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MONO- AND BIS-ADDITION PRODUCTS OF BENZYLMAGNESIUM CHLORIDE TO ACETYLACETONE

A SYNTHESIS OF 1,3-DIMETHYLNAPHTHALENE

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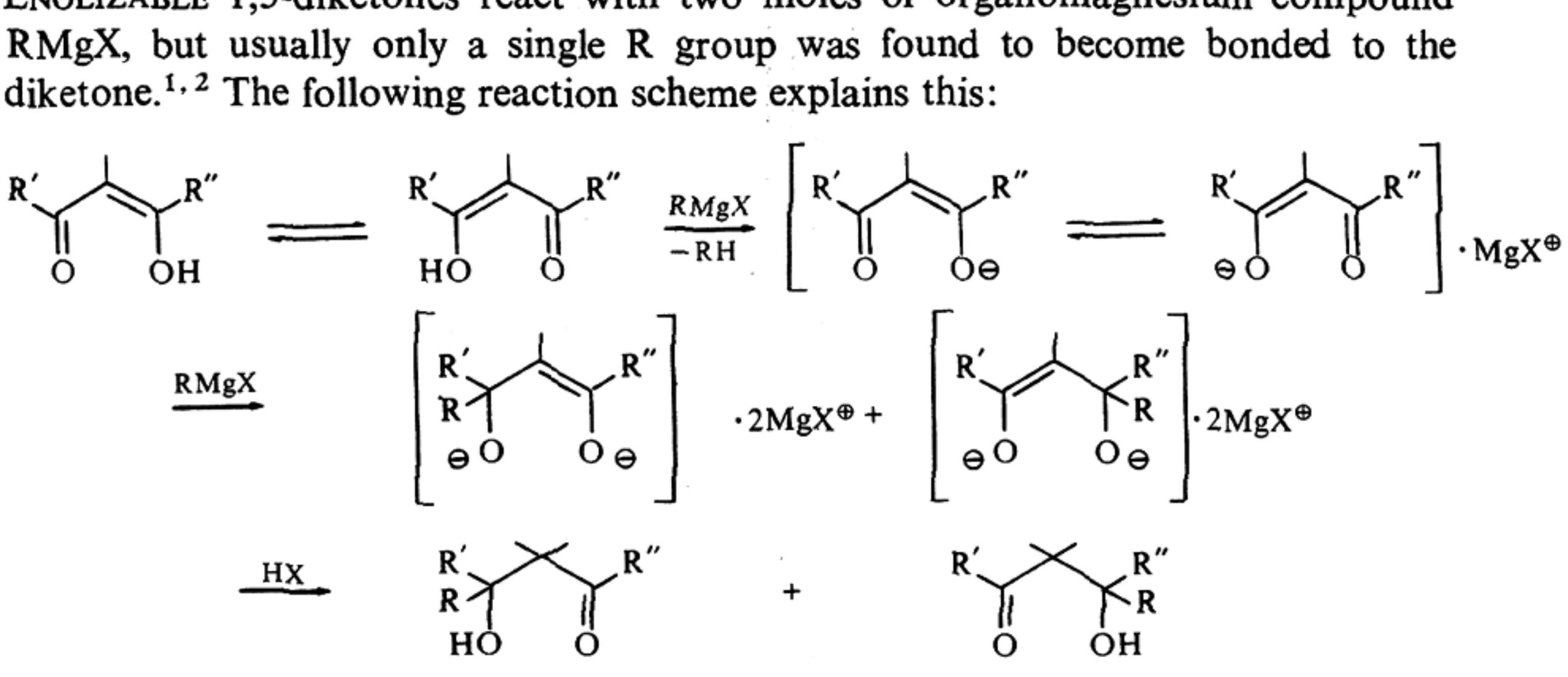
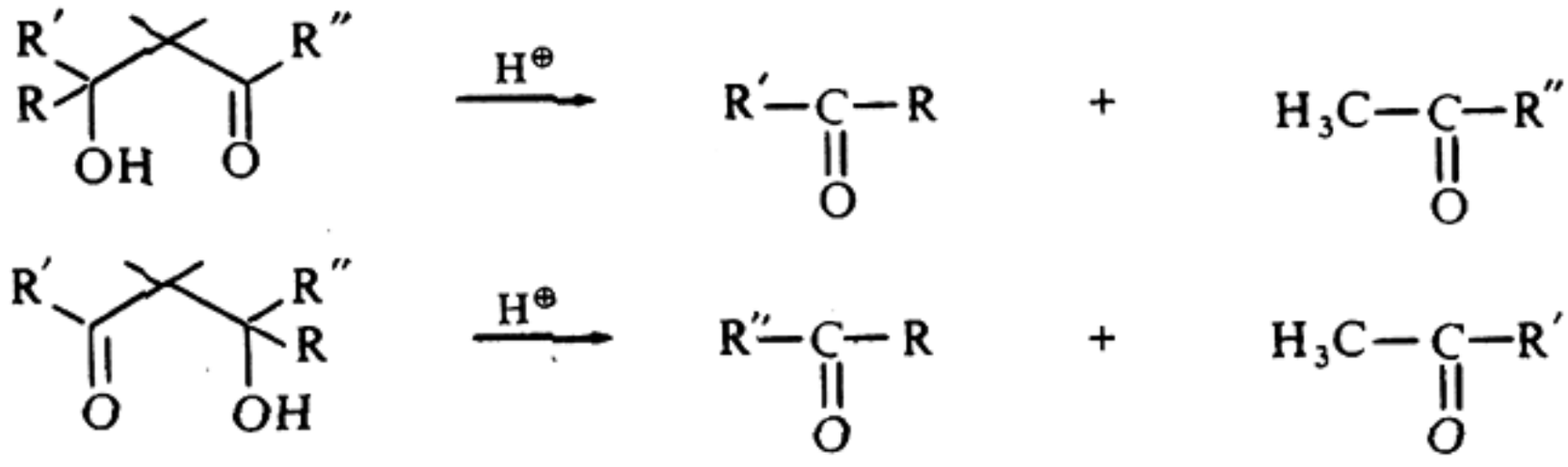
Abstract—The addition of excess benzylmagnesium chloride to acetylacetone affords a mixture of mono- and bis-addition products, whose relative yields suggest that the mono-addition is a reaction of the enol tautomer and the bis-addition a reaction of the diketo-tautomer. 4-Benzyl-4-hydroxypentan-2-one (IV), the primary mono-addition product, is easily dehydrated to *5-phenyl-4-methyl-3-pentene-2-one (XI)*, which was isolated and characterized. This dehydration is a delicate operation; in some runs, only the splitting product, phenylacetone (IX) could be isolated. Acid treatment of the monoaddition products IV or XI causes dehydrative cyclisation to 1,3-dimethylnaphthalene. UV, IR and NMR spectra are discussed. The central methylene group in 2,4-dibenzylpentane-2,4-diol (VII), the bis-addition product, although of type CH_2X_2 (X = HOCMe—CH_2Ph), gives an AB quadruplet in the NMR spectrum, like the benzyl protons; hence the diol is the *meso* form.

