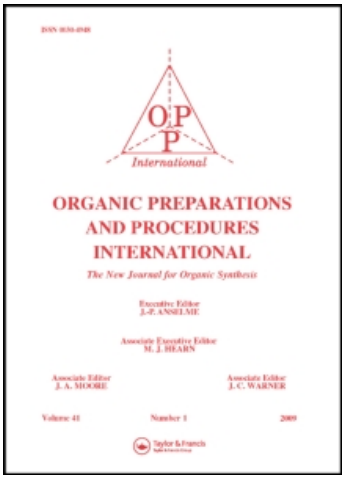

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TRANSFORMATION OF SOME β-TETRALONES TO 1,3-DIFORMYL-2-CHLORONAPTHALENES

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(R)-(+)-2-Methylpiperazine (**4a**).- The above procedure was repeated using (R)-(+)-3-methyl-1-(phenylmethyl)piperazine to give **4a** in 85.5%, mp. 81-84°, $[\alpha]_D^{23}$ = +4.9° (c = 1.0, 2N HCl).
Anal. Calcd for $C_5H_{12}N_2 \cdot 0.14CH_3OH$: C, 58.99; H, 12.10; N, 26.77
Found: C, 58.71; H, 11.98; N, 26.82

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TRANSFORMATION OF SOME β-TETRALONES TO 1,3-DIFORMYL-2-CHLORONAPTHALENES

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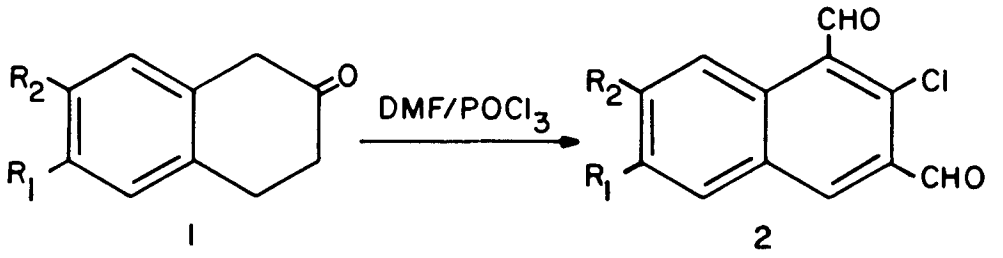
The Vilsmeier reagent is capable of formylating activated aromatic rings,[1] converting aryl benzyl ketones into β-chlorovinyl aldehydes[2] and transforming aryl ketones to aryl dichloroindenes.[2] We now report the formylation and aromatization of a series of β-tetralones under mild conditions by dimethylformamide (DMF) and phosphorous oxychloride ($POCl_3$).



1 2

a) $R_1 = R_2 = H$ b) $R_1 = R_2 = OCH_3$

We found that β-tetralones are converted to their corresponding diformyl naphthalenoid derivatives with DMF-$POCl_3$. Katritzky et al.[3] reported the diformyl aromatization of a series of 2-cyclohexen-1-ones under Vilsmeier reaction conditions and offered a plausible mechanism for the diformyl benzenoid derivatives formed. Paquette[4] reported monoformylation without aromatization with β-tetralone under Vilsmeier conditions. Both the molar ratio of Vilsmeier reagent to starting ketone and the reaction time were greater in our reaction procedure than in the preceding examples. This may serve as a rationale for the difference in the products obtained. α-Tetralone and 6-methoxy-1-tetralone yield the corresponding monoformyl derivatives (1-chloro-3,4-dihydro-2-naphthaldehyde and 6-methoxyl-1-chloro-3,4-dihydro-2-naphthaldehyde) without aromatization

under the reaction conditions utilized in this study.

The NMR spectra of 2a and 2b each contained two sharp one proton resonances below 10 ppm, assigned as aldehydic functions (2a: δ 10.69 and 10.99, 2b: δ 10.64 and 10.98). The spectrum of compound 2a was composed of five additional aromatic resonances: a singlet, two doublets and two doublets of doublets with additional fine structure from meta and para couplings. The singlet was assigned to the only unsubstituted carbon of the newly formed fused aromatic ring. Homonuclear correlation spectra (COSY) contained cross peaks for the expected interactions, including a weak interaction between the aromatic proton singlet and one of the doublets. This was attributed to a peri-coupling found in naphthalene systems. The spectrum of compound 2b was composed completely of singlet resonances. In addition to the two formyl resonances mentioned earlier, the coupled aromatic system of 2a was replaced by three one proton singlets in compound 2b. The aliphatic region contained two singlets with integrated intensities of three protons in each peak. These resonances were assigned to the methoxy methyls (δ 4.07 and 4.01).

