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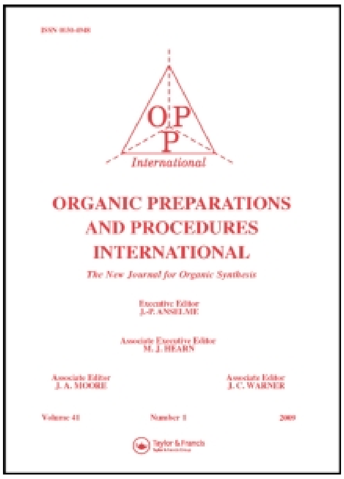

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REACTION OF PIVALOYLACETONITRILE WITH AROMATIC ALDEHYDES

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ORGANIC PREPARATIONS AND PROCEDURES INT., 25 (2), 327-368 (1993)

OPPI BRIEFS

REACTION OF PIVALOYLACETONITRILE WITH AROMATIC ALDEHYDES

Submitted by K. Popandova-Yambolieva* and T. Iossifova
(03/20/92)

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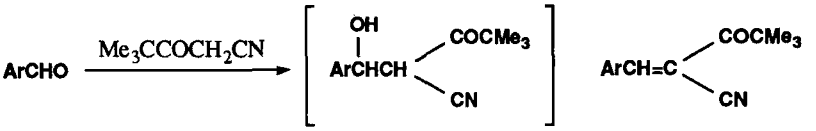
α,β-Unsaturated nitriles having an acyl group in the α-position are useful intermediates in the synthesis of different heterocycles.[1] It was of interest to study the possibility of preparing α,β-Unsaturated nitriles with a carbonyl group in the α-position joined with a bulky group such as a *tert*-butyl. This paper describes our preliminary results on the Knoevenagel condensation of pivaloylacetonitrile (4,4-dimethyl-3-oxopentanenitrile) with aromatic aldehydes.

The reaction was carried out in ethanol in the presence of a catalytic amount of aqueous sodium hydroxide. In all cases, the corresponding nitriles of 2-arylmethylene-4,4-dimethyl-3-oxopentanoic acid (**4a-j**) were obtained in moderate yields (Table 1). The structure of the new compounds was established on the basis of the IR and ^{1}H NMR spectra as well as by combustion analysis data. The reaction failed under the conditions of phase-transfer catalysis (50% aq NaOH, TEBA) in either acetonitrile or dimethylsulfoxide. In both cases, the starting aldehydes were recovered. Cyclization of **4a** under the action of sulfuric acid also proved unsuccessful.



3 4

a) Ar = C_6H_5
b) Ar = $4\text{-}ClC_6H_4$
c) Ar = $4\text{-}MeC_6H_4$
d) Ar = $4\text{-}MeOC_6H_4$
e) Ar = $4\text{-}Me_2NC_6H_4$
f) Ar = $4\text{-}NO_2C_6H_4$
g) Ar = $4\text{-}HOC_6H_4$
h) Ar = $2\text{-}ClC_6H_4$
i) Ar = 2-Naphthyl
j) Ar = 2- Furyl

The conformational study on some β-phenyl-α,β-unasaturated ketones[2] shows a difference between the chemical shifts of the olefinic proton an $CDCl_3$ and C_6D_6. Applying this method for **4a** ($\delta_{CDCl_3} - \delta_{C_6D_6} = 0.27$ ppm), one would be able to assign the stereochemistry as the *s-trans*-(E) compound as depicted below.

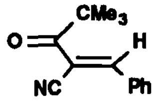
TABLE 1. Yields, mps and Elemental Analyses of Compounds 4

