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THE REACTION OF ALKANE DIAZOTATES WITH GRIGNARD REAGENTS--CONVERSION OF THE C-N TO THE C-C BOND[1]

Robert A. Moss[*] and John Banger

Wright and Rieman Laboratories, School of Chemistry, Rutgers University

The State University of New Jersey, New Brunswick, New Jersey 08903

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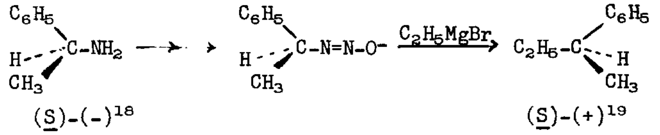
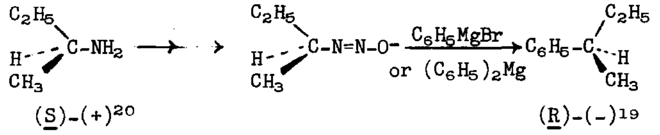
S_N2-like reaction sequences involving unactivated aminoalkanes or their N-substituted derivatives are few, and their development continue to evoke interest.[2-6] Particularly rare are conversions of the C-N to the C-C bond with stereochemical inversion. Older and restricted methods include the von Braun cyanogen bromide reaction[7] and scattered examples of C-alkylation with ammonium salts;[8] these methods have generally been limited to substrates which bear allylic, benzylic, or methyl C-N bonds.

Our approach to the labilization of the amino function involves the facile conversion of aminoalkanes to alkane diazotates.[9] Through the diazotate, an aminoalkane can be hydrolytically converted to an alkanol, with net stereochemical inversion,[10] or ammonolytically converted to its enantiomer.[11] Our discovery of the Li^+-catalyzed lithium azide conversion of octane 2-diazotate to 2-azidooctane, with 73% net inversion,[12] suggested that organometallic Lewis acids should stereoselectively convert alkane diazotates to hydrocarbons. The initial results of this new approach are reported here.

Excess ethereal C_2H_5MgBr was added to ethereal slurries or ether-HMPA solutions of 94.7% optically pure[13] 1-phenylethane diazotate,[14] at temperatures ranging from -30° to +25°; eq. (1). Similarly, 77.0% optically pure[15] butane 2-diazotate[16,17] was treated with C_6H_5MgBr or $(C_6H_5)_2Mg$; eq. (2). Nitrogen evolution was rapid and essentially quantitative. Gas chromatography (20' x 0.25", 7% Carbowax 20M + 3% SF-96 on 60/80 Gaschrom R column, 140°-200°) permitted the isolation of (up to) 25% of 2-phenylbutane, 15% of styrene, and 14% of 1-phenylethanol from re-



(1)



(2)

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[*] Fellow of the Alfred P. Sloan Foundation

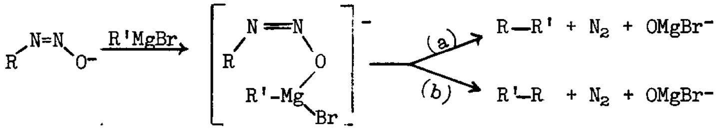
action (1). From reaction (2), gas chromatography (20' x 0.25" 10% SF-96 on 60/80 Gaschrom R column, 120-200°) allowed the isolation of ~19% of 2-phenylbutane. 2-Butanol and butenes were presumably formed,[16] but were not sought. Substantial quantities of high boiling residues account for the low overall yields. The polarimetric results, summarized in Table I, together with the known absolute configurations of 1-phenylethylamine,[18] 2-phenylbutane,[19] and 2-aminobutane[20] define the pictured and tabulated stereochemical courses of reactions (1) and (2).

Table I. Product Stereochemistry: $RCH(CH_3)N{=}NO^-K^+ + R'MgBr \rightarrow C_6H_5CH(CH_3)C_2H_5$

				$C_6H_5CH(CH_3)C_2H_5$			
Run	R	R'	Conditions[a]	α_D	(temp., °C.)[b]	α_D corr.[c]	% Net Inv.[d]
1	C_6H_5	C_2H_5	slurry, 25°	+1.90°	(25)	+2.01°	8.4
2	C_6H_5	C_2H_5	slurry, 25°	+1.99°	(20)	+2.10°	8.8
3	C_6H_5	C_2H_5	slurry, -30°	+2.98°	(23)	+3.15°	13.1[e]
4	C_6H_5	C_2H_5	soln., -5°	+5.52°	(26)	+5.83°	24.3
5	C_2H_5	C_6H_5	soln., -5°	-10.85°	(23)	-14.09°	58.7
6	C_2H_5	C_6H_5	soln., -30°	-11.66°	(22)	-15.14°	63.0
7	C_2H_5	C_6H_5[f]	soln., -30°	-11.77°	(24)	-15.29°	63.6

[a] Grignard added to a diazotate slurry (ether) or to a diazotate solution (ether-HMPA). [b] Rotations were measured with a Perkin-Elmer Model 141 Spectropolarimeter on neat liquids in a 1 cm. cell. α_D is corrected to 1 dm. Readings were reproducible to ±0.02°. [c] Corrected for the optical purities of the initial amine[13] or urethane.[15] A control experiment demonstrated the optical stability of 2-phenylbutane to the reaction conditions. [d] See references 13, 15, 18, 19 and 20, and eqs. (1) and (2). [e] 1-phenylethanol, α_D^{24}-6.73° (neat, 1 dm.), 16.3% net retention,[22] was also isolated. [f] $(C_6H_5)_2Mg$ was used: L.G. Makarova, Organometal. React., 1, 197 (1970).

The results can be analyzed mechanistically with reference to eq. (3), in which the "ate" complex, I, or a "nitrogen separated" ion pair[1,12,23] derived from it, collapses with return of R' [path (a), retention] or is captured from the rear by external Grignard reagent [path (b), inversion].[24,25]



I

(3)

Path (b) dominates in both reactions, (1) and (2), but to a significantly lesser extent in (1). This accords with the behavior of diazotates in ammonolysis reactions:[11] the stereochemical contribution of path (a), return process (more retention, less inversion), is highest when R is most capable of bearing a positive charge [e.g., R=1-phenylethyl, eq. (1)], for here the collapse of species such as I is necessarily fast and most able to compete with inverting capture by external nucleophiles.[1,11,12]

The present report contains the initial examples of a new sequence for the stereoselective conversion of an aminoalkane to a larger hydrocarbon. Beyond the inherent mechanistic interest, there exists potential for the extension of the basic reaction concept to many other organometallic reagents, with the possibility of higher yields and enhanced stereoselectivity.

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(24) Return of $^-$OMgBr or $^-$OMgR' in reaction (1) apparently gives an alkoxide which, after hydrolytic work-up, affords 1-phenylethanol with net retention; Table I, run 3 and note *e*.

(25) Note that replacement of C_6H_5MgBr by $(C_6H_5)_2Mg$ does not affect the stereochemical course of reaction (2); *cf.*, Table I, runs 6 and 7. This suggests, at least, that $MgBr_2$ is not a significant diazotate-labilizing species in the phenyl Grignard runs.

(26) Glass has shown that trifluoromethanesulfonimides derived from benzyl and *n*-hexyl amines can be converted to nitriles (CN^- in HMPA). Iodide ion mediation was required in the latter conversion. Analogous displacements could also be affected with the diethyl malonate anion. These reactions involve the conversion of C-N to C-C bonds; stereochemical aspects, however, were not reported.[4]