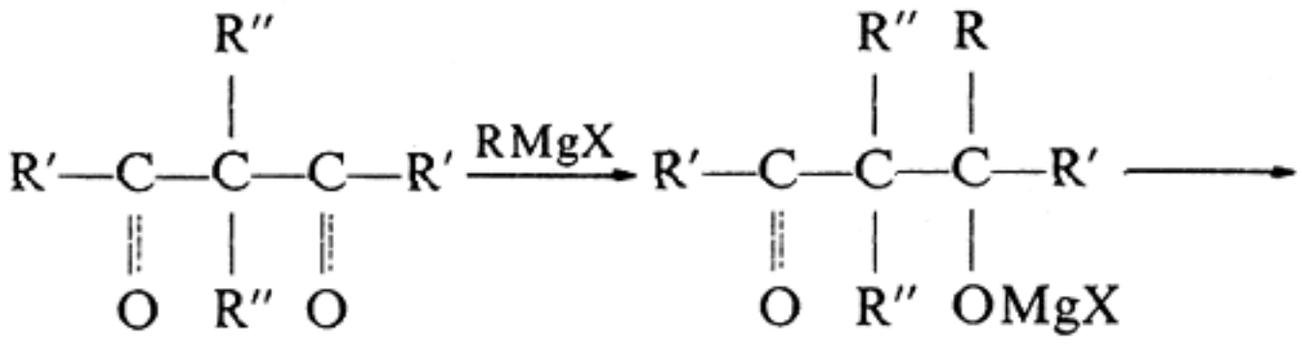
ENOLIZABLE 1,3-diketones react with two moles of organomagnesium compound RMgX, but usually only a single R group was found to become bonded to the diketone.[1,2] The following reaction scheme explains this:

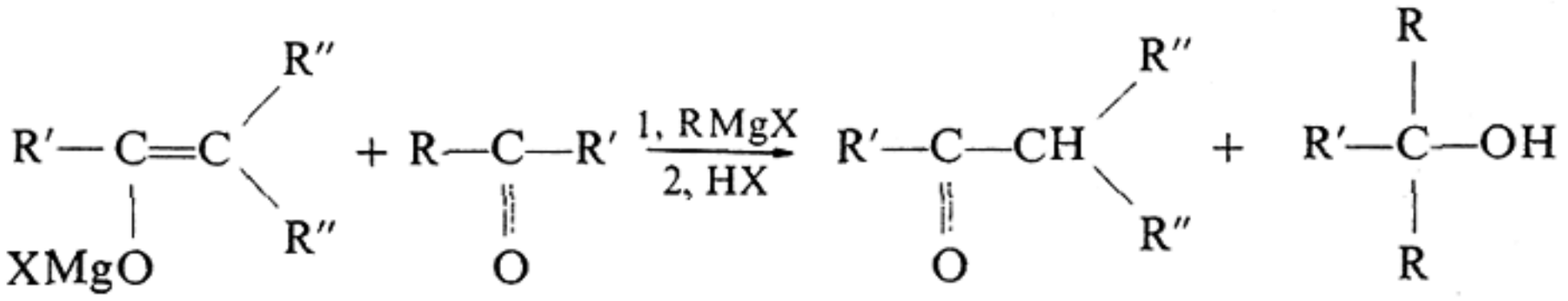


The final acid hydrolysis is a difficult operation; in many cases only the acid splitting products of the carbinols could be isolated:



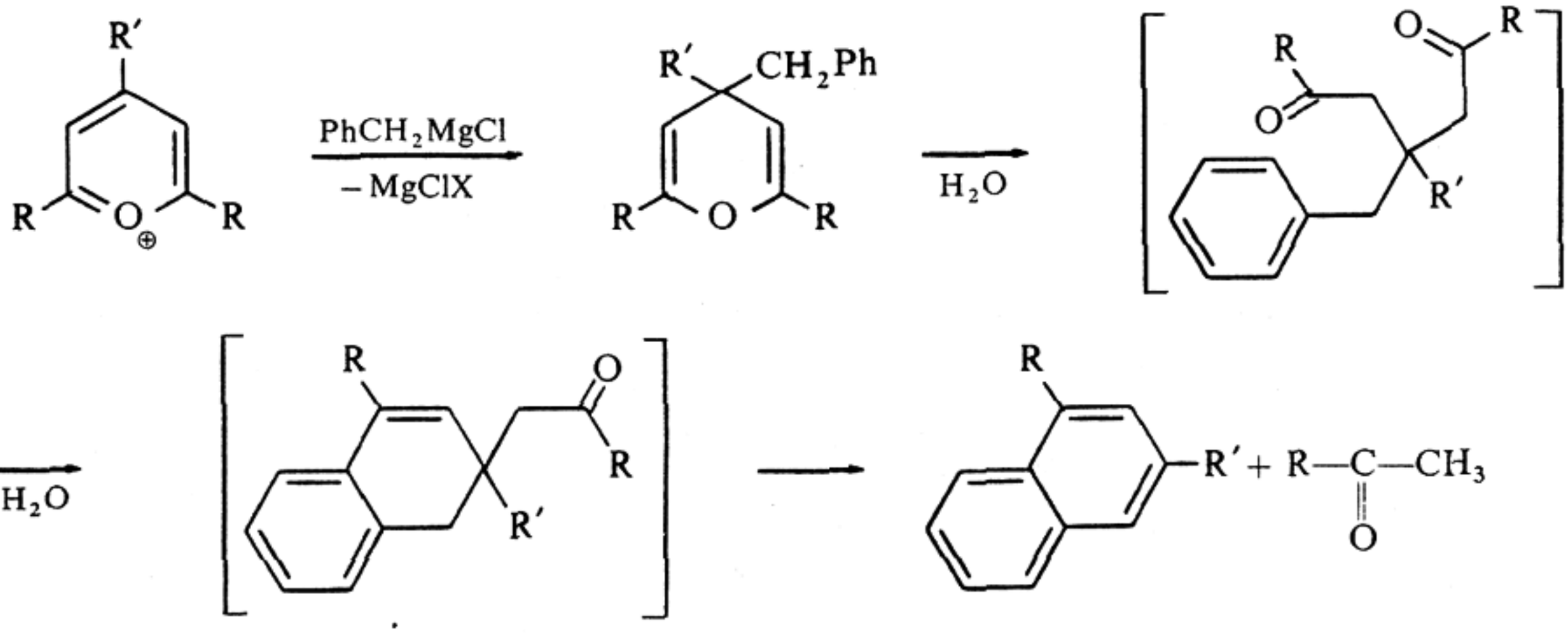
For the non-enolizable 2,2-disubstituted 1,3-diketones the reaction was found to take a different course:[1,2]





There seemed to be no report of "normal" bis-addition of Grignard reagents to 1.3-diketones, when this work was initiated.

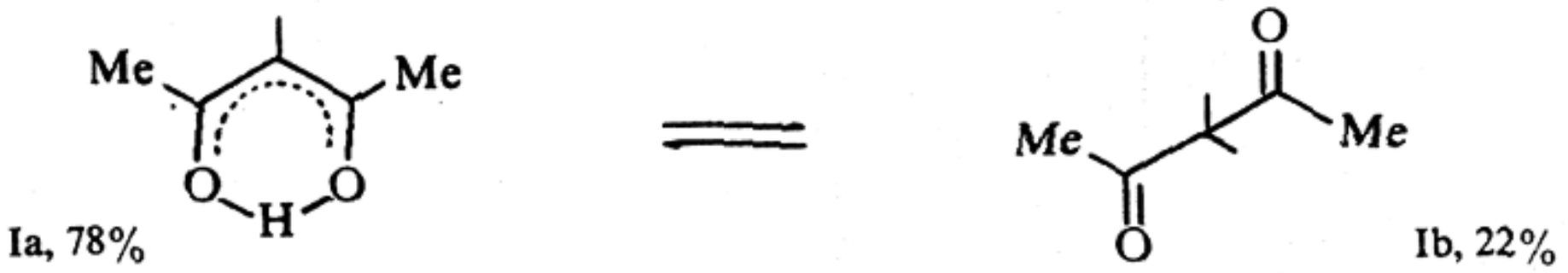
We became interested in the reaction of the benzyl Grignard reagent with 1,3-diketones owing to the following considerations: Dimroth[3] had described the preparation of 1,3-disubstituted naphthalenes starting from 2,4,6-trisubstituted pyrylium salts *via* the following reactions:

