hz, H-9), 5.26 (1H, t, *J* = 6.4 Hz, H-1), 7.03 (H, d, *J* = 7.6 Hz, H-8), 7.10 (H, t , *J* =7.4 Hz, H-7), 7.26 (H, t, *J* = 7.6 Hz, H-6), 8.30 (H, d, *J* = 8.4 Hz H-5); ^{13}C NMR data: **Table I**; EIMS 70 eV: *m/z* (rel. int) 314 (5) [M^+], 291 (7), 273 (30), 253 (5), 228 (25), 209 (14), 185 (10), 149 (15), 129 (20), 104 (75), 83 (54), 57 (100) etc; HREIMS 70 eV: *m/z* 314.4288 [M^+] (calcd. for $C_{19}H_{26}N_2O_2$, *m/z* 314.4292).

Alkaloid 3. White amorphous powder, m.p. 182-183˚C; UV λ_{max} (MeOH) nm: 230, 267, 302; IR (KBr): 3408 (N-H), 1684 (C=O α, β unsaturated) cm^{-1}; ^{1}H NMR (CD_3OD): δ 0.93 (3H, t, H-4′), 1.59 (2H, m, H-3′), 2.15 (2H, m, H-2′), 4.01 (1H, m, NH_2), 4.26 (1H, m, NH_2), 5.11 (1H, t, *J* = 7.2 Hz, H-1′), 7.53 (1H, t, *J* = 7.4 Hz, H-5), 7.75 (1H, d, *J* = 8.0Hz, H-4), 7.82 (1H, t, *J* = 7.2 Hz, H-6), 8.24 (1H, d, *J* = 7.6 Hz, H-7); ^{13}C NMR data: **Table I**; EIMS 70 eV: *m/z* (rel. int) 202 (98) [M^+], 185 (12), 174 (14), 146 (98), 130 (35), 119 (100), 102 (27), 92 (14) etc; HREIMS 70 eV: *m/z* 202.2568 [M^+] (calcd. $C_{12}H_{14}N_2O$, *m/z* 202.2574).

Alkaloid 4. White amorphous powder, m.p. 170-171˚C; UV λ_{max} (MeOH) nm: 243, 280 and 306; IR (KBr): 3540 (O-H) cm^{-1}; ^{1}H NMR (CD_3OD): δ 0.85 (3H, t, H-4′), 1.24 (2 × 2H, s, H-3′, CH_2), 2.07 (H, m, H-2′), 3.62 (2H, d, *J* = 7.2 Hz, H-1′), 5.35 (1H, d H-2), 6.65 (1H, d, *J* = 7.2 Hz, H-4), 6.73 (1H, t, *J* = 7.1 Hz, H-6), 7.05 (1H, d, *J* = 7.2 Hz, H-7), 7.07 (1H, t, *J* = 7.6 Hz, H-5); ^{13}C NMR data: **Table I**; EIMS 70 eV: *m/z* (rel. int) 203 (8) [M^+], 189 (100), 167 (5), 149 (38), 134 (90), 116 (32), 106 (22), 77 (26), 57 (20) etc; HREIMS 70 eV: *m/z* 203.2846 [M^+] (calcd. for $C_{13}H_{17}NO$, *m/z* 203.2850).

References

1 Yusuf M & Kabir M, *Medicinal Plants of Bangladesh*, Bangladesh Council of Scientific and Industrial Research, Dhaka, Bangladesh, **1999**, 226.

2 Kirtiker K R & Basu B D, *Indian medicinal plants,* 2nd Edition, (International book distributors publication, Dehradun, India). Vol. 1, **1981**, 312.

3 Ghosh S & Dutt A, *J Indian Chem Soc,* 7, **1930**, 825.

4 Ghosal S, Chauhan R B P S & Mehta R, *Phytochemistry,* 14, **1975**, 830.

5 Gunatilaka A A L, Sotheeswaran S, Balasubramaniam S, Chandrasekara A I & Badrasriyani H T, *Planta Med*, 39, **1980**, 66.

6 Asha B & Bannerjee N R, *Current Science,* 54, **1985**, 690.

7 Ali M, Ansari S H & Qadry J S, *J Nat Prod,* 54, **1991**, 1271.

8 Finar I L, *Organic Chemistry*, 5th Edition, (Low-priced edition, Singapore), Vol. 2, **1975**, 697.

9 Dhar K L, Jain M P, Koul S K & Atal C K, *Phytochemistry,* 20, **1981**, 319.

10 Scott A I, *Interpretation of UV spectra of Natural Products*, (Pergamon Student Editions, London), Vol. 7, **1964**, 176.