

THE REACTION BETWEEN
2,2-DIPHENYL-1-PICRYLHYDRAZYL FREE STABLE
RADICAL AND N-BROMOSUCCINIMIDE

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ABSTRACT

The reactions of 2,2-diphenyl-1-picrylhydrazyl (DPPH) or 2,2-diphenyl-1-picrylhydrazine (DPPH-H) with N-bromosuccinimide (NBS) were studied. Two main compounds Br-DPPH and (Br)₂DPPH were obtained, by bromination of the starting material in *para*-phenyl position, and also a secondary product, NO₂DPPH. It was shown that the reactions of NBS with DPPH include a substitution at the picryl group of DPPH with liberation *in situ* of NO₂ (*ipso*-substitution of a nitro group with bromine) and subsequently NO₂ is scavenged by DPPH with the formation of NO₂DPPH.

Keywords: DPPH, free radical, bromination, *ipso*-substitution, scavengers

RESUMO

Foram estudadas as reações de 2,2-difenil-1-picrilhidrazila (DPPH) e 2,2-difenil-1-picrilhidrazina (DPPH-H) com N-bromo-succinimida. Foram obtidos dois produtos principais, Br-DPPH e (Br)₂DPPH, através da bromação do reagente inicial na posição *p*-fenila. Também foi obtido um produto secundário, NO₂DPPH. Foi demonstrado que as reações de n-bromosuccinimida (NBS) com DPPH envolvem uma substituição no grupo picrila de DPPH com liberação *in situ* de NO₂ (substituição *ipso* de um grupo nitro com bromo). Subsequentemente, o NO₂ reage com DPPH formando NO₂DPPH.

INTRODUCTION

The synthesis of the substituted derivatives of the 2,2-diphenyl-1-picrylhydrazyl free stable radical (DPPH) involves various methods, including radical-radical reactions.^{1,2}

The scavenger behavior of DPPH, encountered in many physico-chemical processes, afforded the obtaining of the substituted diphenylpicrylhydrazine R-DPPH-H (R-means a substituent in the *para*-phenyl position, -H a hydrazine and a form without -H a hydrazyl radical).³ In this way the bromo- and nitro-substituted derivatives of DPPH were obtained.^{4,5}

Because of its unusual stability, DPPH has focused special interest for a long time; therefore numerous *mono*- and *di*-substituted compounds have been prepared.^{5,6} In particular, the reaction of DPPH with nitrogen dioxide or halogens to form substituted hydrazines has been studied in detail.^{1,4}

The 2-(*p*-bromophenyl)-2-phenyl-1-picrylhydrazyl Br-DPPH and 2-bis-(*p*-bromophenyl)-1-picrylhydrazyl (Br)₂DPPH were obtained by the following reactions: i) the reaction of DPPH with hydrobromic acid in presence of sodium bromide;⁷ ii) the reaction of DPPH or DPPH-H with bromine⁴ and iii) the synthesis of the bromo-derivatives from substituted diphenyl amine.⁵

The mechanism of the reaction between DPPH and N-bromosuccinimide (NBS) proceeds *via* free radical intermediates, as is shown herein. This paper presents a new method for the synthesis of Br-DPPH and (Br)₂DPPH compounds.

EXPERIMENTAL

NBS, DPPH and DPPH-H were Aldrich products. The solvents employed were analytical grade used without purification. In the synthesis, the utilization of DPPH-H instead of DPPH lead to better results.

UV-Vis spectral determinations were performed with a Specord UV-VIS spectrophotometer in methylene chloride. The EPR spectra were recorded at room temperature on a JES-3B (JEOL) spectrometer with 100kHz field modulation using X-band frequency. The parameters of the EPR spectra were measured in comparison with those of Fremy's salt ($a_N=13.0$ Gauss). The NMR spectra were recorded at ambient temperature (ca. 295K) with a Varian Gemini 300BB instrument; the solvent was deuterated chloroform; internal TMS was used as reference both for ¹H-NMR and ¹³C-NMR spectra.

