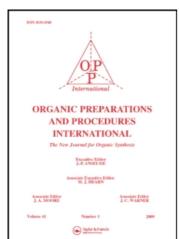
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AN IMPROVED SYNTHETIC ROUTE TO TRIFLUOROMETHYL-6-SUBSTITUTED-2(1H)-PYRIDONES

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AN IMPROVED SYNTHETIC ROUTE TO

TRIFLUOROMETHYL-6-SUBSTITUTED-2(1H)-PYRIDONES†

Submitted by (07/08/92)

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Fluorinated-1,3-dicarbonyl compounds¹ have considerable importance in the synthesis of many biologically active heterocycles. The preparation of fluorinated nitrogen heterocycles *via* cyclization of fluorinated intermediates has been reported in the literature.²⁻⁴ In connection with a program of synthesis of biologically active compounds, we required 4-trifluoromethyl-6-substituted-2(1H)-pyridones (3).

The first reported synthesis⁵ of 3 involves, for example, treatment of 1,1,1-trifluoro-2,4-pentanedione (1a) with cyanoacetamide in the presence of sodium ethoxide, followed by several recrystallizations to obtain 17% pure 3-cyano-6-methyl-4-trifluoromethyl-2(1H)-pyridone. For other pyridones in the series,⁵ the yield ranged from 12-36%. We attempted to improve the yield and purity of the pyridones and found that piperidine acts as a better catalyst in giving 72% in the above preparation

a)
$$R = CH_3$$
 b) $R = C_2H_5$ c) $R = C_6H_5$ d) $R = p-CH_3C_6H_4$ e) $R = p-OCH_3C_6H_4$ f) $R = p-CIC_6H_4$

and better than 70% yield in the preparation of other similar pyridones obtained in this work. The reaction times are shorter, the workup procedures are simpler, and the purity of the products obtained after washing the reaction product with cold ethanol is sufficiently high for further steps. The regioselectivity of the formation of 4CF₃-substituted-2(1H)-pyridones is not affected.

Products 3b, 3d, 3e and 3f are being reported for the first time. The structure of 3a was established by comparison with the work of Lang and Wenk⁶ and the structures of the others follow by analogy. The most electrophilic site is the carbonyl adjacent to the CF₃ group in the diketones and hence the formation of 4-CF₃ substituted regioisomers.

EXPERIMENTAL SECTION

Melting points are uncorrected. Infrared spectra were recorded using a Perkin-Elmer 810 model. ¹H NMR spectra were measured with a Varian (80 MHz) spectrometer in DMSO-d₆. Chemical shifts are reported in ppm, internal standard was tetramethylsilane (δ scale). Mass spectra were recorded on a VG micromass-7070H. Microanalysis were performed by Indian Institute of Chemical Technology, Hyderabad.

Volume 25, No. 1, 1993 OPPI BRIEFS

General Procedure for the Preparation of 3a-f.- To a solution of cyanoacetamide (1.78 g, 0.02 mol) in 95% ethanol (10 mL) was added 1,1,1-trifluoromethyl-2,4-pentanedione (3.08 g, 0.02 mol) with stirring. To the homogenous mixture obtained, piperidine (0.20 mL, 0.002 mol) was then added dropwise, the reaction mixture was refluxed for 2 hrs and cooled to room temperature. The resulting solid was collected, washed with small portions of cold ethanol and dried at 85°.

- 3a: Yield 72%, white powdery crystals, mp 234°, lit.⁶ mp. 232-234°. ¹H NMR: δ 2.37 (s, 3H, CH₃-C(6)), 6.62 (s, 1H, H-C(5)); IR (Nujol): 3320, 2225, 1655 cm⁻¹. MS: m/z 202.
- 3b: Yield 71%, white crystals, mp. 215°. ¹H NMR: δ 1.18 (d, 3H, CH₃), 2.62 (q, 2H, CH₂), 6.56 (s, 1H, H-C(5)); IR (Nujol): 3300, 2218, 1650 cm⁻¹. MS: m/z 216.
- Anal. Calcd. for C₉H₇F₃N₂O: C, 50.00; H, 3.26; F, 26.36; N, 12.95

Found: C, 50.01; H, 3.26; F, 26.35; N, 12.95

- 3c: Yield 73%, yellow needles, mp. 301°. ¹H NMR: δ 7.22 (s, 1H, H-C(5)), 7.56 (m, 3H, ArH), 7.93 (m, 2H, ArH); v IR(Nujol): 3350, 2225, 1648cm⁻¹. MS: m/z 264.
- **3d**: Yield 73%, yellow needles, mp. > 305°. ¹H NMR: δ 2.43 (s, 3H, CH₃), 7.21 (s, 1H, H-C(5)), 7.41 (d, 2H, ArH), 7.91 (d, 2H, ArH); IR (Nujol): 3150, 2200, 1648 cm⁻¹. MS: m/z 278.
- Anal. Calcd. for C₁₄H₉F₃N₂O: C, 60.43; H, 3.26; F, 20.48; N, 10.06 Found: C, 60.42; H, 3.25; F, 20.48; N, 10.06
- **3e**: Yield 72%, yellow needles, mp. 285°. ¹H NMR: δ 3.87 (s, 3H, OCH₃), 7.21 (s, 1H, H-C(5)) 7.11 (d, 2H, ArH) 7.97 (d, 2H, ArH); IR (Nujol): 3150, 2210, 1645 cm⁻¹. MS: m/z 294.
- Anal. Calcd. for C₁₄H₉F₃N₂O₂: C, 57.15; H, 3.08; F, 19.37; N, 9.52 Found: C, 57.14; H, 3.08; F, 19.36; N, 9.51
- **3f**: Yield 71%, yellow needles, mp. 287°. ¹H NMR: δ 7.37 (s, 1H, H-C(5)), 7.37 (d, 2H, ArH), 8.03 (d, 2H, ArH); IR (Nujol): 3375, 2200, 1645 cm⁻¹. MS: m/z 298.
- Anal. Calcd. for C₁₃H₆ClF₃N₂O: C, 52.28; H, 2.02; Cl, 11.87; F, 19.08; N, 9.38 Found: C, 52.28; H, 2.02; Cl, 11.86; F, 19.08; N, 9.37

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REFERENCES

- [†] IICT Communication No.3062.
- 1. J. C. Reid and M. Calvin, J. Am. Chem. Soc., 72, 2948 (1950).
- 2. A Giner-Sorolla and A. Bendich, ibid., 80, 5744 (1958).
- 3. E. D. Bergmann, S. Cohen and I. Shahak, J. Chem. Soc., 3278 (1959).
- 4. S. Llnoue, A. J. Saggiomo and E. A. Nodiff, J. Org. Chem., 26, 4504 (1961).
- 5. S Portnoy, *ibid.*, **30**, 3377 (1965).
- 6. R. W. Lang and P. F. Wenk, *Helv. Chim. Acta*, 71, 596 (1988).