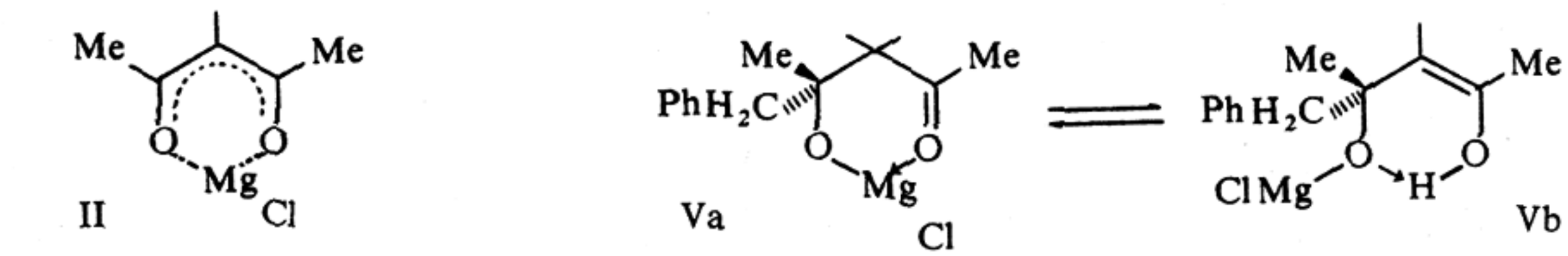


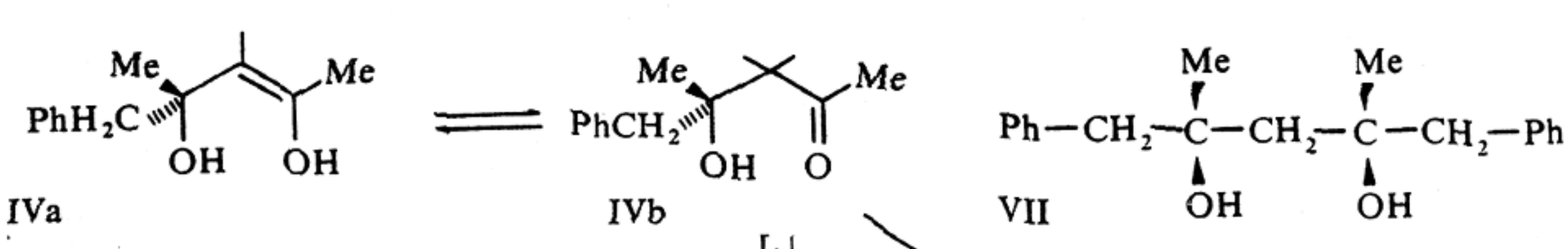
In this reaction one mole of methyl ketone is split off. Subtracting this fragment theoretically from the starting pyrylium salt, results in a 1,3-diketone. The interesting point to note is that pyrylium salts are in fact prepared[4–6] by reacting a methyl ketone with a 1,3-diketone. The logical conclusion was to try the preparation of 1,3-disubstituted naphthalenes from 1,3-diketones and benzylmagnesium chloride. The results of our investigations have been reported in preliminary form.[7,8] Independently, L. C. Leitch and P. Canonne came to essentially the same conclusions,[9] and described compounds IV and VII below.