The NMR and ESR spectra were identical with those in literature.^{4,8}

The reaction of DPPH-H with NBS in carbon tetrachloride

Br-DPPH

Five hundred milligrams of DPPH-H (1.25 mmol) dissolved in carbon tetrachloride was allowed to react with 240 mg N-bromosuccinimide (1.3 mmol) at 0-5°C. After 24 hrs. the carbon tetrachloride solution was filtered off, stirred with an aqueous solution of ascorbic acid until the color changed to red-brown, and the organic phase separated; the solvent was removed and the residue chromatographed on silica gel GF 254 (Merck). (Br)₂DPPH-H (14%), Br-DPPH-H (39%), DPPH-H (12%), and NO₂-DPPH-H (5%) were obtained. By oxidation of the hydrazine with solid potassium permanganate in methylene chloride the free stable radicals were obtained in 95% yield. Elemental analysis for Br-DPPH-H (C₁₈H₁₂N₅O₆Br): calculated (C, H, N, Br %): 45.59; 2.55; 14.77; 16.85; found

P. Ionita

45.45; 2.50; 14.90; 16.73. Melting point 181-3°C (literature data 182-4 °C); UV-Vis $\lambda_{\text{max}}=320$ nm, in basic media $\lambda_{\text{max}}=424$ nm, for the corresponding free radical $\lambda_{\text{max}}=520$ nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent, $R_f=0.60$, for the free radical $R_f=0.68$.

(Br)₂DPPH

Samples of 500 mg DPPH-H (1.25 mmol) was treated with 460 mg NBS (2.6 mmol), and the reaction mixture worked up similarly. (Br)₂DPPH-H (32%), Br-DPPH-H (15%), DPPH-H (12%), and NO₂-DPPH-H (11%) were obtained. By oxidation in methylene chloride the corresponding free radicals are obtained with 95% yield. Elemental analysis for Br₂DPPH-H (C₁₈H₁₁N₅O₆Br₂): calculated (C, H, N, Br %) 39.09; 2.00; 12.66; 28.89; found 38.45; 2.00; 12.70; 28.73. Melting point 158-60°C (literature data 158-62°C); UV-Vis $\lambda_{\text{max}}=319$ nm, in basic media $\lambda_{\text{max}}=432$ nm, for the corresponding free radical $\lambda_{\text{max}}=520$ nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent $R_f=0.66$, for the free radical $R_f=0.78$.

The reaction of DPPH-H with NBS in DMF

Br-DPPH

Samples of 500 mg DPPH-H (1.25 mmol) and 230 mg NBS (1.3 mmol) were dissolved at 0-5°C in DMF. After 1 hr. water and ascorbic acid were added until a yellow-red precipitate appeared, which was filtered off, dried and chromatographed under the same conditions as described above. The products were isolated with the following yields: (Br)₂DPPH-H (12%), Br-DPPH-H (42%), DPPH-H (10%), and NO₂-DPPH-H (5%). Oxidation in methylene chloride give the corresponding free radicals with 95% yield. Elemental analysis for Br-DPPH-H (C₁₈H₁₂N₅O₆Br): calculated (C, H, N, Br %) 45.59; 2.55; 14.77; 16.85; found 45.55; 2.50; 14.92; 16.83. Melting point 183°C (literature data 182-4 °C); UV-Vis $\lambda_{\text{max}}=320$ nm, in basic media $\lambda_{\text{max}}=424$ nm, for the corresponding free radical $\lambda_{\text{max}}=520$ nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent $R_f=0.60$, for the free radical $R_f=0.68$.