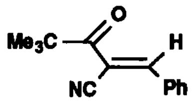
Cmpd	Yield (%)	mp. (°C)	Elemental Analyses Calcd. (Found) C	H	N
4a	60	66-68	78.84 (79.14)	7.09 (7.27)	6.57 (6.21)
4b	58	88-89	67.88 (67.77)	5.66 (5.39)	5.68 (5.51)
4c	70	65-67	79.26 (79.40)	7.54 (7.45)	6.16 (5.91)
4d	60	80-82	74.05 (74.23)	7.04 (6.82)	5.76 (5.65)
4e	41	122-124	74.96 (74.97)	7.86 (7.98)	10.93 (10.66)
4f	79	107-109	65.10 (65.40)	5.46 (5.76)	10.85 (10.63)
4g	57	175-177	73.34 (73.04)	6.59 (6.48)	6.11 (6.08)
4h	42	oil	67.88 (68.07)	5.66 (5.43)	5.68 (5.40)
4i	52	83-85	82.10 (82.39)	6.51 (6.80)	5.32 (5.31)
4j	46	57-58	70.91 (71.09)	6.45 (6.18)	6.89 (6.66)

TABLE 2. IR and ^{1}H NMR Spectra of Compounds 4

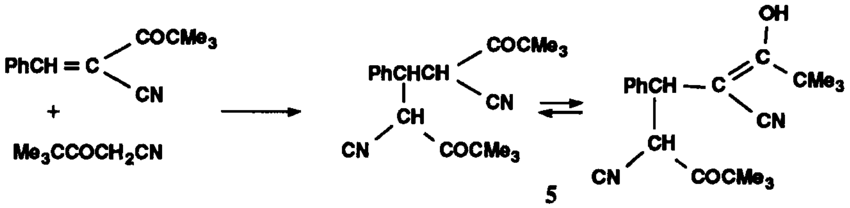
Cmpd	IR (nujol) (cm^{-1})	^{1}HNMR (δ)
4a	1700, 2220	1.40 (s, 9), 7.50 (m, 3), 7.98 (t, 2) 8.23 (s, 1)[a]
4b	1700, 2230	1.40 (s, 9), 7.43 (d, 2), 7.92 (d, 2), 8.15 (s, 1)
4c	1690, 2210	1.38 (s, 9), 2.48 (s, 3), 7.19 (d, 2) 7.gO (d, 2), 8.20 (s, 1)
4d	1680, 2205	1.39 (s, 9), 3.91 (s, 3), 7.01 (d, 2) 8.04 (d, 2), 8.23 (s, 1)
4e	1675, 2220	1.36 (s, 9), 3.13 (s, 6), 6.70 (d, 2), 7.98 (d, 2), 8.18 (s, 1)
4f	1705, 2205	1.39 (s, 9), 7.85 (d, 2), 8.25 (d, 2), 8.05 (s , 1)
4g	1685, 2205	1.86 (s, 9), 6.56 (br s, 1, OH),[b] 6.86 (d, 2), 7.85 (d, 2), 8.09 (s, 1)
4h	1690, 2220	1.89 (s, 9), 7.18-8.15 (m, 4), 8.47 (s, 1)
4i	1695, 2220	1.40 (s, 9), 7.28-8.05 (m, 7), 8.15 (s, 1)
4j	1690, 2220	1.35 (s, 9), 6.51 (s, 1, β-furyl), 7.29 (d, 1), 7.55 (s, 1), 7.89 (s, 1)

a) ^{1}H-NMR (C_6D_6): δ 1.20 (s, 9), 6.85 (m, 3), 7.55 (t, 2), 7.95 (s, 1); b) D_2O exchange.


s-*trans*-(E)


s-*cis*-(E)

In order to assess the possibility of isolating intermediate **3a**, the reaction was performed at low temperature (0-3°); instead, diketone **5**, a product of Michael addition of pivaloylacetonitrile to **4a** was isolated. The IR spectrum ($CHCl_3$) suggested that **5** exists as an equilibrium mixture of two compounds. The *enolic* form is stabilized by a cyano group, a result which is in a good agreement with the known behavior of such compounds.[1a] Diketone **5** was characterized by elemental analysis, IR and ^1H NMR spectra. Attempts to purify it by recrystallization lead to **4a** as the main product, resulting from a *retro*-Michael reaction.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Pharmacological activity might be expected on the basis of that reported for compounds of similar structure.[3]

EXPERIMENTAL SECTION

Melting points were determined on a Kofler micro hot stage "Böoecius". IR spectra were obtained on a Specord-71. ^1H NMR s pectra were taken on a 80 MHz TESLA BS 487 instrument, using TMS as internal standard. All starting reagents are commercial products.

