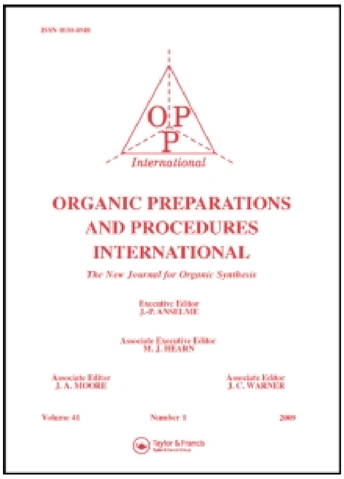

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NEW PREPARATION OF N-METHYLIMIDAZOLE-4,5-DICARBOXALDEHYDES AND SOME OF ITS REACTIONS

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by evaporation of the mother liquor.

REFERENCES

1. M. J. Hearn and J. E. Grimwade, Org. Prep. Proced. Int., 12, 249 (1980).
2. T. Curtius and G. Dedichen, J. prakt. Chem., 50, 241 (1894).
3. N. D. Cheronis, Mikrochim. Acta, 925 (1956).
4. A. F. Hegarty and F. L. Scott, J. Org. Chem., 33, 753 (1968).
5. A. F. Hegarty, M. Cashman and F. L. Scott, J. Chem. Soc., Perkin Trans. 2, 1381 (1972). The compounds were prepared by conversion of an acid to the corresponding acyl halide, using a large excess of thionyl chloride, followed by reaction with the hydrazine.
6. R. H. Clark and E. C. Wagner, J. Org. Chem., 9, 55 (1944); see also G. M. Coppola, Synthesis, 505 (1980).
7. It has previously been reported that β-acyl groups have little effect on the UV spectra of phenylhydrazines, although α-acylation caused radical changes [N. I. Latosh and Z. V. Pushkareva, Trudy Ural. Politekh. Inst. im.S.M. Kirova, 42 (1959); Chem. Abstr., 55, 8038 (1961)].

NEW PREPARATION OF N-METHYLIMIDAZOLE-4,5-DICARBOXALDEHYDES AND SOME OF ITS REACTIONS

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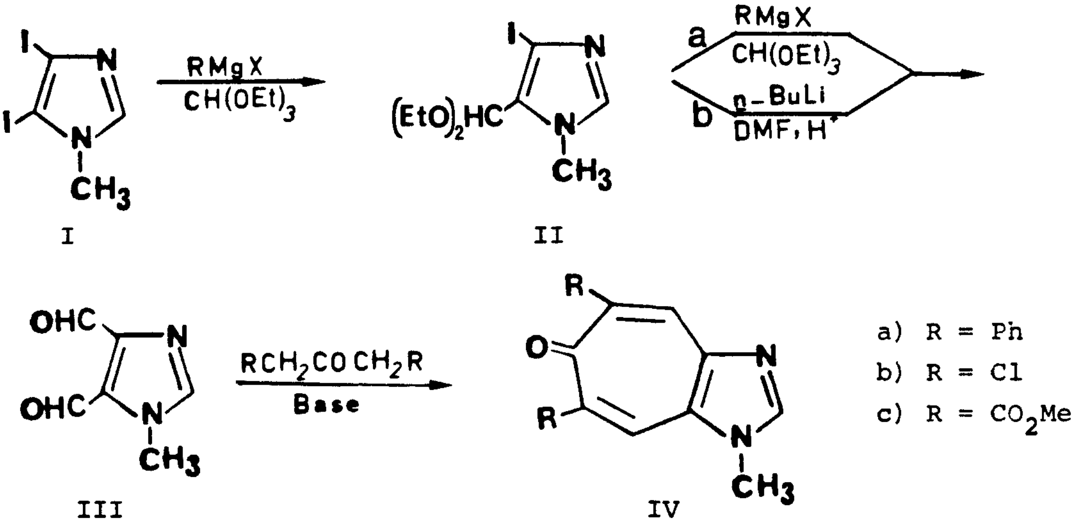
In the context of our interest in imidazoles,[1] we now report a new method for the preparation of N-methylimidazole-4,5-dicarboxaldehyde (III) from 4,5-diiodo-N-methylimidazole (I) in very good yield. This compound was previously prepared by Schubert et al.,[2] by a lengthy method starting from N-substituted ethyl glycinate hydrochloride. Compound III was obtained from the action of either a Grignard reagent and triethyl orthoformate (*method a*) or n-butyllithium and DMF (*method b*) on II, prepared by the reaction of I with triethyl orthoformate and a Grignard reagent. Condensation of III with ketones gave the corresponding N-methylimidazo[4,5-d]cycloheptatrienones (IV).