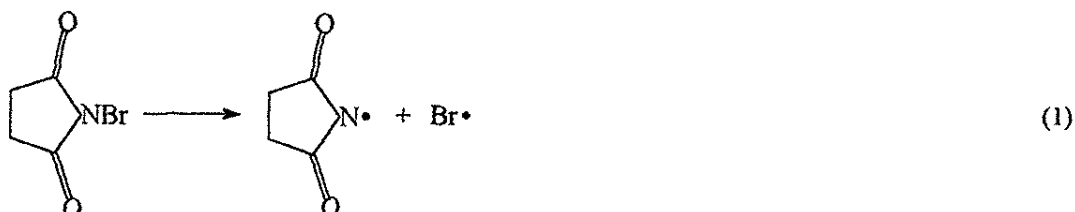
(Br)₂DPPH

Samples of 500 mg DPPH-H (1.25 mmol) and 460 mg NBS (2.6 mmol) were processed similarly as described above. (Br)₂DPPH-H (37%), Br-DPPH-H (14%), DPPH-H (8%), and NO₂-DPPH-H (10%) were obtained. By oxidation in methylene chloride the corresponding free radicals are obtained in 95% yield. Elemental analysis of Br₂DPPH-H (C₁₈H₁₁N₅O₆Br₂): calculated (C, H, N, Br %) 39.09; 2.00; 12.66; 28.89; found 38.65; 2.10; 12.70; 28.75. Melting point 161°C (literature data 158-162°C); UV-Vis $\lambda_{\text{max}}=319$ nm, in basic media $\lambda_{\text{max}}=432$ nm, for the corresponding free radical $\lambda_{\text{max}}=520$ nm. TLC analysis on silica gel GF 254 (Merck), toluene eluent $R_f=0.66$, for the free radical $R_f=0.78$.

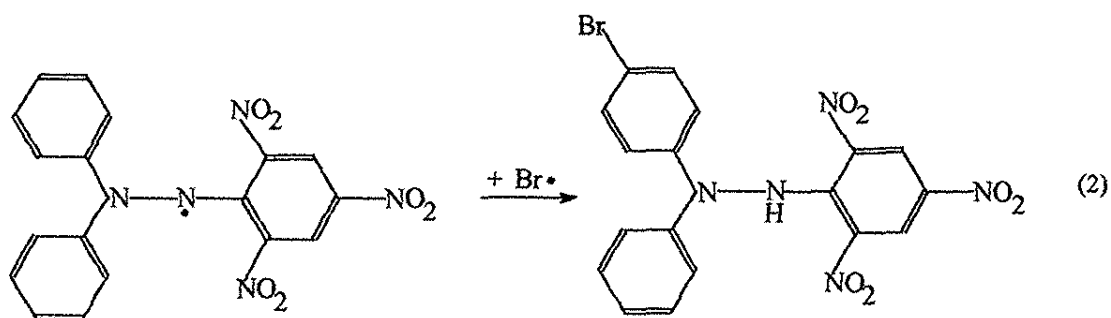
The compound NO₂-DPPH-H was isolated in the same conditions at $R_f=0.26$ ($\lambda_{\text{max}}=352$ nm), for free radical $R_f=0.46$ ($\lambda_{\text{max}}=505$ nm).

RESULTS AND DISCUSSION

NBS is widely used in the preparation of a bromoderivatives originating in active substrates, the bromination occurring by a radical mechanism (Eq. 1).



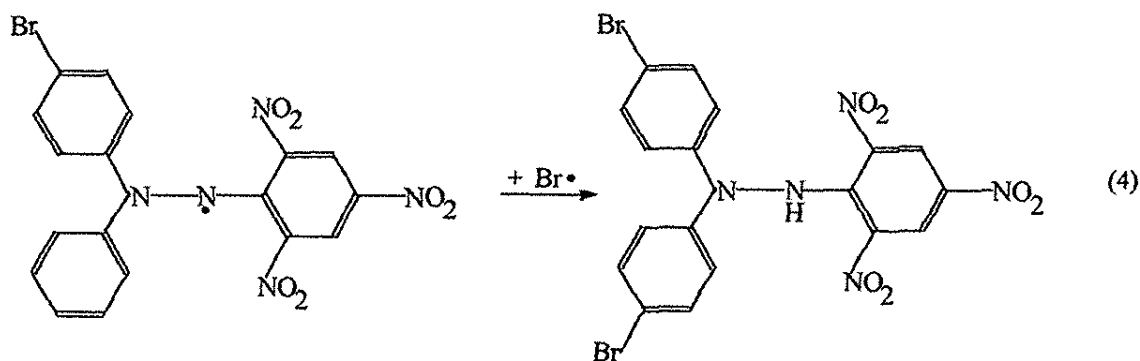
Both free radicals generated may interact with DPPH, but only the bromine radical yields the compound shown in the next equation (the bromine radical is scavanged by DPPH, which requires both combination and H-transfer, Eq. 2):



The free radicals involved in the processes (R may be the free radicals derived from succinimide, bromine or nitrogen dioxide free radical) allowed the oxidation of hydrazine species to the hydrazyl free radical (Eq.3):



If an excess of NBS is employed (Br)₂DPPH is expected to form (Eq. 4):



