The transformation of 2,6-di-tert-butyl-4-(alkylamino)methylphenols to *N,N*-bis(3,5-di-tert-butyl-4-hydroxylbenzyl)-*N*-alkylamines

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Several derivatives of *N,N*-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-*N*-alkylamines were isolated in the reduction of the imines obtained from 3,5-di-tert-butyl-4-hydroxylbenzaldehyde and primary amines. Experimental results showed that they were transformed from the corresponding 2,6-di-tert-butyl-4-alkylaminomethylphenols.

Keywords: 2,6-di-tert-butyl-4-(alkylamino)methylphenols, *N,N*-bis(3,5-di-tert-butyl-4-hydroxylbenzyl)-*N*-alkylamines

Hindered phenols (compounds **a**) are widely used as antioxidants while hindered amines (compounds **b**) are used as light stabilisers in polymers and lubricants because of their special hindered structures.[1-7] Recently new compounds with hindered phenol or hindered amine groups have been examined. In our project, we aimed to synthesise a series of compounds with both of hindered phenol and hindered amine groups (compounds **c**) as showed in Fig. 1, and evaluate their performances in polymers. A series of secondary benzyl amines with hindered phenol groups (compounds **2**) were required as the key intermediates.

Firstly, we tried to synthesise them through a replacement reaction of the hindered phenol benzyl halide with primary amines, but the major product was tertiary amines with bis phenol groups,[8] even when the reactions were carried out under 0°C and 4–5 equivalents of the primary amine was used. Although the reason for this result is unknown, we sought an alternative method for the synthesis of these intermediates. In the light of reports on the synthesis of the similar compounds,[9] we examined the reductive amination of 3,5-di-tert-butyl-4-hydroxybenzaldehyde with aliphatic amines and sodium borohydride. However, some surprising results were obtained (Scheme 1).

2,6-Di-tert-butyl-4-(butyliminomethyl)-phenol (**1a**) was obtained in nearly quantitative yield by the condensation of 3,5-di-tert-butyl-4-hydroxybenzaldehyde with *n*-butylamine in refluxing toluene.[10] Then the imine was reduced by sodium borohydride in dry ethanol at –5–0°C. Besides the expected product 2,6-di-tert-butyl-4-(butylamino)methylphenol (**2a**), another compound was isolated at the same time. Its structure was determined by the NMR spectrum and X-ray diffraction of its single crystal (Fig. 2).[11] The results indicated that it was the *N,N*-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-*N*-butylamine (**3a**).

The reaction was repeated and studied in details, the results showed that the yield of **3a** increased as the reaction was prolonged. When the reaction time was limited in 0.5 h, yield of **2a** was 75%, and the yield of **3a** was only 20.8%. When the reaction was carried out over 3 hours, the yield of compound **3a** increased to 49%, while the yield of compound **2a** was only 46%.

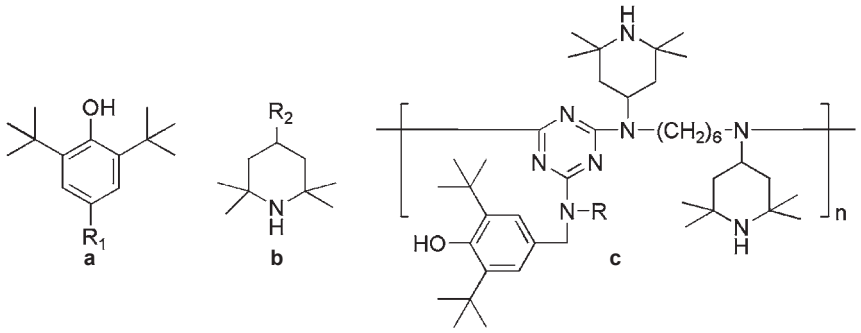
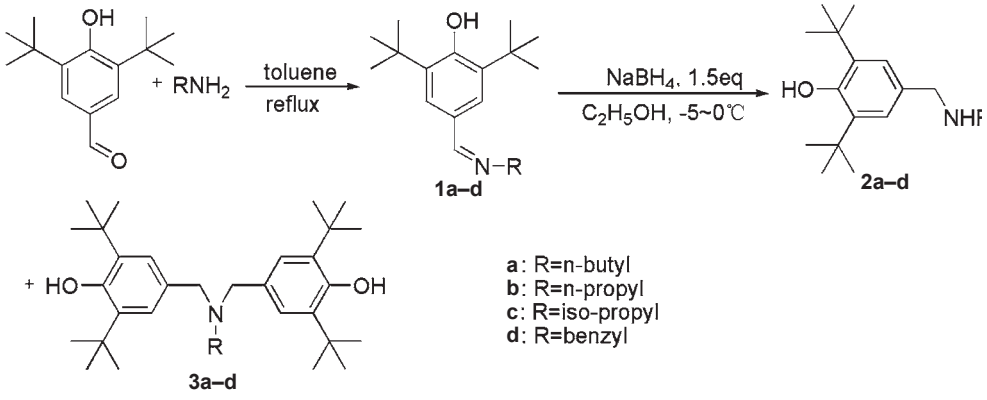


Fig. 1 Compounds with hindered phenol and/or hindered amine groups.



