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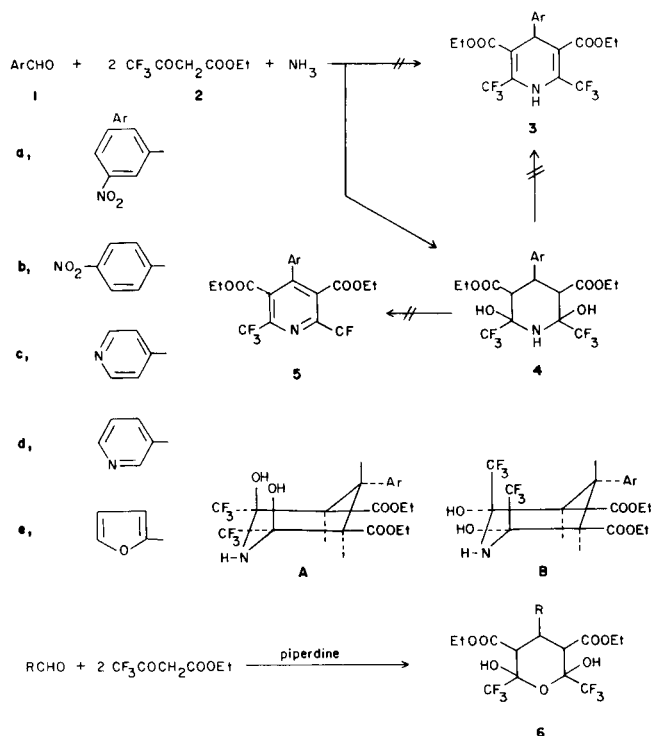
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Reaction of ethyl 4,4,4-trifluoroacetoacetate with aromatic aldehydes and ammonia gives diethyl 4-aryl-2,6-dihydroxy-2,6-bis(trifluoromethyl)-3,5-piperidinedicarboxylates (**4**) instead of diethyl 4-aryl-1,4-dihydro-2,6-bis(trifluoromethyl)-3,5-pyridinedicarboxylates (**3**) as reported previously (1).

J. Heterocyclic Chem., 17, 1109 (1980).

Balicki, *et al.* (1), have reported the preparation of a series of diethyl 4-aryl-1,4-dihydro-2,6-bis(trifluoromethyl)-3,5-pyridinedicarboxylates (**3**) by the reaction of ethyl 4,4,4-trifluoroacetoacetate (**2**) with arylaldehydes (**1**) and aqueous ammonia in ethanol [Hantzsch pyridine synthesis (2)]. They have made their structural assignments on the basis of microanalyses and unspecified spectroscopic data. We have now shown unequivocally that products formed by the above reaction do not have structure **3**, but rather, are diethyl 4-aryl-2,6-dihydroxy-2,6-bis(trifluoromethyl)-3,5-piperidinedicarboxylates (**4**).



In our laboratory, from the reaction of ethyl 4,4,4-trifluoroacetate (**2**) with 3-nitrobenzaldehyde (**1a**) and aqueous ammonia or ammonium acetate in ethanol [essentially the same conditions used by Balicki, *et al.* (1)] we obtained a compound in the form of colorless prisms, m.p. 128-130°; ms: M^+ at m/e 518 and elemental analysis of $\text{C}_{19}\text{H}_{20}\text{F}_6\text{N}_2\text{O}_8$ (molecular weight 518), the molecular form-

ula of **4a**. The ^1H nmr ($\text{DMSO}-d_6$) spectrum of this compound displayed signals consistent with structure **4a**: δ 7.5-8.4 (4H, aromatic), 6.42 (2H, s, OH), 4.23 (1H, t, $J = 12$ Hz, H-4), 3.82 (4H, q, OCH_2CH_3), 3.52 (2H, d, $J = 12$ Hz, H-3, H-5), 3.46 (1H, s, NH), and 0.83 ppm (6H, t, OCH_2CH_3).

