A Synthesis of Conjugated Dienes from Aromatic, Five-membered Heterocycles

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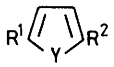
Reactions of furan, thiophene, selenophene, and tellurophene as well as 2-methyl and 2,5-dimethyl derivatives of the first two heterocycles with phenyl-, methyl-, and n-butyl-magnesium bromides in the presence of ligated nickel dichloride are shown to yield buta-1,3-dienes mostly with retention of configuration.

The facile, alkylative ring opening of benzofuran, thianaphthalene, and dibenzothiophene by the reactions of these substances with Grignard reagents in the presence of ligated, low-valent nickel species formed a part of the recent discovery of carbon–carbon bond formation by replacement of trigonal carbon–oxygen[1] and –sulphur[2] bonds. In continuation of this work a comparative study of the chemistry of the heterocycles furan (**1a**), thiophene (**1b**), selenophene (**1c**), and tellurophene (**1d**) as well as some of their methyl derivatives (**1e**—**h**) has been undertaken, the results of which are reported in the present communication.

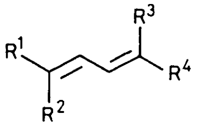
Reactions between the heterocycles and the Grignard reagents phenylmagnesium bromide [under the influence of bis(triphenylphosphino)nickel dichloride catalysis], methylmagnesium bromide [in the presence of 1,3-bis-(diphenylphosphino)propanenickel dichloride], and n-butylmagnesium bromide [under the influence of 1,3-bis(diphenylphosphino)propanenickel dichloride] were carried out in refluxing benzene for periods of 2—72 h. The products and their yields are listed in Table 1.

As in earlier cases of heteroatom replacement from olefinic or aromatic carbon atoms by nickel-mediated Grignard reactions[1,2] phenylmagnesium bromide proved to be the most active reagent, requiring the less accelerating catalyst, and among the aliphatic Grignard reagents the less bulky methylmagnesium bromide was faster than the n-butyl equivalent.



(1) a; $R^1 = R^2 = H, Y = O$
b; $R^1 = R^2 = H, Y = S$
c; $R^1 = R^2 = H, Y = Se$
d; $R^1 = R^2 = H, Y = Te$
e; $R^1 = Me, R^2 = H, Y = O$
f; $R^1 = Me, R^2 = H, Y = S$
g; $R^1 = R^2 = Me, Y = O$
h; $R^1 = R^2 = Me, Y = S$

For each of the Grignard reagents the heterocycles showed the following order of reactivity: (**1d**) > (**1c**) > (**1b**) > (**1a**). No reaction took place between n-butylmagnesium bromide and furan, *i.e.* the slowest reagent and substrate. The unravelling of the rings occurred with full retention of configuration, leading to *Z,Z*-dienes, except for the reactions of phenylmagnesium bromide, which showed a trend toward *E,E*-diene formation in the (**1d**)-to-(**1a**) series, manifesting itself most dramatically in the transformation of furan (**1a**) exclusively into an *E,E*-diene (**2a**). Since, in principle, a reaction involving only a 1 : 1 heterocycle–Grignard reagent molar ratio was expected to produce a dienolate or its sulphur, selenium, or tellurium equivalents and hence an unsaturated aldehyde on work-up, the reactions were executed under



(2) a; $R^1 = R^4 = Ph, R^2 = R^3 = H$
b; $R^1 = R^4 = H, R^2 = R^3 = Ph$
c; $R^1 = Me, R^2 = R^3 = Ph, R^4 = H$
d; $R^1 = R^4 = Me, R^2 = R^3 = Ph$
e; $R^1 = R^4 = H, R^2 = R^3 = Me$
f; $R^1 = R^2 = R^3 = Me, R^4 = H$
g; $R^1 = R^2 = R^3 = R^4 = Me$
h; $R^1 = R^4 = H, R^2 = R^3 = Bu^n$
i; $R^1 = Me, R^2 = R^3 = Bu^n, R^4 = H$
j; $R^1 = R^4 = Me, R^2 = R^3 = Bu^n$
k; $R^1 = R^4 = H, R^2 = Me, R^3 = Ph$
l; $R^1 = Me, R^2 = R^3 = H, R^4 = Ph$
m; $R^1 = R^2 = Me, R^3 = Ph, R^4 = H$
n; $R^1 = R^2 = R^4 = Me, R^3 = Ph$
o; $R^1 = R^4 = H, R^2 = Bu^n, R^3 = Ph$
p; $R^1 = Bu^n, R^2 = R^3 = H, R^4 = Ph$
q; $R^1 = Me, R^2 = Bu^n, R^3 = Ph, R^4 = H$
r; $R^1 = R^4 = Me, R^2 = Bu^n, R^3 = Ph$
s; $R^1 = R^4 = H, R^2 = Bu^n, R^3 = p\text{-}MeC_6H_4$

Table 1. Reactions between heterocycles (**1a**—**h**) and Grignard reagents.[a]

	PhMgBr			MeMgBr			Bu^{n}MgBr		
	Reaction time (h)	Product	Yield (%)	Reaction time (h)	Product	Yield[b] (%)	Reaction time (h)	Product	Yield (%)
(**1a**)	72	(**2a**)	49	72	(**2e**)	5			
(**1b**)	24	(**2b**) (**2a**)	8 76	24	(**2e**)	80	24	(**2h**)	58
(**1c**)	8	(**2b**) (**2a**)	44 44	8	(**2e**)	85	12	(**2h**)	60
(**1d**)	2	(**2b**)	88	6	(**2e**)	88	6	(**2h**)	66
(**1e**)	72	(**2c**)	45	72	(**2f**)	8			
(**1f**)	36	(**2c**)	78	24	(**2f**)	58	24	(**2i**)	47
(**1g**)	72	(**2d**)	39	72	(**2g**)	15			
(**1h**)	36	(**2d**)	72	24	(**2g**)	68	72	(**2j**)	17

[a] Molar ratio 1 : 2.1 : 0.1 heterocycle : Grignard reagent : catalyst. The stereochemistry of the buta-1,3-dienic products was determined by high-resolution ^1H and ^{13}C n.m.r. spectroscopy. [b] Based on g.l.c. analysis.

these constraints. However, nothing other than dienes were obtained, indicating that the Grignard reaction on the 1:1 product complex is faster than the one leading to the complex.

The reactions of the aliphatic Grignard reagents with all the heterocycles except the furans furnished phenylated dienes as side-products in up to 10% yield. Thus the reactions of methylmagnesium bromide with (**1b**) and (**1c**) gave mixtures of dienes (**2k**) and (**2l**), with (**1d**) afforded (**2k**), with (**1f**) yielded (**2m**) and with (**1h**) led to (**2n**), while the reactions of n-butylmagnesium bromide with (**1b—d**) furnished mixtures of (**2o**) and (**2p**), with (**1f**) produced (**2q**) and with (**1h**) formed (**2r**). The phenyl groups of the side-products could be shown to be derived from the catalyst ligand[3] by the observation of the formation of side-product (**2s**) (6%) accompanying the major product (**2h**) (56%) in a reaction of n-butylmagnesium bromide with tellurophene (**1d**) under the influence of 1,3-bis(di-*p*-tolylphosphino)propanenickel dichloride.

In conclusion it is worth noting that the reactions of Grignard reagents with the aromatic, five-membered heterocycles constitute a new, fast method of synthesis of *Z,Z*-buta-1,3-dienes.

Received, 24th January 1984; Com. 101

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