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Isotopic exchange of active methyl hydrogens. IV(1). Preparation of 1,3-di-d_3-methylnaphthalene, d_9-mesitylene and d_9-mesitylene derivatives from 2,4,6-tri-d_3-methylpyrylium perchlorate

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SUMMARY

Starting from the easily available 2,4,6-tri-d_3-methylpyrylium perchlorate, the following methyl-deuterated compounds were prepared : 1,3-dimethylnaphthalene III, nitromesitylene IV, mesidine V, mesitylenediazonium hydrogen sulphate VI, mesitylene VII, mesitol VIII and 1-mesityleneazo-2-naphthol IX. Their infrared spectra and deuterium analyses show that some dedeuteration occurs during the reaction of pyrylium salts.

A new naphthalene synthesis from benzylmagnesium chloride and 1,3-diketones is reported.

INTRODUCTION

By recrystallization from deuterium oxide, the readily accessible 2,4,6-trimethylpyrylium perchlorate (2) (I*a*) is converted (3) into 2,4,6-tri-d_3-methylpyrylium perchlorate (I) * which thus is easily available in large amounts.

Its easy purification, stability and ready conversion into various other aliphatic, aromatic or heterocyclic compounds (4,5) make this compound a suitable and convenient starting material for the preparation of many methyl-deuterated substances. One can thus take advantage of the presence of the pyrylium ring: on one hand by facilitating the carbon-bonded hydrogen exchange, and on the other hand by converting the deuterated salt into other deuteromethyl compounds which are unable to be deuterated by direct hydrogen exchange.

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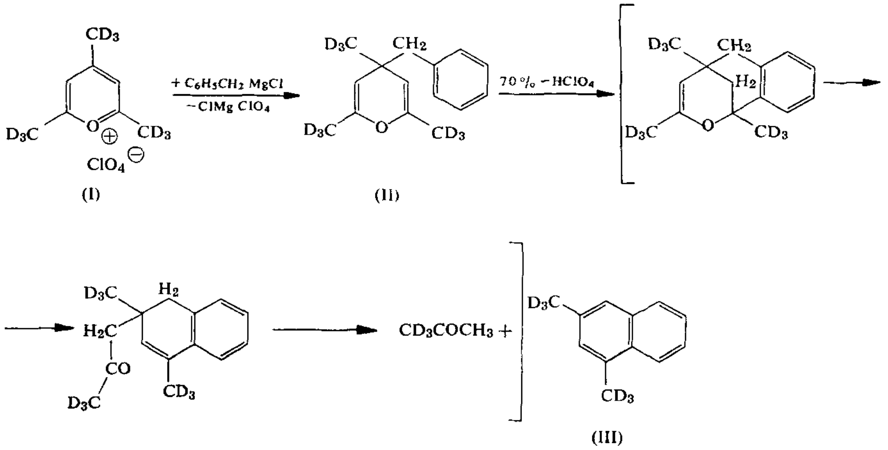
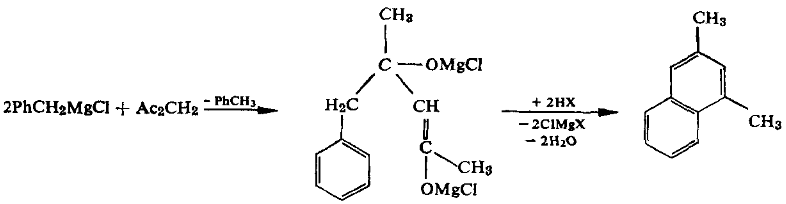
* As in the previous paper (1) the letter "a" following a roman numeral denotes the non-deuterated counterpart of the compound indicated by that numeral.

In continuation of previous studies,⁽¹⁾ the present paper reports the preparation of two aromatic hydrocarbons deuterated in the side-chain: 1,3-di-d_3-methylnaphthalene (III) and d_9-mesitylene (VII). The former was prepared from I and benzylmagnesium chloride, followed by treatment with 70% perchloric acid.⁽⁶⁾ The mechanism proposed by Dimroth is outlined in the following reaction sequence.