Scheme 1 The reduction of imines **1a–d**.

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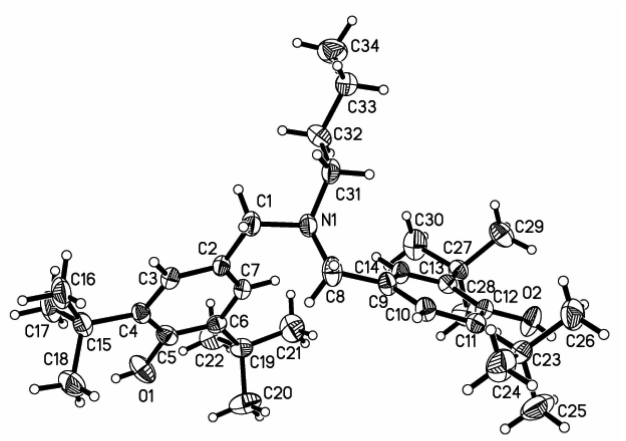


Fig. 2 The crystal structure of **3a**.

A series of different primary amines including *n*-propylamine, iso-propylamine and benzylamine were examined in this reaction the similar results were observed (as Table 1 showed).

Two experiments were designed to explore the transformation of compounds **2** to compounds **3**. The mixture of the pure imine **1a** (5 mmol) and the secondary amine **2a** (5 mmol) was stirred in dry ethanol at 20°C for 24 h, while in another experiment only the secondary amine **2a** (5 mmol) was stirred in dry ethanol under the same conditions. The result of the former experiment showed that although the tertiary amine **3a** was obtained, the imine **1a** was isolated quantitatively. However, in the latter experiment, compound **3a** was obtained in a yield of 34%.

When compounds **2b**, **2c**, **2d** were tested in the two experiments, the similar results were obtained. Thus we drew the conclusion that the tertiary amine **3** was obtained from the corresponding secondary amine **2**, instead of the reaction between the imine **1** and the primary amine **2**.

Hereby we propose the mechanism of this transformation as follows according to the experimental results and the structure characteristics of the hindered phenol derivatives (Scheme 2).

Experimental

Starting material obtained form J&K Chemical company. Melting point were determined by BKSPII apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz (Bruker AM), respectively. The high resolution mass spectra were recorded on a Fourier transform ion cyclotron resonance mass spectrometer (Bruker Apex). Toluene was distilled from CaH_2 and ethanol was distilled from Mg according to handbook.

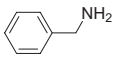
General procedure

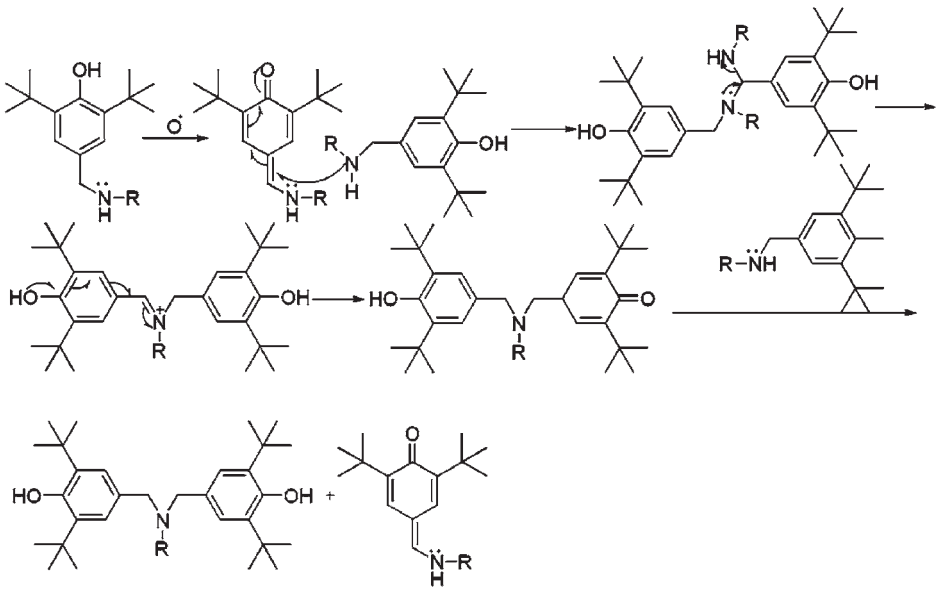
The imine (compound **1a**–**d**) 0.02 mol was dissolved in 100 ml dry ethanol and cooled to –5–0°C, the sodium borohydride (1.15 g, 0.03 mol) was added, the mixture was stirred for 0.5 h. Then 10 ml was added and the ethanol was evaporated. The product was extracted with ether (3 × 100 ml) and dried with $MgSO_4$ and ether was evaporated. The product was separated by silica gel flash column chromatography (petroleum ether/ethyl acetate = 10 : 1 (V/V)).

