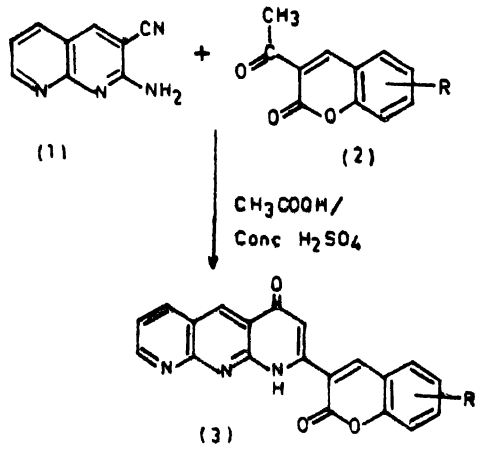



Scheme 1

precursors **1** and **2** was used as an indirect evidence for the structure elucidation of **3**. The ir spectra of **3** exhibited characteristic bands at 1 680 (C=O), 1 720 (lactonic C=O), 3 320 (NH) and an intense band at 1 600 (C=N), in addition to 1 460, 1 375, 1 230, 1 110, 1 025, 950, 870, 810 and 760 $cm^{-1}$. The absence of C≡N band at 2 200 $cm^{-1}$ provided additional proof for the structural assignment of **3**. The mass spectra of **2** showed a strong molecular ion peak at *m/z* 371 which corresponds to the molecular formula $C_{21}H_{13}N_3O_4$. The characterisation data of these compounds are given in Table 1.

TABLE 1—PHYSICAL DATA OF 2-(3-COUMARINYL)-4(1*H*)ANTHYRIDINONES (3)*

| R | M.p. °C | Yield % | Mol. formula |
|---|---|---|---|
| H | >300 | 60 | $C_{20}H_{11}N_3O_3$ |
| 8-$OCH_3$ | >300 | 80 | $C_{21}H_{13}N_3O_4$ |
| 7-OH | >300 | 66 | $C_{20}H_{11}N_3O_4$ |
| 6-Cl | >300 | 80 | $C_{20}H_{10}N_3O_3Cl$ |
| 6-Br | >300 | 76 | $C_{20}H_{10}N_3O_3Br$ |
| 6,8-Di-Cl | >300 | 75 | $C_{20}H_9N_3O_3Cl_2$ |
| 6,8-Di-Br | >300 | 74 | $C_{20}H_9N_3O_3Br_2$ |
| 6-$NO_2$ | >300 | 63 | $C_{20}H_{10}N_4O_5$ |
| 8-$NO_2$ | >300 | 63 | $C_{20}H_{10}N_4O_5$ |
| 8-$OCH_3$-6-$NO_2$ | >300 | 68 | $C_{21}H_{12}N_4O_5$ |
| 6-Br-8-$OCH_3$ | >300 | 70 | $C_{21}H_{12}N_3O_4Br$ |
| 5,6-Benzo | >300 | 68 | $C_{24}H_{13}N_3O_3$ |

*C, H, N analyses satisfactory.

## Experimental

M. ps. are uncorrected. The homogeneity and purity of the compounds were tested by tlc Ir spectra (nujol) were recorded on a Perkin–Elmer 283 spectrophotometer.

*3-Acetylcoumarins* (**2**) : Various substituted-3-acetylcoumarins derived from salicylaldehydes and ethyl acetoacetate were prepared by the literature method[6-8].

*2-(3-Coumarinyl)-4(1H)anthyridinones* (**3**) : A mixture of **1** (0.1 mol) and appropriate 3-acetyl coumarin (**2** ; 0.1 mol) was refluxed in glacial acetic acid (25 ml) in presence of a trace of concentrated $H_2SO_4$ for 4 h. The reaction mixture was cooled, poured onto crushed ice and the separated solid filtered and recrystallised from aqueous acetic acid to give **3**.

## Acknowledgement

The authors are thankful to Prof. E. V. Sundaram, Head, Department of Chemistry and Dean, Faculty of Science, Kakatiya University, Warangal, for facilities. Two of the authors (K. R. R. and K. M.) are thankful to C.S.I.R., New Delhi, for the award of Senior Research Fellowship and Pool Officership, respectively.