a) $R = Ph$
b) $R = Cl$
c) $R = CO_2Me$

EXPERIMENTAL SECTION

The ^1H NMR spectra were recorded on a Varian A-60 in DMSO d-6 with TMS as internal reference. IR spectra were recorded on a Beckman IR-4 using KBr wafer technique. Mass spectra were recorded on a Finnigan 3000 at 70 eV with direct inlet and a source of temperature of 90°. All mps were taken on a Thomas-Hoover apparatus and are uncorrected.

Compound I was prepared according to the method cited in literature.[3] The usual work-up procedure consisted of dilution with water, extraction with methylene chloride, drying over magnesium sulphate, evaporation of solvent under reduced pressure and purification by column chromatography on silica G 60 (Merck)

5-(Diethoxymethyl)-4-iodo-N-methylimidazole(II).- To a solution of ethyl magnesium bromide (0.12 mole) 33.4 g (0.1 mole) in 200 ml dry ether of I was slowly added at room temperature. The reaction mixture was refluxed for 2 hrs, 200 ml dry benzene was added and the ether was evaporated in vacuo. The ethyl orthoformate (18 g, 0.12 mole) was then slowly added and the reaction mixture was refluxed for 4 hrs. The reaction mixture was hydrolyzed at 0^o with 10% NH_4Cl solution and worked up as usual. The product was purified by chromatography using ether-hexane (1:2) as eluent, and crystallized from ether-hexane (1:1) to give 21 g (68%) of II, mp. 66^o.

NMR (δ ppm): 7.62 (ArH, s, 1H), 5.32 ($CH(OEt)_2$, s, 1H), 3.44 (CH_2, q, 4H), 1.18 (CH_3, t, 6H), 3.74 (NCH_3, s, 3H).

Anal. Calcd. for $C_{19}H_{15}IN_2O_2$: C, 34.48; H, 4.48; I, 40.96; N, 9.03.

Found: C, 34.78; H, 4.80; I, 40.78; N, 9.23.

N-Methylimidazole-4,5-dicarboxaldehyde (III)

Method a.- The action of ethylmagnesium bromide (0.12 mole) and ethyl orthoformate (0.12 mole) on 31 g (0.1 mole) of II as described above, gave 4,5-(diethoxymethyl)-N-methylimidazole as a yellow liquid which was purified by distillation to give 18 g (58%) of liquid, bp. $78\text{-}80^o$/2mm.

Anal. Calcd. for $C_{14}H_{26}N_2O_4$: C, 58.74; H, 9.09; N, 9.79.

Found: C, 58.96; H, 9.22; N, 9.92.

To a solution of 10 g of the above prepared compound in 100 ml dry methylene chloride, 20 ml of 6N HCl was slowly added. The reaction mixture was refluxed for 2 hrs, and then worked up as usual. The product was purified by chromatography using ether-hexane (2:1) as eluent, and crystallized from benzene-hexane (1:1) to give 3.1 g (58%) of III, mp. 115°, lit.[2] mp. 88°.

Method b.- To (0.1 mole) of n-BuLi in dry ether at -30° under a nitrogen atmosphere, was added a solution of 31 g (0.1 mole) of II in 200 ml dry ether. The organolithium intermediate was treated with 9 g (0.12 mole) of DMF in 20 ml dry ether, and the temperature was kept at -30° for 2 hrs. The reaction mixture was hydrolyzed at 0° and worked up as usual. The product obtained was treated with HCl as described above, to give after purification and crystallization the desired III in 47% yield, mp. 115°, mixed mp. with the product prepared by method a shows no depression.

IR (cm^{-1}): 1695 and 1688 (C-O); NMR (δ ppm): 7.75 (ArH, s, 1H), 9.85 and 9.65 (CHO, d, 2H, J = 0.8 Hz), 3.88 (NCH_3, s, 3H).