EXPERIMENTAL SECTION

Mps. were taken on a MelTemp apparatus and are uncorrected. IR spectra were recorded as chloroform solutions on a Perkin-Elmer 1300 spectrophotometer. ^{1}H NMR spectra were obtained on a standard Varian XL 200 spectrometer. Microanalyses were carried out by Desert Analytics, Tucson, Arizona.

1,3-Diformyl-2-chloronaphthalene (2a).- β-Tetralone (2.0 g, 0.0137 mole) was added to an ice-cooled solution of DMF (15 mL)-$POCl_3$ (6 mL) and heated on a water bath for 5 min. The reaction mixture was stirred overnight at room temperature. The dark brown solution was added to ice water (200 mL) and the suspension was stirred overnight. The crude product was collected and recrystallized from ethanol-water to afford 1.6 g (54%) of yellow crystals, mp. 124-125°. IR ($CHCl_3$): 1696, 1683 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.65 (dd, 1H, J = 8.2, 8.7, 2.1Hz), 7.81 (dd, 1H, J = 8.8, 8.7 1.9 Hz), 8.01 (m, 1H, J = 8.2, 1.9, 0.9 Hz), 8.65 (s, 1H), 9.05 (m, 1H, J = 8.8, 2.1, 0.9 Hz), 10.69 (s, 1H), 10.99 (s, 1H): mass spectrum: 220, 218 M$^+$, base peak).

Anal. Calcd for $C_{12}H_7ClO_2$: C, 65.92; H, 3.23; Cl, 16.22. Found: C, 65.94; H, 3.11; Cl, 16.04

6,7-Dimethoxy-1,3-diformyl-1-2-chloronaphthalene (2b).- $POCl_3$ (6 mL) was added over a period of 20 min. to an ice-cooled solution of DMF (15 mL) in tetrahydrofuran (20 mL). 6,7-Dimethoxy–β-tetralone (2 g, 0.0097 mole) was added to the cool solution and the mixture was stirred overnight at room temperature. The dark brown solution was poured into ice water (200 mL) and stirred overnight. The crude product was collected and recrystallized from ethanol-water to yield 0.8 g (30%) of white crystals, mp. 208-209°; IR ($CHCl_3$): 1686, 1673 cm^{-1}; ^{1}H NMR: δ 4.01 (s, 3H), 4.07 (s, 3H), 8.47 (s, 1H), 8.68 (s, 1H), 10.64 (s, 1H), 10.98 (s, 1H); mass spectrum: 280, 278 (M$^+$, base peak).

Anal. Calcd for $C_{14}H_{11}ClO_4$: C, 60.33; H, 3.98; Cl, 12.72

Found: C, 60.29; H, 3.92; Cl, 12.65

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A CONVENIENT PREPARATION OF ETHYL 3,3-DIMETHYL-3H-INDOLE-2-CARBOXYLATE

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We required access to 2-alkoxycarbonyl-substituted 3H-indoles as dipole precursors for an investigation into the 1,3-dipolar cycloadditions of 3H-indolium-N-methylides.[1] However, the literature methods[2] for the preparation of ethyl 3,3-dimethyl-3H-indole-2-carboxylate (1) which center around the Japp-Klingmann modification of the Fischer indole synthesis[3] proved to be highly unsatisfactory. We now describe a convenient and high yielding route to 1 utilizing cheap, readily available reagents.

Our retrosynthetic analysis of 1 was based on a Fischer indole cyclization of hydrazone 4 derived from α-ketoester 3. The numerous routes to α-ketoesters[4] are usually multi-step procedures. A recent method reported by Singh[5] proved to be very convenient for the preparation of α-ketoester 3, by addition of a solution of isopropylmagnesium chloride to diethyl oxalate 2 in ether at -70° to afford the desired α-ketoester 3 cleanly and in excellent yield. Formation of hydrazone 4 was achieved in high yield by heating a solution of α-ketoester 3 and phenylhydrazine in benzene at reflux over 4Å molecular sieves. Fischer cyclization of the hydrazone 4 was accomplished by heat-