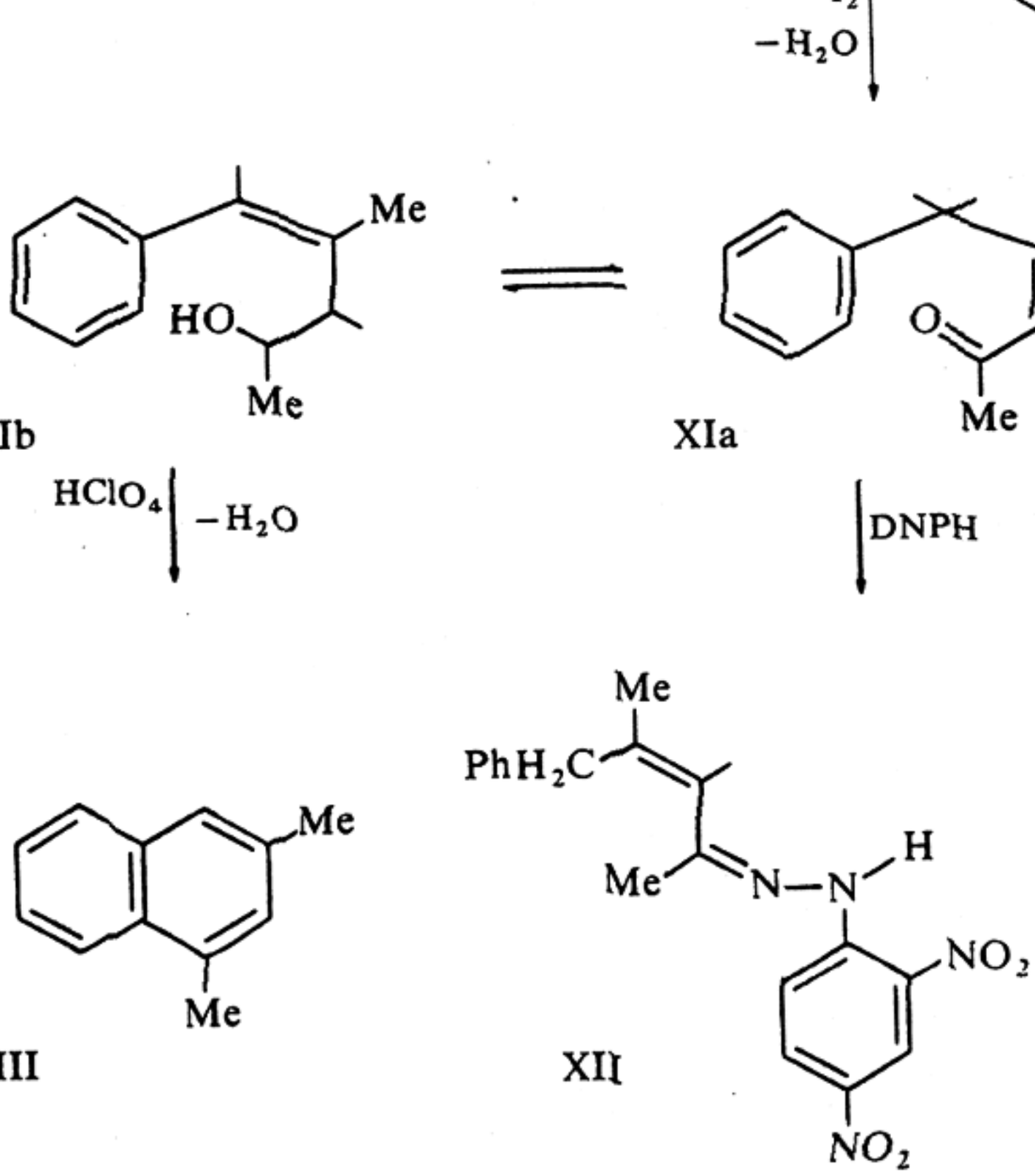
DISCUSSION

The products isolated from the reaction between acetylacetone (I) and $PhCH_2MgCl$ prove that both mono- and bis-addition of the Grignard reagent to the 1,3-diketone takes place. The addition and subsequent synthesis of 1,3-dimethylnaphthalene is believed to proceed *via* the following reactions (tautomers are noted by *a* and *b*):


Me
Me
O
H
O
Ia, 78%
Me
Me
O
O
Ib, 22%
very fast
PhCH2MgCl
−PhCH3
fast
PhCH2MgCl


Me
Me
O
O
Mg
Cl
II
PhCH2MgCl
slow
Me
PhH2C
Me
O
O
Mg
Cl
Va
Me
PhH2C
Me
O
Cl Mg
H
O
Vb
PhCH2MgCl
Me
PhH2C
Me
O
O
ClMg
MgCl
III
2HCl
Me
PhH2C
Me
CH2Ph
O
O
ClMg
MgCl
VI
2HCl


Me
PhH2C
OH
OH
IVa
Me
PhCH2
Me
OH
O
IVb
I2
−H2O
Ph—CH2—C—CH2—C—CH2—Ph
Me
Me
OH
OH
VII
Me
HO
Me
XIb
HClO4
−H2O
Me
O
Me
XIa
DNPH
Me—C—Me
O
VIII
+
PhCH2—C—Me
O
IX
DNPH


Me
Me
XIII
Me
PhH2C
Me
N
N
H
NO2
NO2
XII
PhH2C—C—Me
N
N
H
NO2
NO2

The ratio of yields in the bis-addition product VII relative to the mono-addition product XI (IV was not isolated pure) amounted in two separate runs to 0·22 and 0·215, which stands very close to the known equilibrium content of the diketo-form in liquid acetylacetone.[10, 11] Admitting that the reaction of the Grignard reagent with the enolic hydrogen (Ia → II) is instantaneous, one can conclude that at least the first addition step (Ib → V) is a much faster reaction than the tautomerization process (Ia ⇌ Ib).[9a]

The structures of the purified products VII, IX–XIII were established by elementary analysis and spectroscopy.

Electronic spectra clearly differentiate between the two 2,4-dinitrophenylhydrazones X (yellow, λ_{max} = 359 nm, EtOH) and XII (red solid, yellow solution, λ_{max} = 381 nm, in EtOH, 388 nm in 1,2-dichloroethane), showing X to possess a less extended delocalized electronic system, thus deriving from a simpler ketone.

A number of major IR bands could be assigned to individual vibrations (Table 1).