(I) (II) (III)

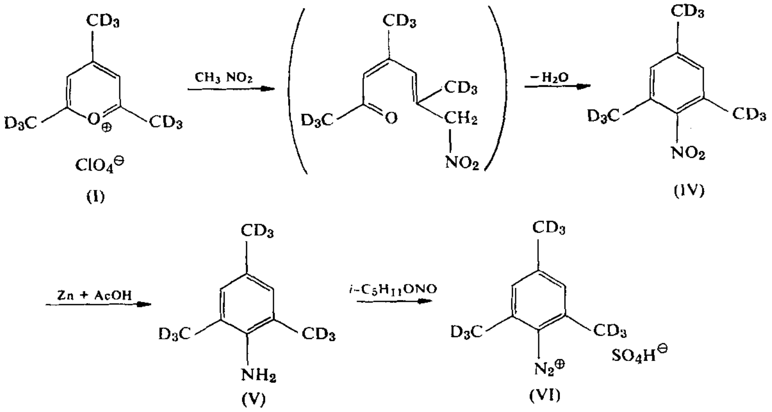
Taking into account the above reaction and the fact that acids convert mixtures of a methylketone and a 1,3-diketone into pyrylium salts,⁽⁷⁾ it appeared possible to devise a new naphthalene synthesis by reaction of 1,3-diketones with benzylmagnesium chloride. This synthesis was indeed successful and differs from the previous one by the absence of a ketonic splitting.



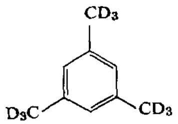
(III*a*)

This reaction is being extended to other 1,3-diketones and will be reported in detail in a forthcoming paper.

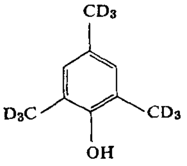
From pyrylium salts and nitromethane, after Dimroth and coworkers ⁽⁸,⁹⁾ aromatic nitroderivatives are formed, e.g. I*a* affords nitromesitylene ⁽⁸⁾ identical with the nitration product of mesitylene. (10,11) Analogously, I yields d_9-nitromesitylene IV whose reduction leads to d_9-mesidine V.



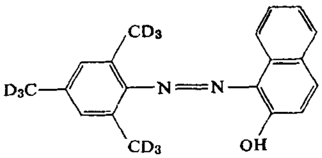
From this deuterated amine, by diazotization the relatively stable diazonium sulphate VI was obtained. This leads to d_9-mesitylene VII by reduction, to d_9-mesitol VIII by hydrolysis, and to deuterated azoderivatives, e.g. IX, by azoic coupling.



(VII)



(VIII)



(IX)

EXPERIMENTAL PART

2,4,6-Tri-d_3-methylpyrylium perchlorate (I). The dry * non-deuterated perchlorate (I*a*) (1 mole) is refluxed in 50 moles deuterium oxide for 45 minutes, cooled, filtered off, dried, and the procedure is repeated with a fresh portion of D_2O. The isotopic analysis and NMR spectrum indicate that deuteration of the side-chains is complete (with a small amount of ring-deuteration as well).

1,3-Di-d_3-methylnaphthalene (III). Perfectly dry (over P_2O_5 in vacuum) I (10 g, 35 mmoles) is suspended in 250 ml absolute ether. Into the stirred suspension, and in nitrogen atmosphere, a filtered solution was added of benzylmagnesium chloride prepared (12) from 2.4 g (100 matom-grams) magnesium turnings. After 5 hrs' stirring at room temp., the ethereal solution is filtered from the precipitate, washed with 1n hydrochloric acid and several times with water, and dried over calcium chloride. After evaporation of the ether, the brown oil affords II, b.p. 125-130°/12 mm, 6.5 g (70%). This 4H-pyran II was heated for 5 min with 70%-perchloric acid at 50°. After cooling and dilution with water the product was extracted with benzene, washed with water, dried over calcium chloride and distilled in vacuum, b.p. 120-123°/9 mm, affording 2.2 g III (50% yield). A final purification may be made by distillation over sodium.

1,3-Dimethylnaphtalene (III*a*) *from acetylacetone*. Into a solution of benzylmagnesium chloride, prepared from 9.6 g (0.4 gram-atoms) of magnesium turnings and 48 ml (52 g, 0.4 moles) benzyl chloride in 200 ml anhydrous ether, a solution of 20 ml (20 g, 0.2 moles) acetylacetone in 50 ml ether was introduced dropwise with stirring at reflux temperature. The magnesium salt which precipitated was filtered off, washed with absolute ether and hydrolysed with 500 g ice and 0.4 moles hydrochloric acid. The aqueous solution was extracted with ether and the ethereal extract was dried over sodium sulphate. After removal of the solvent on the water bath, the yellow liquid residue was heated for 10 min at 50° with 60 ml 70%-perchloric acid with occasional stirring, then poured into 300 ml cold water and extracted with petroleum ether. The ethereal extract dried over potassium carbonate was fractionated in vacuum, affording a fraction b.p. 107-110° at 3 mm (2.3 g, 7% yield). This fraction was redistilled over sodium and the infrared absorption spectrum was identical with that of 1,3-dimethylnaphthalene prepared after Dimroth. (6)

