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DEHYDRODIMERIZATION OF IMINES VIA α-BROMOIMINES USING LITHIUM DIISOPROPYLAMIDE

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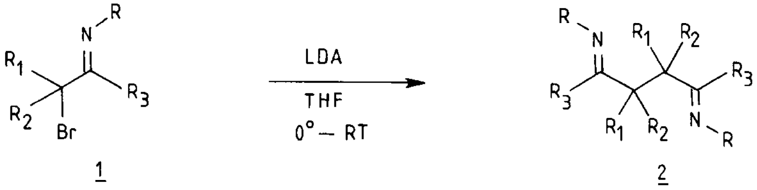
Abstract : α-Bromoimines were transformed into 1,4-diimines under soft conditions using lithium diisopropylamide in tetrahydrofuran.

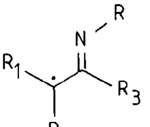
Dehydrodimerization of carbonyl compounds to afford 1,4-dicarbonyl derivatives is a well-documented transformation. This reaction is frequently performed by radical initiation[1] or by oxidative coupling of α-anions derived from these carbonyl compounds.[2] The latter process can occur by S_N2 type reactions or by dimerization of the appropriate radicals. Some recent results demonstrated that capto-datively substituted substrates dimerize probably via the radical pathway.[3]

We have found now a novel dehydrodimerization reaction of imines presumptively via an electron-transfer process of their α-bromo derivatives.[4]



Treatment of α-bromoimines 1 with lithium diisopropylamide (2 molar equiv.) (LDA) in tetrahydrofuran (0°C-RT; 1.5-2h) resulted in the formation of 1,4-diimines 2 in 48-89% isolated yield (Table I). In some cases, minor side reactions involving 1,2-dehydrobromination (formation of α,β-unsaturated imines) (4-15%) and reduction of the bromide (10%) took place[7] but compounds 2 could be easily purified by distillation or crystallization.

The mechanism of the reaction may be interpreted as a single electron-transfer from LDA to α-bromoimine 1 followed by bromide expulsion to generate imidoyl-substituted radicals 3. Dimerization of these radicals leads to



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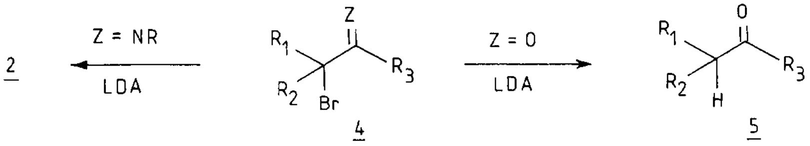
1,4-diimines 4 in analogous way as exemplified extensively for the corresponding acyl-substituted radicals.[1,7] A S_N2 type dimerization involving initial bromide-metal exchange and subsequent nucleophilic substitution can be ruled out because of the sterical hindrance in the substrates (see for instance 1b by which the reaction is not limited to geminally dimethylsubstituted compounds). All attempts to identify the LDA derived oxidation product (if formed) were unsuccessful. Single electron-transfer processes with LDA have been shown recently to afford N-(2-propylidene)isopropylamine[8,9] but this substance was undoubtedly not present in the organic fraction of the reaction mixtures. In order to avoid the possible loss of this LDA-derived ketimine (aqueous work-up; volatility), the conversion of N-(2-bromo-2-methyl-1-propylidene)*t*-butylamine 1a into 1,4-diimine 2a was performed using lithium dicyclohexylamide in tetrahydrofuran under similar conditions. The exclusive reaction product was 2a and no trace of N-(cyclohexylidene)cyclohexylamine was found (GLC analysis;



comparison with authentic material). The conversion of α-bromoimines 1 into 1,4-diimines 2 contrasts clearly with the reactive behavior of the corresponding oxygen-analogues, i.e. α-bromoketones 4, which exclusively afford reduction into the corresponding debrominated ketones 5 with LDA in tetrahydrofuran.[10] However, α-bromoketones 4 (Z=O) can be coupled to 1,4-diketones using $Fe(CO)_5$ in 1,2-dimethoxyethane.[14]

Table I. Synthesis of 1,4-Diimines 2 from α-Bromoimines 1

	R_1	R_2	R_3	R	Reaction conditions	Yield of diimine 2[a]	Other reaction products
a	Me	Me	H	t-Bu	2h/RT	89%[b]	-
b	$(CH_2)_5$		H	t-Bu	1.5h/0°C	48%[c]	15% 1,2-dehydrobromination
c	Me	Me	i-Pr	i-Pr	2h/RT	62%[d]	-
d	Me	Me	Ph	i-Pr	1.5h/0°C	72%[e]	4% 1,2-dehydrobromination and 10% reduction of the halide

a) Isolated yields after distillation or crystallization. b) Bp 74-78°C/0,3 mmHg (Lit.[11] Bp 130-135°C/12 mmHg). c) Mp 124°C. d) Mp 143°C (Lit.[12] mp 143°C). e) Bp 120-130°C/0,05 mmHg.[13]

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4. α-Bromoimines 1 are easily accessible by two major procedures, namely by 1) bromination of aldimines with N-bromosuccinimide in CCl_4 (1a, 1b)[5] or by 2) condensation of α-bromoketones with primary amines in the presence

of titanium(IV) chloride (1c, 1d).[6]

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13. As an example, the spectrometric data of compound 2d are presented here. IR (NaCl) : 1631 cm^{-1} ($\nu_{C=N}$). ^{1}H NMR (δ, CDCl$_3$) : 0.96 (12H, d, J=6Hz, Me$_2$C-N); 3.00 (2H, septet, J=6Hz, NCH); 1.16 (12H, s, Me$_2$C-C=N); 6.9-7.4 (10H, m, Ph). ^{13}C NMR (δ, CDCl$_3$) : 23.8 (q, Me); 26.1 (q, Me); 48.1 (s, CMe$_2$); 52.4 (d, NCH); 126.6 (d, para C); 127.3 and 127.4 (each d, ortho and meta C); 139.5 (s, arom. C quat.); 174.7 (s, C=N). Mass spectrum m/z (%) : 376 (M^+; 1), 333(5), 230(7), 215(11), 189(28), 188(34), 175(7), 174(10), 160(4), 146(15), 131(8), 104(100), 91(8), 77(8), 43(15), 41(10).
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