## References

1. S. CARBONI, A. DA SETTIMO, D. BERTINI, P. L. FERRACINI, O. LIVI and I. TONETTI, *J. Heterocycl. Chem.*, 1972, **9**, 801, and references therein
2. S. CARBONI, A. DA SETTIMO and I. TONETTI, *J. Heterocycl. Chem.*, 1970, **7**, 875.
3. P. CALUWE and T. G. MAJEWICZ, *J. Org. Chem.*, 1977, **42**, 3410.
4. K. MOGILAIAH, K. RAJENDAR REDDY, K. VIJAYENDER REDDY and B. SREENIVASULU, *J. Indian Chem. Soc.*, 1986, **63**, 345.
5. E. M. HAWES and D. G. WIBBERLEY, *J. Chem. Soc. (C)*, 1967, 1564.
6. K. P. RAJANIBALA and C. P. KANTILAL, *Agra University J. Research*, 1955, **4**, 305 (*Chem. Abstr.*, 1956, **50**, 4121).
7. NG. PH. BUU-HOI, T. B. LOC and NG. D. XUONG, *Bull. Soc. Chim. Fr.*, 1957, **3**, 561.
8. N. V. SUBBA RAO and V. SUNDARAMURTHY, *Proc. Indian Acad Sci., Sect. A*, 1961. **54**, 321.

# Substituted-1,8-naphthyridines. Part-VII. Synthesis and Biological Activity of 4-Arylazo-2-(1,8-naphthyridin-2-yl)phenols

G. RAMA RAO, K. MOGILAIAH, K. RAJENDAR REDDY

and

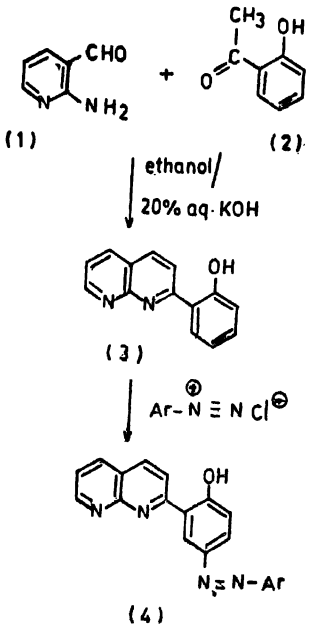
B. SREENIVASULU*

Department of Chemistry, Kakatiya University, Warangal-506 009

*Manuscript received 25 May 1987, accepted 18 September 1987*

IN continuation of our studies on the synthesis and antimicrobial activity of substituted[1-4] and fused[5-7] 1,8-naphthyridines, we report herein the synthesis of 4-arylazo-2-(1,8-naphthyridin-2-yl)phenols and evaluation of their biological activity. The reaction sequence is shown in Scheme 1.

The required 2-*o*-hydroxyphenyl-1,8-naphthyridine[1] (**3**) was obtained by the Friedlander's condensation of 2-aminonicotinaldehyde (**1**) with *o*-hydroxyacetophenone (**2**) in presence of ethanol containing a few drops of aqueous 20% KOH The intermediate **3** on coupling with diazotised arylamines




Scheme 1

at 0–5° resulted in the formation of 4-arylazo-2-(1,8-naphthyridine-2-yl)phenols (**4**). The compounds are all coloured crystalline solids and almost all the compounds are insoluble in common organic solvents at room temperature. The structures of the compounds were established on the basis of their elemental analyses and ir spectral data. The ir spectra of the compounds showed characteristic band at 1 540–1 570 $cm^{-1}$ due to N=N stretching and a broad band at 3 210–3 400 $cm^{-1}$ indicating the presence of phenolic hydroxyl group. All the compounds were obtained in good yields and pertinent data are recorded in Table 1.

*Biological activity :* All the compounds were tested for their antibacterial (against *Escherichia coli* and *Bacillus substilus*) and antifungal (against *Paecilomyces* sp and *Fusarium heterosporum*) activities[8] at a concentration of 400–600 $\mu g\ ml^{-1}$. None of the compounds showed any noteworthy activity.

## Experimental

M.ps. are uncorrected. Ir spectra (nujol) were taken on a Perkin–Elmer 283 spectrophotometer. The homogeneity and purity of the compounds were tested through tlc.

*2-o-Hydroxyphenyl-1,8-naphthyridine* (**3**) *:* A mixture of 2-aminonicotinaldehyde (**1** ; 0.1 mol) and *o*-hydroxyacetophenone (**2** ; 0.1 mol) was refluxed in ethanol (30 ml) in the presence of a catalytic amount of aqueous 20% KOH for 4 h. The reaction mixture was allowed to cool and poured onto crushed ice. The separated solid was filtered, dried and recrystallised from benzene, m.p. 188°.

*4-Arylazo-2-(1,8-naphthyridin-2-yl)phenols* (**4**) *:* The appropriate arylamine (0.1 mol) was dissolved in HCl (1 : 1, 20 ml) and cooled to 0–5°. Cold sodium nitrite solution (20%, 10 ml) was gradually added with stirring below 5°. The diazotised arylamine solution was added with stirring to a cold solution of **3** (0.1 mol) in NaOH solution (10%, 30 ml) at 0–5°. The resulting reddish orange reaction mixture was stirred for further 1 h. The solution was acidified with concentrated HCl and the precipitate obtained was filtered and washed with water. The products were airdried and recrystallised from ethanol.