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* Contrary to the warnings expressed by the Editorial Board of Organic Syntheses, (2) the present authors have never experienced any hazard owing to the explosion of 2,4,6-trimethylpyrylium perchlorate, although it was handled and stored for ten years in amounts as high as 2 kg in dry condition. It is the authors' belief that 2,4,6-trisubstituted pyrylium salts can be handled without exaggerate precautions, unlike the unsubstituted pyrylium or tropylium perchlorates which, being "secondary carbonium perchlorates," require greater caution.

d_9-Nitromesitylene (IV). Perchlorate I (30 g, 130 mmoles) is dissolved in 100 ml boiling nitromethane and the hot solution is treated with a warm solution of 11 g NaOH in 300 ml ethanol. After 5 min standing (a longer time leads to dark-coloured solutions) the mixture is poured into 1 l water. After extraction with petroleum ether, the extract is washed with 20% NaOH, dried over sodium sulphate and concentrated in vacuum. The brown crystals m.p. 40-42°, (yield 18 g, 85%), of IV can be used without further purification for the next step. The purification is performed by pressing on a porous plate and recrystallization from dil. ethanol; the pure product has m.p. 43°. (lit. (10) m.p. 43-4°).

d_9-Mesidine (V). Crude IV (17 g, 100 mmoles) is dissolved in 200 ml ethanol and 32 g (0.5 gram-atoms) zinc powder are added. With vigorous stirring, 40 ml glacial acetic acid are added with external cooling (internal temperature 5-10 °C). The reaction may proceed violently, therefore the addition must be carried out cautiously; a run with the above amounts in which the acetic acid was added when the internal temperature was −10° led to an explosive temperature rise after the addition of 15 ml acetic acid. After 5 hrs' stirring at 5-10°, the mixture is allowed to reach room temperature and is poured into an excess of aqueous sodium hydroxide. The mixture is extracted with petroleum ether and the extract is dried over sodium sulphate. The product is fractionated on an efficient column yielding V, b.p. 90-92°/7 mm, yield 9.6 g (70%). For analysis the product was refractionated, b.p. 90°/7 mm. (13)

d_9-Mesityldiazonium hydrogen sulphate (VI). d_9-Mesidine V (7.3 g, 40 mmoles) was dissolved in 60 ml absolute ethanol containing 5 ml (9 g, 100 mmoles) conc. sulphuric acid; after cooling at 0°-5°, the solution was treated with 8 ml (6 g, 15% excess) isopentyl nitrite. After 15 min, 200 ml ether is added, and the precipitated diazonium salt VI is filtered off and washed with ether. Yield 12 g (95%), white crystals which can be stored in a dessicator for a few days.

d_9-Mesitylene (VII). The diazonium salt VI (9 g, 35 mmoles) dissolved in 50 ml ethanol is treated gradually with 5 g zinc powder. The mixture foams strongly. Then the solution is refluxed 30 min on the water bath. The decanted solution is poured into water and the solution is extracted with benzene. The precipitate is washed with benzene and the combined benzenic extracts dried over $CaCl_2$ are distilled at normal pressure on an efficient column. After adding 4 g diphenylmethane, the mesitylene is distilled at 80 mm, b.p. 90-95°, yield 1.2 g (25%). A final purification can be done by heating with sodium and vacuum distillation.

d_9-Mesitol (VIII). The diazonium salt VI (1.7 g, 7 mmoles) dissolved in 50 ml water is heated slowly until the nitrogen evolution ceases, then it is distilled until no more mesitol crystallizes in the distillate. The distillate affords on filtration white crystals of VIII, m.p. 70° (lit. (14) m.p. 68-69°) which require no

further purification. For analysis the product was sublimed at 70°/7 mm. Yield 0.5 g, 55%.

1-d_9-Mesityleneazo-2-naphthol (IX). 2-Naphthol (0.6 g, 4 mmoles) is dissolved in 10 ml dil. NaOH and is treated at 0° with a solution of 1 g (4 mmoles) VI in 10 ml water. The alkaline solution is acidified with acetic acid. The product IX is filtered off and washed with cold water, then dried in vacuum. After recrystallization from ethanol one obtains red needles of IX, m.p. 135°, in 85% yield (1.0 g). Lit. m.p. 134-5°. (15)

Infrared spectra were recorded by Elena Romas, with a Jena UR-10 double-beam spectrophotometer.

