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^{1}H NMR of (α-Substituted benzyl-t-butyl)hydroxylamines and EPR of Their Oxidized Forms

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^{1}H NMR study of several (benzyl-t-butyl)hydroxylamine derivatives (BBHA) was performed, which were obtained through the addition of Grignard agents to α-phenyl-N-t-butylnitrone (PBN) or the reduction of PBN. Concomitantly, EPR of their oxidized forms (nitroxide radicals, BBN) was measured. It was proved that the joint application of ^{1}H NMR and EPR provides decisive evidences to assign the α-substituents.

PBN is a famous spin trap and widely used to detect short-lived free radicals formed in various reactions. In spin-trapping experiments, produced spin adducts of PBN, i.e. nitroxide radicals, are characterized by EPR in most cases. In the spin trap-EPR, however, the assignment of the trapped radical is sometimes obscured when the hyperfine parameters of several candidates are very close. In this case, if ^{1}H NMR is applicable, it must present decisive information to the assignment. Therefore, as the first stage of this trial, we studied the ^{1}H NMR of (benzyl-t-butyl)hydroxylamine derivatives which are easily converted from the corresponding nitroxide radicals through reduction. In this study, the hydroxylamine derivatives were synthesized from PBN by reduction or addition of Grignard agents, not by way of nitroxide radicals, for the simplicity of identification. Moreover, produced hydroxylamines were oxidized and their EPR was measured to make assurance of the product assignment.

(Benzyl-t-butyl)hydroxylamine was produced through the reduction of PBN with an equi-molar $LiAlH_4$ in ether solution. After 2h reflux at room temperature, the reactant solution was treated with HCl and then neutralized with NaOH, and the organic phase was separated and evacuated to dryness. The product was recrystallized from ligroin and the obtained white crystal was supplied for NMR measurements in $CDCl_3$ solution. On the other hand, this product was dissolved into benzene in an EPR sample tube and oxygen was bubbled through the solution for 2 or 3 min. The solution was finally outgassed with nitrogen for 10 min and EPR of this sample was measured. Besides, methyl and ethyl adduct of PBN were synthesized by the addition of methyl magnesium iodide or ethyl magnesium bromide which was made in ordinary methods. The obtained products were dissolved into $CDCl_3$ and the ^1H NMR measurements were executed. Another portion of these products were dissolved into benzene and treated with oxygen and nitrogen in order to prepare samples for EPR measurements.

^1H NMR and EPR spectra of BBHA and its oxidized form (BBN) recorded on the Hitachi R-250 and JES-RE2X spectrophotometers, respectively, are shown in Fig. 1. The chemical shifts of BBHA protons are characteristic in comparison with those of PBN's as follows: (1) the signal of benzyl-CH_2 was at 3.77 ppm diamagnetically shifted from 7.54 ppm of Ph-CH= of PBN, drastically; (2) Phenyl protons showed diamagnetic shift and variations of the chemical shift of each proton are reduced; (3) ^tBu-H showed diamagnetic shift from 1.62 ppm of PBN to 1.20 ppm. It is noticeable that the chemical shifts of the protons of BBHA are very close to those of N-t-butylbenzylamine ($\delta(^tBu\text{-}H) = 1.19$, $\delta(PhCH_2) = 3.72$, $\delta(Ph\text{-}H) = 7.15\text{-}7.40$ ppm).[1] The EPR spectrum of BBN consists of seven lines (1: 2: 2: 2: 2: 2: 1) and the obtained hf parameters (Table 1) accorded with the reported values.[2]

^1H NMR spectra of MeBBHA and EtBBHA showed the expected splitting of benzyl proton and peaks of methyl and ethyl protons were also observed