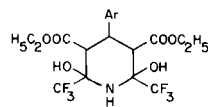
Attempts to convert **4a** to **3a** by dehydration with sulfuric acid, acetic anhydride, titanium tetrachloride or *N,N*-dicyclohexylcarbodiimide were unsuccessful. Starting material was recovered at lower temperatures while higher temperatures resulted in decomposition. Compound **4a** also failed to give **5a** on oxidation with nitric acid, a reagent commonly used to convert 1,4-dihydropyridines (**3**) to the corresponding pyridines (**5**).

While we were investigating the chemistry of **4a**, the work, of Balicki and co-workers (1) came to our attention. Their work did not include the reaction with 3-nitrobenzaldehyde (**1a**); therefore, we were prompted to repeat some of their work. In general, our yields were considerably lower but melting points slightly higher than theirs. All our compounds gave elemental analyses, nmr and mass spectra compatible with structures **4** (Table I and II). The Knoevenagel condensation of aldehydes with ethyl 4,4,4-trifluoroacetoacetate has been reported (3) to give the analogous diethyl 4-substituted-2,6-dihydroxy-2,6-bis(trifluoromethyl)tetrahydropyran-3,5-dicarboxylates (**6**). These compounds decomposed instead of giving the dehydrated products on treatment with sulfuric acid.

Stereochemistry.

The ^1H nmr spectra of these compounds show a triplet for H-4 and a superimposed doublet for H-3 and H-5 ($J = 12$ Hz) which suggests that these compounds have a plane of symmetry passing through N and C-4. The large coupling constant ($J_{3,4} = J_{5,3} = 12$ Hz) indicates that H-4 occupies trans axial position with respect to H-3 and H-5. These data suggest that the stereochemistry of these molecules may be represented by either of the symmetrical structures **A** or **B**.

Table I



| Compound No. | Ar | Formula | Yield (lit. (1) yield) % | M.p. (lit. (1) m.p.)°C (a) | Ms M ⁺ (m/e) |
|--------------|----|--|-----------------------------|-------------------------------|----------------------------|
| 4a | | C ₁₉ H ₂₀ F ₆ N ₂ O ₈ | 20 | 128-130 | 518 |
| 4b | | C ₁₉ H ₂₀ F ₆ N ₂ O ₈ | 24 (54) | 174-176 (168-169) | 518 |
| 4c | | C ₁₈ H ₂₀ F ₆ N ₂ O ₆ | 50 (70) | 184-186 (177-178) | 474 |
| 4d | | C ₁₈ H ₂₀ F ₆ N ₂ O ₆ | 54 (62) | 137-139 (129-130) | 474 |
| 4e | | C ₁₇ H ₁₉ F ₆ NO ₇ | 40 (65) | 128-130 (128-129) | 463 |

(a) Melting points are uncorrected.

Table II

¹H Nmr [δ ppm, J (Hz) (a)]

| Compound No. | OH | H-4 | OCH ₂ CH ₃ | NH | H-3, H-5 | OCH ₂ CH ₃ |
|--------------|--------------|----------------------|----------------------------------|--------------|-------------------------|----------------------------------|
| 4b | 6.47 (2H, s) | 4.22 (1H, t, J = 12) | 3.81 (4H, q) | 3.49 (1H, s) | 3.42 (2H, d, J = 12) | 0.85 (6H, t) |
| 4c | 6.46 (2H, s) | 4.04 (1H, t, J = 12) | 3.82 (4H, q) | 3.46 (1H, s) | 3.35 (2H, d, J = 12) | 0.84 (6H, t) |
| 4d | 6.46 (2H, s) | 4.05 (1H, t, J = 12) | 3.79 (4H, q) | 3.44 (1H, s) | 3.37 (2H, d, J = 12) | 0.83 (6H, t) |
| 4e | 6.42 (2H, s) | 4.18 (1H, t, J = 12) | 3.96 (4H, q) | 3.45 (1H, s) | 3.19 (2H, d, J = 12) | 1.02 (6H, t) |

(a) In DMSO-d₆-TMS.

REFERENCES AND NOTES

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- (3) A. S. Dey and M. M. Joulie, *J. Org. Chem.*, **30**, 3237 (1965).

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