Isotopic analyses were performed by burning the sample, condensing the water, and analyzing it by means of the refractive index (16) with an immersion refractometer graduated with standard samples of D_2O of various concentrations. The water obtained from the combustion contains 30 ± 2% D_2O for 1,3-dimethyl-naphthalene, 62.5 ± 2% D_2O for mesitylene and 52.3 ± 2% D_2O for mesitol.

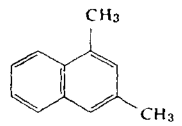
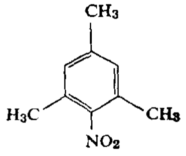
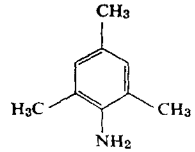
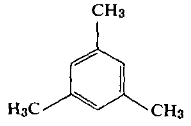
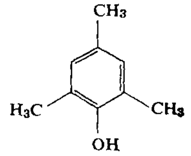
RESULTS AND DISCUSSION

The formation of deuterated compounds was evidenced by isotopic analysis for III, VII and VIII, and by infrared spectroscopy for III-IX.

The isotopic analysis indicates that during the above reactions partial dedeuteration takes place. Thus the deuterium content of 1,3-dimethylnaphthalene corresponds (the calculation was performed as outlined in ref. 17) to 60% III + 40% III*a*, while that of mesitylene corresponds to 83%VII + 17% VII*a*. Mesitol has a deuterium content leading to 70% VIII + 30% VIII*a*. The reactions which account for the dedeuteration must involve either the back exchange of the pyrylium salt (I-I*a*) or an acyclic ketonic intermediate product. In the synthesis of III, the dedeuteration can occur during the heating of II with aqueous perchloric acid, since with acids (HCl + ether) 4H-pyrans can be converted back into pyrylium salts. In the synthesis of mesitylene derivatives, the dedeuteration occurs probably during the reaction of I with nitromethane by isotopic exchange between the d_3-methyl groups of I and the ethanolic hydroxyl groups. Indeed, the IR spectrum of nitromesitylene IV evidences saturated ν C-H bands, which appear in all subsequent steps for V-IX. However, their low intensity as well as the absence or the low intensity of δ C-H bands (cf. Table 1) is in accord with the isotopic analysis and shows that the dedeuteration is not extensive. By employing $DClO_4$ in D_2O in the first, and C_2H_5OD in the second reaction, one could presumably avoid the dedeuteration.

The infrared bands presented in table 1 concern only the νCH, νCD, δCH_3 and δCD_3 ranges as in part III; (1) detailed assignments will be discussed in a forthcoming paper. The spectra described in table 1 are consistent with the results of isotopic analyses.

Table 1. Pertinent infrared absorption bands in the range 1000-1550 and 2000-3000 cm^{-1}

Compound / Assignments										
	H	D	H	D	H	D	H	D	H	D
$\delta_s CD_3$				1118 w		1202 w		1192 w		1180 s
$\delta_{as} CD_3$		1304 w		1258 w		1287 m		1285 w	1232 m	
$\delta_s CH_3$	1390 s 1424 s	1390 w 1410 s	1430 m		1388 m	1390 vw	1385 m	1386 vw	1386 m	
$\delta_{as} CH_3$	1456 vs	1454 w	1464 s 1488 s		1451 vs 1495 vs	1452 sh 1478 vs	1480 s		1453 m 1498 vs	1440 m 1480 s
νCD		2070 m 2115 m 2126 m 2143 m 2210 s 2230 s		2070 w 2115 w 2172 w 2220 w 2240 w		2063 s 2096 sh 2110 m 2140 m 2190 s 2225 s		2069 m 2110 m 2140 m 2155 m 2205 m 2230 m		2066 m 2110 m 2129 m 2150 w 2210 m 2230 m 2240 w
νCH sat	2735 w 2868 s 2922 vs 2950 vs 2980 vs	2864 vw 2928 m 2950 m	2740 w 2870 m 2954 m 2980 m	2875 w 2965 vw	2732 w 2860 vs 2920 vs 2970 s	2862 w 2920 m	2730 m 2860 s 2920 vs	2868 vw 2928 m	2730 m 2860 m 2920 s 2950 m 2972 m	2925 m 2960 w

1,3-Di-d_3-methylnaphthalene was prepared by Dizabo and Leitch (18) and its infrared spectra have been discussed. (19) No preparation of the other deuterated compounds has as yet been reported.

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