Table 1—Analytical and Physical Data of 4-Arylazo-2-(1,8-naphthyridin-2-yl)phenols (**4**)*

| Ar | M.p. °C | Yield % | Mol. formula | N %: Found/(Calcd.) |
|---|---|---|---|---|
| $C_6H_5$ | 220 | 67 | $C_{20}H_{14}N_4O$ | 17.29 (17.17) |
| *o*-$CH_3.C_6H_4$ | 235 | 76 | $C_{21}H_{16}N_4O$ | 16.26 (16.47) |
| *p*-$CH_3.C_6H_4$ | 245 | 80 | $C_{21}H_{16}N_4O$ | 16.28 (16.47) |
| *m*-$CH_3O.C_6H_4$ | 215 | 72 | $C_{21}H_{16}N_4O_2$ | 15.85 (15.78) |
| *p*-$CH_3O.C_6H_4$ | 222 | 75 | $C_{21}H_{16}N_4O_2$ | 15.87 (15.73) |
| *m*-$NO_2-C_6H_4$ | 250 | 68 | $C_{20}H_{13}N_5O_2$ | 18.63 (18.86) |
| *p*-$NO_2-C_6H_4$ | 235 | 65 | $C_{20}H_{13}N_5O_2$ | 18.65 (18.86) |
| *o*-$Cl.C_6H_4$ | 208 | 70 | $C_{20}H_{13}N_4OCl$ | 15.67 (15.55) |
| *m*-$Cl.C_6H_4$ | 242 | 68 | $C_{20}H_{13}N_4OCl$ | 15.69 (15.55) |
| *m*-$OH.C_6H_4$ | 265 | 71 | $C_{20}H_{14}N_4O_2$ | 16.55 (16.37) |
| *p*-$SO_3H-C_6H_4$ | 278 | 70 | $C_{20}H_{14}N_4O_4S$ | 13.61 (13.79) |
| *p*-$SO_2NH_2.C_6H_4$ | 275 | 67 | $C_{20}H_{15}N_5O_3S$ | 17.11 (17.28) |
| *o*-$COOH.C_6H_4$ | 272 | 60 | $C_{21}H_{16}N_4O_3$ | 15.18 (15.09) |
| *p*-Thiazole-2-aminosulphonylphenyl | 295 | 67 | $C_{18}H_{13}N_5O_3S_2$ | 17.39 (17.21) |
| *p*-5-Methyloxazole-2-aminosulphonyl phenyl | 280 | 70 | $C_{24}H_{18}N_6O_4S$ | 17.85 (17.28) |
| *p*-4,5-Dimethylpyrimidin-2-aminosulphonylphenyl | 290 | 68 | $C_{28}H_{21}N_7O_3S$ | 19.08 (19.17) |

*All compounds gave satisfactory analyses for C and H.

## Acknowledgement

The authors are thankful to Prof. E. V. Sundaram, Head, Department of Chemistry, Kakatiya University, Warangal, for facilities and to C.S.I.R., New Delhi, for financial assistance.

## References

1. B. Sreenivasulu and K. Vijayender Reddy, *Curr. Sci.*, 1977, **46**, 597.

2. K. MOGILAIAH and B. SREENIVASULU, *Indian J. Chem., Sect. B*, 1982, **21**, 479.
3. K. MOGILAIAH, K. VIJAYENDER REDDY and B. SREENIVASULU, *Indian J. Chem., Sect. B*, 1983, **22**, 178.
4. K. RAJENDAR REDDY, K. MOGILAIAH and B. SREENIVASULU, *J. Indian Chem. Soc.*, 1987, **64**, 193.
5. K. MOGILAIAH and B. SREENIVASULU, *Indian J. Chem., Sect. B*, 1982, **21**, 582.
6. K. VIJAYENDER REDDY, K. MOGILAIAH and B. SREENIVASULU, *J. Indian Chem. Soc.*, 1984, **61**, 888.
7. E. J. S. REDDY, S. M. REDDY, K. MOGILAIAH and B. SREENIVASULU. *Nat. Acad. Sci. Letters*, 1985, **8**, 19.
8. J. C VENCENT and H. W. VINCENT, *Proc Soc. Exptl. Biol. Med.*, 1944, **55**, 162.