TABLE 1. IR ABSORPTION SPECTRA OF THE ADDITION PRODUCTS AND THEIR DERIVATIVES

Compound				Assignment
X[a]	XI[b]	XII[a]	VII[a]	
—	3500 vs	—	3470 s	*ν*, OH
3320 m	—	3315 ms	—	*ν*, NH
3100 w	—	3115 mw	—	*ν*, CH aromatic, olefinic and overtones
3090 mw	3090 m	—	3080 vw	
3060 vw	3065 ms	3060 mw	3060 vw	
3020 vw	3030 vs	3030 mw	3000 mw	
—	2980 s	—	2982 mw	
—	—	2950 mw	2965 m	*ν*, CH aliphatic and overtones
2928 w	2930 s	2930 mw	2935 m	
—	—	2900 mw	2910 m	
2850 vw	2860 m	—	2865 w	
—	1715 vs	—	—	*ν*, C=O
—	1700 vs	—	—	
1620 vs	1630 vs	1620 vs	1615 w	*ν*, C=C aromatic, olefinic, *ν*, C=N
1595 s	1612 vs	1595 vs	—	
—	—	1540 m	—	
1520 ms	—	1520 vs	—	*ν* as, NO_2
1496 s	1503 vs	—	1503 m	*ν*, C=C aromatic
1460 m	1465 vs	1460 m	1465 m	
1430 m	—	1422 s	1408 m	*δ*as, CH_3
1370 m	1360 vs	1360 ms	1382 m	*δ*s, CH_3
1335 vs	—	1332 vs	—	*ν*s, NO_2
1318 vs	—	1320 vs	—	
1287 vs	—	1287 vs	1290 m	
1250 mw	1260 m	1250 ms	—	
1228 m	1220 s	1230 ms	1230 m	*γ*, CH_2

TABLE 1—*continued*

Compound				Assignment
X[a]	XI[b]	XII[a]	VII[a]	
—	—	1192 mw	—	
—	1180 vs	—	1180 m	ν, C—OH[9a]
—	—	1165 mw	1162 s	
1139 m	1130 s	1140 s	1138 s	γ, CH_3
—	1107 s	1101 s	1108 m	
1090 m	1085 m	—	—	
1076 m	—	—	1070 w	
1060 mw	1060 w	1066 m	—	
1035 mw	1039 ms	1038 m	1040 w	ρ, CH_3
—	1020 m	1010 w	1010 w	
—	972 m	980 w	970 w	
942 mw	942 m	930 mw	945 mw	
930 w	920 mw	918 m	922 w	
885 vw	895 mw	890 w	880 ms	
872 vw	860 w	875 mw	—	
841 ms	—	838 m	—	ν, C—NO_2
—	820 w	795 w	810 mw	
770 mw	800 w	768 w	770 m	δ, CH aromatic out-of-plane
760 m	745 vs	748 ms	755 ms	
750 ms	—	—	748 vs	
720 m	710 vs	—	710 vs	
705 ms	—	702 m	—	
656 w	645 mw	668 w	—	
628 mw	630 mw	652 w	625 w	
615 w	610 m	595 ms	612 w	
565 m	580 mw	560 w	—	
530 mw	522 s	526 mw	520 ms	

[a] In KBr pellet

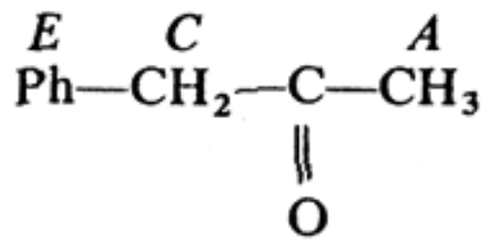
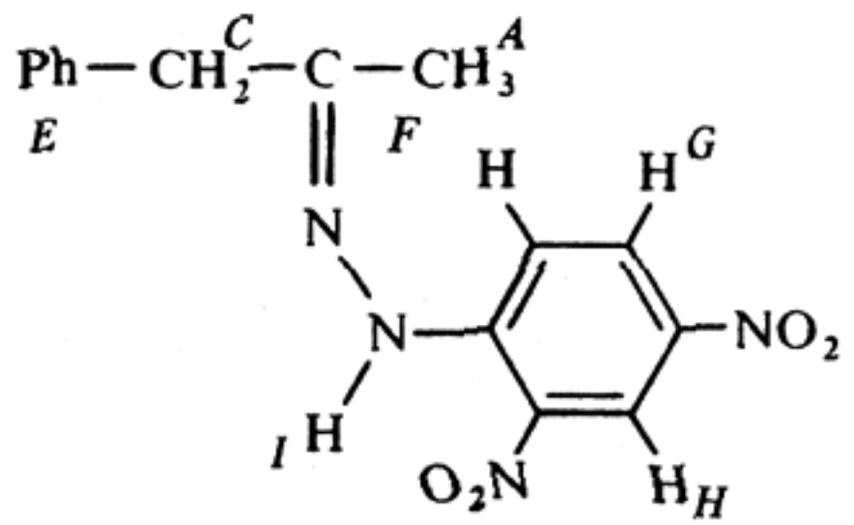
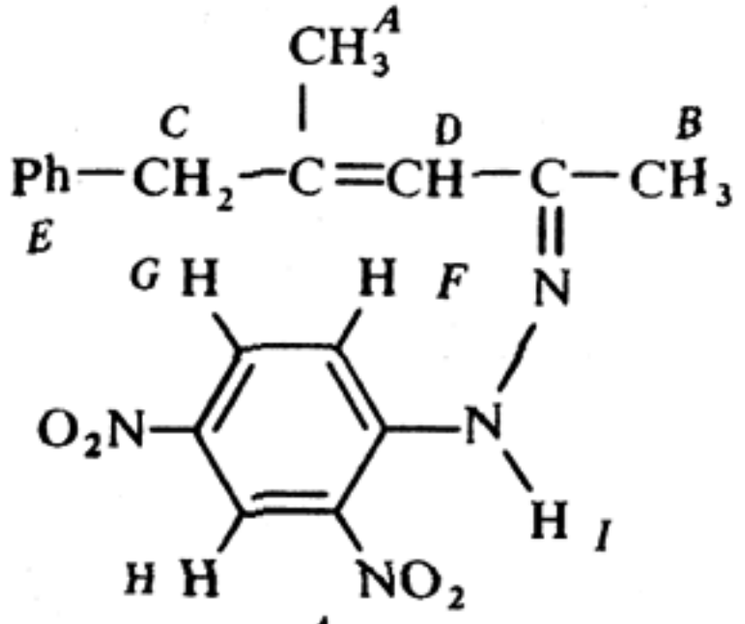
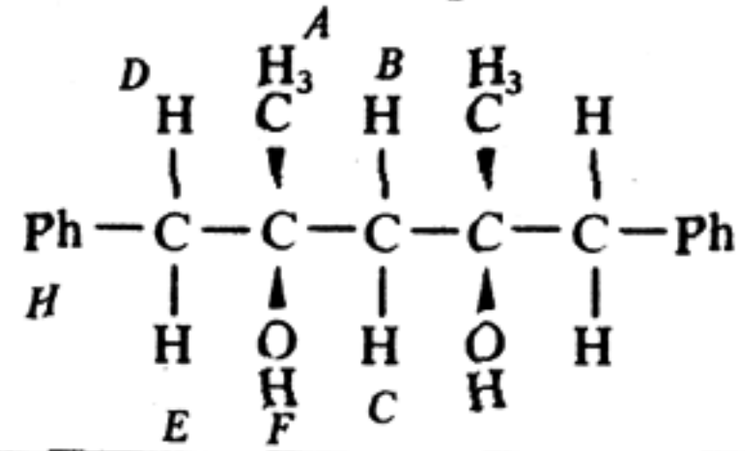
[b] In liquid film