5,7-Diphenyl-N-methylimidazo[4,5-d]cycloheptatrien-6-one (IVa).- A mixture of 1.38 g (0.01 mole) of III and 2.2 g (0.011 mole) of 1,3-diphenylacetone in 30 ml ethanol was added very slowly to a solution of 10 ml 10% NaOH. The reaction mixture was stirred for 12 hrs at room temperature, and then refluxed for 1 hr. The reaction mixture was worked up as usual. The product was purified by chromatography using ether-hexane (3:1) as eluent, and crystallized from benzene-hexane (2:1) to give 2.18 g (70%) of IVa, mp. 168°.

Anal. Calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97.
Found: C, 80.59; H, 5.22; N, 8.89.

5,7-Dichloro-N-methylimidazo 4,5-d cycloheptatrien-6-one (IVb).- A mixture of (0.01 mole) of III and (0.012 mole) of 1,3-dichloroacetone was added to 10 ml 10% NaOH solution as mentioned above. The product was purified by chromatography using methylene chloride-hexane (2:1) as eluent and crystallized from benzene-hexane (3:1) to give 1.26 g (55%), of IVb, mp. 227°.

<u>Anal</u>. Calcd. for $C_9H_6Cl_2N_2O$: C, 47.16; H, 2.62; Cl, 31.00; N, 12.27.

Found: C, 47.32; H, 2.84; Cl, 31.42; N, 12.54.

TABLE 1. Spectral Data of 5,7-Diphenyl-, 5,7-dichloro-, and 5,7-dicarbomethoxy-N-methylimidazole[4,5-d]cycloheptatrien-6-one (IV).

Cmpd	IR (cm^{-1})	'H nmr (δ ppm)	Mass Spectrum
IVa	1592 1578 (C=O)	7.74 (H_2, s, 1H), 7.96 (H_4, s, 1H), 7.80 (H_8, s, 1H), 7.47 (Ph, m, 10H), 3.78 (NCH_3, s, 3H)	m/e = 312 (100%); m/e = 285 $[M^{+\cdot}-HCN^{\cdot}]$ (18.8%); m/e = 270 $[M^{+\cdot}-CHNCH_3^{\cdot}]$(11.6%).
IVb	1612 1586 (C=O)	7.75 (H_2, s, 1H), 7.94 (H_4, s, 1H), 7.82 (H_8, s, 1H), 3.80 (NCH_3, s, 3H)	m/e = 229 (100%); m/e = 202 $[M^{+\cdot}-HCN^{\cdot}]$ (17.4%).
IVc	1618 1592 (C=O)	7.74 (H_2, s, 1H), 8.08 (H_4, s, 1H), 7.98 (H_8, s, 1H), 1.40 (Me, s, 6H), 3.82 (NCH_3, s, 3H)	

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a) s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet.

<u>5,7-Dimethylcarboxylate-N-methylimidazo[4,5-d]cycloheptatrien-6-one (IVc)</u>.- A mixture of 1.38 g (0.01 mole) of III and 2.1 g (0.012 mole) of dimethylacetone-1,3-dicarboxylate and a few drops of piperidine in 100 ml dry benzene was refluxed for 3 hrs. The reaction mixture was worked up as usual. The product was purified by chromatography using methylene chloride-hexane (2:1) as eluent and crystallized from benzene hexane (3:1) to give 1.7 g (62%) of IVc, mp. 212-213°.

<u>Anal</u>. Calcd. for $C_{13}H_{12}N_2O_5$: C, 56.52; H, 4.34; N, 10.14.
Found: C, 56.68; H, 4.48; N, 10.32.

REFERENCES

1. M. El Borai, A. H. Moustafa, M. Anwar and A. G. Ghattas, Croat. Chem. Acta., 54, 211 (1981); Chem. Abstr. 95, 150541c, (1981).

2. H. Schubert and W. D. Rudorf, Z. Chem., 11, 175 (1971).

3. M. S. Shvartsberg, L. N. Bizhan, E. E. Zave and I. L. Kotylarevskii, Izv. Akad. Nauk, Ser. Khim., 472 (1972); Chem. Abstr. 77, 34422 (1972).

SYNTHESIS OF 7-HYDROXYBENZO[a]PYRENE

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7-Hydroxybenzo[a]pyrene (<u>3a</u>) is a metabolite of the potent carcinogen benzo[a]pyrene.[1] Synthesis of <u>3a</u> by dehydrogenation of 7-oxo-7,8,9,10-tetrahydrobenzo[a]pyrene (<u>1</u>) with sulfur[2] or palladium black[3] in yields of 30% and 62%, respec-