# Azatriterpenes. Part-VII. Synthesis of 2-Eno-[2,3-*g*]tetrazolo[1,5 *a*]pyrimidines of Pentacyclic Triterpenes†

B. SUDHAKAR, P. RAJARAM and T. SUNDARA RAMAIAH*

Department of Chemistry, Nizam College, Hyderabad-500 001

and

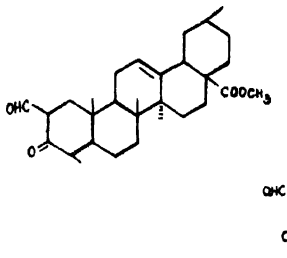
K. LAXMAN RAO and S. K. RAMRAJ

Department of Chemistry, Vivek Vardhini College, Hyderabad-500 195

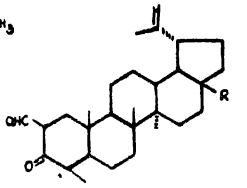
*Manuscript received 5 November 1986, accepted 18 September 1987*

HETEROSTEROIDS in recent years have gained great importance because of their modified physiological activity and sometimes with completely changed biological activity[1-4]. To develop new azasteroids of biological interest, Bajwa and Sykes[5] synthesised various steroidal 2-eno[2,3-*g*]-tetrazolol[1,5-*a*]pyrimidines by the reaction of steroidal 3-keto-2-hydroxymethylene derivatives with 5-aminotetrazole. As an application of this approach[5] we report herein some 2-eno[2,3-*g*]-tetrazolo[1,5-*a*]pyrimidines of pentacyclic triterpenes.

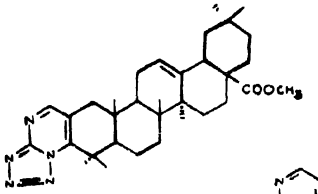
2-Hydroxymethylene derivatives[6] of methyl oleonate (**1**), lupenone (**2**) and methyl betulonate (**3**) were condensed with 5-aminotetrazole in absolute ethanol to obtain the desired compounds **4**–**6**. The assignment of structures was based on the observation of Bajwa and Sykes[5] for 2-eno[2,3-*g*]-tetrazolo[1,5-*a*]pyrimidines. Thus in the nmr spectra of **4**–**6**, a sharp signal around $\delta$ 8.67 (5'–H) conforms to the angular isomers as according to Bajwa and Sykes[5] the other isomeric structure ([3,2-*f*]tetrazolo[1,5-*a*]pyrimidine) is expected to give a broadened singlet for 7'–H due to a small longrange coupling with methylene protons. Also, in agreement to Bajwa and Sykes[5], in the present case tetrazolopyrimidines (**4**–**6**) exist in equilibrium with their azido forms in solution which is demonstrated in the ir spectra of the compounds in chloroform ($\nu_{max}$ 2 140 $cm^{-1}$ for azide function). The nmr spectra of all the three 2-eno[2,3-*g*]tetrazolo-[1,5-*a*]pyrimidines (**4**–**6**) showed a sharp signal around $\delta$ 8.1 (1H, 6'–H of azido form) and another around $\delta$ 8 6 (1H, 5'–H of tetrazolo form). The spectral data clearly indicate that the tetrazolo form and the azido form exist in equilibrium in solution. This is also supported by presence of two spots on the tlc of the condensation products.



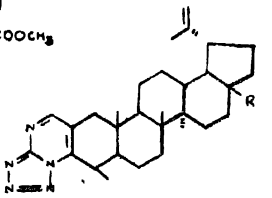

1




2, R=CH$_3$
3; R=COOCH$_3$




4




5; R=CH$_3$
6, R=COOCH$_3$

## Experimental

M.ps. were recorded using Bio-chem melting point apparatus and are uncorrected. The nmr spectra ($CDCl_3$) were recorded on a EM-360 (60 MHz) nmr spectrometer with TMS as the internal standard. Ir spectra were recorded on a Perkin–Elmer Infracord 237 spectrophotometer.

3-Keto-2-hydroxymethylene derivatives of pentacyclic triterpenes were prepared by the usual method[6].

*A typical experiment for the condensation of 5-aminotetrazole with 3-keto-2-hydroxymethylene derivatives of pentacyclic triterpenes* (**1**–**3**). *Isolation of 2-eno[2,3-g]tetrazolo[1 5-a]pyrimidines of pentacyclic triterpenes* (**4**–**6**) : A solution of the compound **1**–**3** (700 mg) 5-aminotetrazole (250 mg) in absolute ethanol (25 ml) was refluxed for 12 h and then evaporated to dryness in vacuum. The residue was adsorbed over neutral alumina (Acme) and eluted with petroleum ether (500 $cm^3$) and benzene (1.5 $dm^3$). Petroleum ether eluate did not yield any residue. Benzene eluate yielded 2-eno[2,3-*g*]-

†Part presented at 5th. Annual Convention of Indian Council of Chemists, 1985.