The presence of a strong OH band in the spectrum of compound XI leads us to suppose a tautomeric equilibrium XIa ⇌ XIb in solution. The doublet structure of the C=O absorption band for ketones like IX and XI is known in the literature and was assigned to rotational isomerism.[12–19]

NMR spectra gave convincing structural evidence for compounds VII, IX, X and XII, (Table 2). The agreement with literature data[20,21] on X is fairly good, except that we have found in $CDCl_3$ none or only very small signals attributable to the *anti* isomer of X (Me group A, δ 2·20, less than 4%). For compound XII no evidence for stereoisomerism was obtained.

The coupling constants J were verified by double resonance experiments using spin decoupling and INDOR techniques as shown in Fig. 1. The small coupling found between the NH proton (I) and the dinitrophenyl ring proton in *meta* position to it (G) is an interesting feature.

TABLE 2. NMR SPECTRA OF THE ADDITION PRODUCTS AND THEIR DERIVATIVES IN $CDCl_3$, AT 80 AND 100 MHz

Compound	Formula	Chemical shifts, (δ)									Coupling constants, (Hz)					
		A	*B*	*C*	*D*	*E*	*F*	*G*	*H*	*I*	J_{AD}	J_{BC}	J_{DE}	J_{FG}	J_{GH}	J_{GI}
IX		2·11	—	3·65	—	7·0–7·4	—	—	—	—	—	—	—	—	—	—
syn-X		2·00	—	3·75	—	7·31	8·00	8·32	9·11	11·05[a]	—	—	—	9·5	2·3	0·7
XII		2·08	2·18	3·51	5·90	7·27	7·86	8·29	9·11	11·17[a]	1·3	—	—	10·0	2·5	0·8
VII		1·28	1·53	1·88	2·68	2·77	3·61[b]	—	7·11	—	—	15·0	13·0	—	—	—

[a] slightly broadened signal;

[b] this band appears at δ 3·23 on heating to 50° and vanishes after shaking with D_2O, thus confirming the above assignment. No other change occurs on heating.

HOCMe—CH_2Ph, also appears as an AB quadruplet. The diol (VII) can exist in a *meso* or racemic form. Benzylic protons of both these forms are diastereotopic,[22] hence magnetically non-equivalent in chiral or achiral solvents.[23, 24] However the central methylene protons (*BC*) of the enantiometric forms are equivalent, whereas those of the *meso* form are diastereotopic. Therefore the diol VII is the *meso* form. Its formation can be rationalized by stereospecific attack of the benzyl Grignard reagent on one of the diastereotopic carbonylic faces of the monoaddition intermediate V, namely the face with the benzyl group.

The synthesis of 1,3-dimethylnaphthalene starting from acetylacetone and $PhCH_2MgCl$ is similar to the Combes synthesis[25–27] of 2,4-dimethylquinoline from acetylacetone and aniline. Starting from methyl-deuterated 2,4,6-trimethylpyrylium perchlorate we prepared 1,3-bis(d_3-methyl)-naphthalene, and reported its IR spectrum[28] in agreement with literature data.[29]

EXPERIMENTAL

UV-Spectra were recorded with a CF 4-Optica Milano spectrophotometer, IR-spectra with an UR-10 Carl Zeiss Jena instrument. NMR-Spectra at 60 and 100 MHz were recorded on JEOL instruments, those at 80 MHz, including double resonance experiments, on a TESLA BS-487-B (Brno, Czechoslovakia) spectrometer. The reproducibility was about $\pm 0{\cdot}2$ Hz.