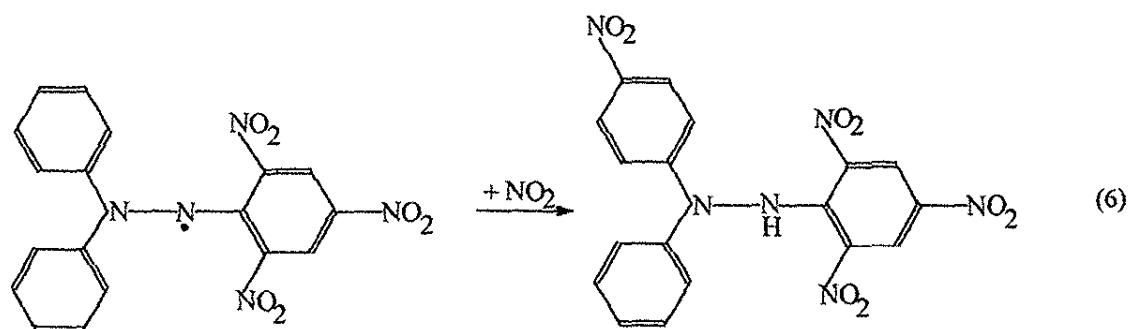
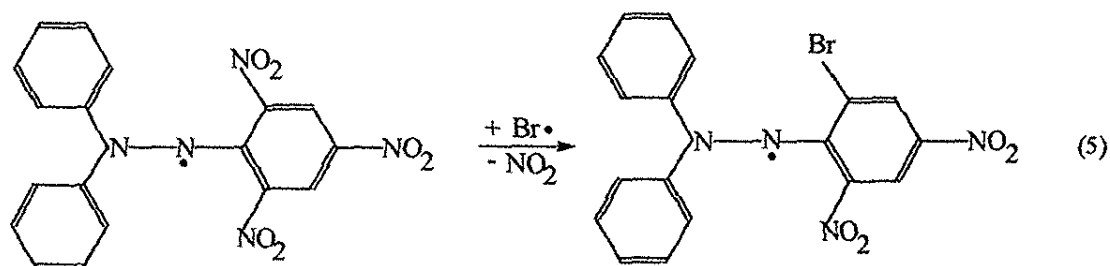
P. Ionita

The study showed that for the DPPH, Br-DPPH and (Br)₂DPPH compounds, the relative ease of oxidation of the hydrazines to the corresponding free radical decreases as the bromo groups are added (Weil observed the same behaviour for the nitrocompounds NO₂-DPPH and (NO₂)₂DPPH).¹

The reactions were carried out in carbon tetrachloride or dimethylformamide (DMF). Although bromination with NBS takes place in carbon tetrachloride, utilization of DMF offers some advantages, because the process is faster, occurs in homogeneous phase and one can easily separate the reaction products by water addition.

An attempt was made to increase the yield and the selectivity of the reaction for one or the other product (Br-DPPH and (Br)₂DPPH); the reaction was carried out at low temperature (0-5° C). This processes favoured the obtention of brominated compounds and decreased the yield of the *ipso*-substituted derivatives.⁴ The average yield of brominated derivatives increases about 10% when the reaction occurs at low temperature.

All the experiments have shown the formation of NO₂-DPPH, by *ipso*-substitution process (bromine radical *ipso*-substituted one *ortho*-nitro group), followed by NO₂ radical scavenged by DPPH (Eqs. 5 and 6).^{3,4,6,8}



After the isolation of the bromoderivatives, elementary analysis, melting point and the UV-Vis, NMR and ESR spectra were identical with the literature data.^{1-3,9} In basic media the hydrazinic hydrogen is removed (because it has an acidic character),^{10,11} and the anion formed exhibits a different absorption spectrum (see experimental part).

The use of the corresponding hydrazine DPPH-H instead of DPPH gave better results as far as the reduction of secondary compounds concerned, as shown by TLC analysis.

In conclusion, although the reaction between DPPH-H and NBS is quite complex, the proposed method is a viable alternative for the DPPH bromination. The reaction involves the generation of bromine radical which is scavenged by DPPH or Br-DPPH. The *ipso*-substitution of a nitro group from picryl moiety with bromine yields NO₂DPPH.

*Reactions of Picrylhydrazine***ACKNOWLEDGEMENT**

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