General Procedure.- Aqueous sodium hydroxide (1N, 1 mL) was added to a solution of pivaloylacetonitrile (1.25 g, 10 mmol) and the corresponding aldehyde (10 mmol) in ethanol (10 mL). The mixture was refiuxed for 10 min (only 2 min f or **4b** and **4e**). After 1 hr at room temperature, water (100 mL) was added and the precipitate was collected, washed with water until neutral and recrytallized from methanol (Tables 1 and 2).

Preparation of 2,2,8,8-Tetramethyl-5-phenyl-4,6-dicyano-3,7-nonadione (5).- Aqueous sodium hydroxide (1 M, 0.5 mL) was added to a solution of benzaldehyde (0.53 g, 5 mmol) and pivaloylacetonitrile (0.63 g, 5 mmol) in 5 mL ethanol cooled to 0° (ice-water bath). The mixture was stirred for 10 min at 0-3° and 50 g of crushed ice was added. The precipitate was collected, washed with water and air-dried., mp. 89-95°. The crude crystals were washed with methanol at room temperatu re and dried to yield 0.50 g (60%), mp. 93-95°. IR($CHCl_3$): 1605, 1720 (C=O), 2210 (C≡N), 2240 (unconjugated C≡N), 3590 (OH) cm^{-1}. ^{1}HNMR (CDCl$_3$): δ 0.94 and 1.15 (2s, 18H); 1.55 (d, 1H, J = 8 Hz); 4.24 (d, 1H, J = 8 Hz); 4.30 (s, 1H, D_2O exchange); 6.98-7.30 (m, 5H).

Anal. Calcd. for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74 ; N, 8.28. Found: C, 74.77; H, 7.46; N, 8.02

REFERENCES

1. a) J. L. Soto, C. Aparicio, C. Seoane and J. Vales, *Heterocycles*, **20**, 2393 (1983); b) S. Kambe and K. Saito, *Synthesis*, 839 (**1980**); c) V. O. Aran and J. L. Soto, *ibid.*, 513 (**1982**); d) H. N. Elnagdi, N. M. Abed, M. H. Elmoghayar and D. H. Fleta, *Indian J. Chem.*, **14B**, 422 (1976).

2. P. Baas and H. Cerfontain, *Tetrahedron*, **33**, 1509 (1977).

3. H. L. Holmes and P. J. Currie, *Can. J. Chem.*, **47**, 4076 (1969).

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A CONVENIENT SYNTHESIS OF (±)-10-METHYL-2-TRIDECANONE, THE PHEROMONE OF SOUTHERN CORN ROOTWORM

Submitted by (10/01/92)

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The pheromone secreted by the females of southern corn rootworm *Diabrotica undecimpunctata* has been identified[1] as (R)-10-methyltridecan-2-one (7). Effective control and eradication of this harmful pest *via* an integrated pest management program necessitated its pheromone be available in sufficient amount. In view of the non-detrimental effect exhibited[2] by its antipode, preparation and use of the pheromone in racemic form seemed to be economically appealing. We have formulated a simple strategy for the synthesis of (±) **7** utilizing the terminal bifunctionality of 10-undecenoic acid (1). This readily accessible acid (1) was used by us earlier for the synthesis of prostanoid synthons[3] and other bioactive compounds.[4,5] To the best of our knowledge this constitutes the first report of the synthesis of racemic 7, although chiral syntheses of 7 have been reported.[6-8]

The methyl ester of **1** was converted[3] to the ketoester **2** by *in situ* oxidation of its mercurated intermediate. Wittig olefination of **2** with *n*-propyltriphenylphosphonium bromide followed by hydrogenation of the double bond of the resultant methyl (10-methyl)-10-tridecenoate gave an excellent yield of ester **3** which on subsequent reduction gave the alcohol **4**. After tosylation, the resultant tosylate **5** was subjected to base-catalyzed elimination to furnish **6** in 90% yield. Surprisingly, this simple