Addition of acetylacetone to benzylmagnesium chloride. Benzylmagnesium chloride was prepared as usual[30] from 19·2 g Mg turnings and 96 ml (0·8 moles) $PhCH_2Cl$ in ether. To this solution 40 ml (0·4 moles) of acetylacetone in 50 ml ether were introduced dropwise under vigorous stirring at a rate which allows the mixture to reflux gently. The stirring under reflux was maintained for an additional 6 hr period by heating. The mixture was then cooled by an ice-salt bath and 200 ml of ice-cold, sat. NH_4Cl aq added under vigorous stirring, continued till nearly all solid material dissolved. The cold solution was filtered and the precipitate washed several times with fresh NH_4Cl aq. The ethereal layer of the filtrate was separated and the aqueous phase extracted with ether. Combined organic layers were dried (Na_2SO_4) and the ether evaporated at room temperature. About 150 ml of yellowish oil was obtained, consisting mainly of 4-benzyl-4-hydroxypentan-2-one (IV),[9b] which could not be purified because it underwent dehydration.

Preparation of 5-phenyl-4-methyl-3-pentene-2-one, (4-benzyl-3-pentene-2-one), XI. The oily 4-benzyl-4-hydroxypentan-2-one (4-hydroxy-4-methyl-5-phenyl-2-pentanone, methyl-benzyl-acetonyl carbinol, IV) was heated carefully in a distillation apparatus with a trace of I_2, to 130° for a short time. An exothermal reaction took place and a mixture of water and toluene passed over. From the residue, 35 g of a colourless liquid was obtained by distillation at 140°/20, 130°/7, 110°/3 mm. The literature[31] indicates for compound (XIa) b.p. of 140°/9 mm. This product was refractionated at 126°/7 mm, for analytical purposes.

Preparation of the 2,4-dinitrophenylhydrazone (XII) *of 5-phenyl-4-methyl-3-pentene-2-one.* Product XI (3 ml) prior or subsequent to refractionation was introduced into a boiling mixture of 4 g dinitrophenylhydrazine (DNPH), 1 ml conc. H_2SO_4 and 60 ml EtOH. From the resulting dark-red solution needle-like red crystals were deposited after 48 hr. These were purified by column chromatography on alumina in C_6H_6 and finally recrystallized from EtOH, m.p. 141–2°, (Found: C, 61·90; H, 5·46; N, 16·03; $C_{18}H_{18}N_4O_4$ requires: C, 61·01; H, 5·12; N, 15·81%).

Splitting of benzyl-methyl-acetonyl carbinol (IV) *to benzyl methyl ketone (phenylacetone,* IX). By heating product IV without I_2 (or in a few irreproducible runs even with I_2), 40 ml of a different distillate, b.p. 100–130°/10 mm was obtained. Its main component, IX, could be obtained by refractionation at 80°/6 mm or 71°/3 mm and yielded on treating with DNPH only a yellow adduct, which after several recrystallizations from dioxane melted at 156° (all m.p. in this paper were taken on a Kofler micro hot stage and are therefore corrected). Literature[32–34] m.p. for X, 152–4°.

Isolation of the 2,4-dimethyl-1,5-diphenylpentane-2,4-diol (2,4-dibenzyl-2,4-pentanediol, VII). The residue from the distillation described under item 2 or item 4, consisted of a dark coloured viscous oil, which deposited on standing about 16 g of white crystalline material. After several recrystallizations from ligroin the analytically pure compound VII melted at 93°.[9a] (Found: C, 80·11; 80·52; H, 8·25; 8·46; Calc. for $C_{19}H_{14}O_2$, C, 80·24; H, 8·51%).

Preparation of 1,3-dimethylnaphthalene, (XIII), *from* IV. The crude IV was heated 10 min. at 60° with

excess 70% $HClO_4$. The resulting black oil was poured into 500 ml cold water and the mixture extracted with petroleum ether. The organic layer dried over K_2CO_3 was fractionated in vacuum, affording a fraction b.p. 107–110°/3 mm (2·3 g, 7% yield relatively to I). This fraction was redistilled over Na and identified as 1,3-dimethylnaphthalene by IR spectroscopy.

Preparation of 1,3-*dimethylnaphthalene* (XIII) *from* 5-*phenyl*-4-*methyl*-3-*pentene*-2-*one*, (XI). 13 g of ketone XI, and 60 ml of 70% $HClO_4$ were heated 10 min. at 60° with stirring. After cooling, the mixture was poured into 500 ml of cold water and the organic layer extracted with petroleum ether. The extract was washed with Na_2CO_3 aq and dried over $CaCl_2$. The fraction boiling between 110 and 125°/9 mm was redistilled over Na at 125°/9 mm, yielding 5 g (43% yield) of 1,3-dimethylnaphthalene identified by means of IR spectroscopy.

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