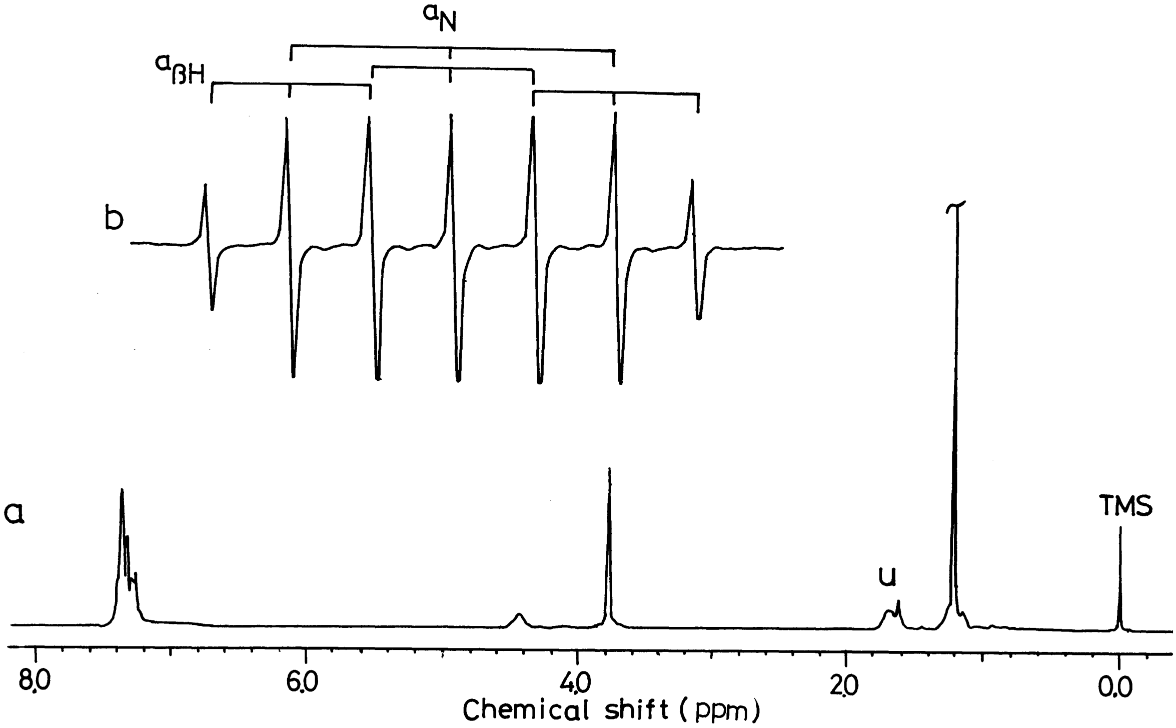

Fig. 1. ^1H NMR and EPR spectra of BBHA (a) and oxidized BBHA (b). u: unknown peaks.

Table 1. ^{1}H NMR chemical shifts$^{a)}$ and EPR parameters$^{b)}$ of BBHA: Ph-CHR-N(OH)-^{t}Bu and BBN: Ph-CHR-N(O•)-^{t}Bu

R	H	CH_3	CH_2CH_3
^{1}H NMR			
^{t}Bu-H	1.20	1.07	0.98
PhCR-H	3.77 (s)	4.13-4.21 (q)	3.75-3.80 (t)
R-H	3.77 (s)	1.48, 1.51 (d)	1.87, 2.04 (d, m) 0.76-0.82 (t)
Ph-H	7.28-7.39 (m)	7.22-7.32 (m)	7.21-7.28 (m)
NO-H	4.44	-	-
EPR$^{b)}$			
a_N	14.9	14.6	14.58
$a_{\beta H}$	7.46	3.48	3.21

a) in units of ppm in $CDCl_3$ solution. Chemical shifts of PBN protons: 1.62 (^{t}Bu-H), 7.54 (PhCR-H), 7.39-7.42 (Ph-H, m, 3H), 8.27-8.31 (Ph-H, m, 2H) ppm. b) in units of gauss in benzene solution.

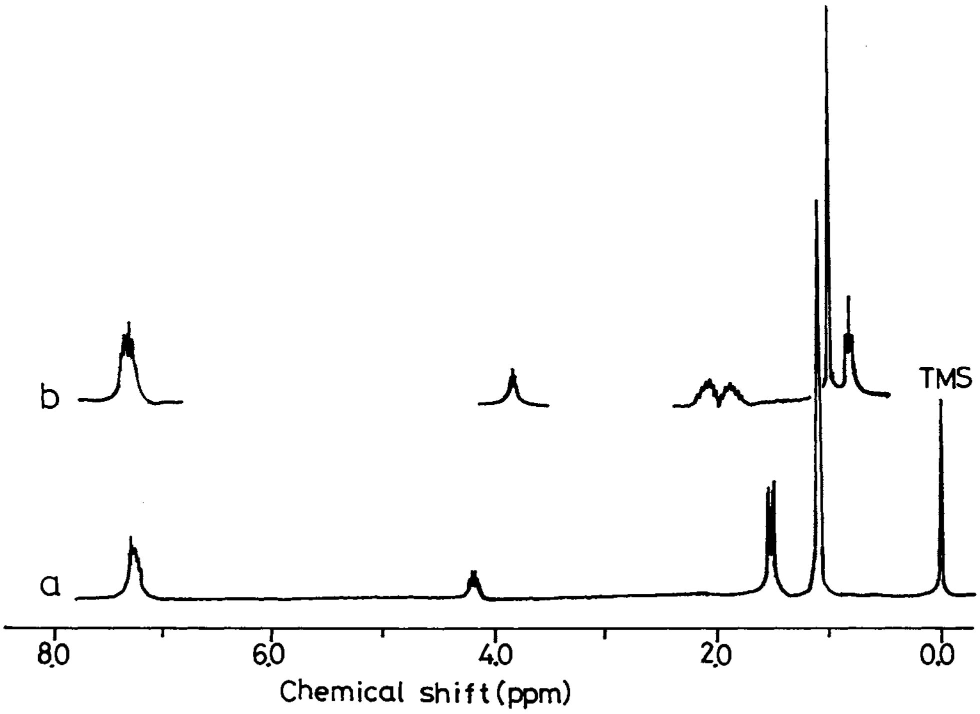

Fig. 2. ^{1}H NMR spectra of MeBBHA (a) and EtBBHA (b).

(Fig. 2). In these cases, ^{t}Bu-H showed small diamagnetic shift from that of BBHA. EPR measurements of the oxidized form of BBHA's, i.e. MeBBN and EtBBN, gave the typical six-line spectra with the same intensity and the hf parameters obtained also showed good accordance with the reported values.[2)]

This is the first report on the proton chemical shifts of BBHA derivatives and even ^{1}H NMR studies of hydroxylamines homologous to BBHA are very rare,[3)] whereas systematic study of arylnitrones[4)] and intimate study of nitrone spin traps containing PBN have been reported.[5)]

As already mentioned, in the application of ^{1}H NMR method to the assignment of PBN-spin adducts, reduction of the adducts is indispensable. This process often produces the by-products, e.g. ^{t}BuNO (δ = 1.25 ppm), $(^t\mathrm{BuNO})_2$ (δ = 1.62 ppm),[6)] and unreacted PBN and its reduced form, BBHA. Therefore, it can be said that the result shown in Table 1 is the fundamental data to advance the spin trap-NMR studies, hereafter.

References

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