2,6-Di-tert-butyl-4-(butylamino)methyl-phenol **2a**: M.p. 36°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.92 (t, *J* = 7.2 Hz, 3H), 1.38 (m, 2H) 1.41 (s, 18H,), 1.51 (m, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 3.70 (s, 2H), 5.12 (s, 1H), 6.02 (s, 1H), 7.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.02, 20.53, 30.32, 32.13, 34.31, 49.38, 54.42, 124.89, 131.02, 135.82, 152.75. HRMS: C19H33NO calcd: 291.2562, found: 291.2564.

2,6-Di-tert-butyl-4-(propylamino)methyl-phenol **2b**: M.p. 47°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.92 (t, *J* = 7.2 Hz, 3H), 1.41 (s, 18H), 1.55 (m, 2H), 2.63 (t, *J* = 7.6 Hz, 2H), 3.44

Table 1 The results of the reduction of the imines **1a–d**

Entry	Amine	Product	Yield/%	Product	Yield/%
1a		2a	75.52	**3a**	20.8
1b		2b	73.5	**3b**	22.9
1c		2c	71.8	**3c**	23.6
1d		2d	78.5	**3d**	19.6



Scheme 2 The proposed mechanism of the transformation from compounds **2** to compounds **3**.

(s, 2H), 5.14 (s, 1H), 6.01 (s, 1H), 7.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 12.14, 20.56, 30.57, 34.57, 51.88, 55.07, 125.18, 131.20, 135.64, 153.01. HRMS: C18H31NO calcd: 277.2406, found: 277.2407.

2,6-Di-tert-butyl-4-(isopropylamino)methyl-phenol **2c**: M.p. 42°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.11 (d, J = 2.8 Hz, 3H), 1.13 (d, J = 1.6 Hz, 3H), 1.45 (s, 18H), 2.89 (m, 1H), 3.69 (s,2H), 5.12 (s, 1H), 5.99 (s, 1H), 7.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 23.15, 30.54, 30.63, 34.54, 48.65, 52.28, 125.10, 131.12, 136.06, 152.95. HRMS: C18H31NO calcd: 277.2406, found: 277.2408.

2,6-Di-tert-butyl-4-(benzylamino)methyl-phenol **2d**: M.p. 53°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.45 (s, 18H), 3.74 (s, 2H), 3.85 (s, 2H), 5.15 (s, 1H), 6.02 (s, 1H), 7.14 (s, 2H), 7.27 (t, J = 5.6 Hz, 1H), 7.34 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 30.60, 34.57, 53.48, 53.65, 125.21, 127.17, 128.49, 128.62, 131.06, 135.89, 136.05, 153.04. HRMS: C22H31NO calcd: 325.2406, found: 325.2407.

N,N-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-N-butylamine **3a**: M.p. 125°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.822 (t, J = 7.2 Hz, 3H), 1.32 (m, 2H), 1.44 (s, 36H), 1.52 (m, 2H), 2.40 (t, J = 6.8 Hz), 3.48 (s, 4H), 5.06 (s, 2H), 7.17 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.48, 20.76, 29.76, 30.77, 34.62, 53.28, 58.78, 125.46, 131.19, 135.68, 152.71. HRMS: C34H55NO2 calcd: 509.4233, found: 509.4235.

N,N-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-N-propylamine **3b**: M.p. 146°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.91 (t, 9.6 Hz, 3H); 1.43 (s, 36H), 1.54 (m, 2H), 2.35 (t, J = 7.2 Hz, 2H), 3.44 (s, 4H), 5.04 (s, 2H), 7.16 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 12.19, 20.56, 30.66, 34.51, 55.45, 58.57, 125.34, 131.09, 135.61, 152.61. HRMS: C33H53NO2 calcd: 495.4076, found: 495.4072.

N,N-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-N-isopropylamine **3c**: M.p. 139°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.07 (d, J = 5.2 Hz, 6H), 1.41 (s, 36H), 2.99 (s, 1H), 3.50 (s, 4H), 5.04 (s, 2H), 7.20 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.81, 30.64, 34.52, 48.23, 53.31, 124.91, 131.79, 135.58, 152.46. HRMS: C33H53NO2 calcd: 495.4076, found: 495.4082.

N,N-bis(3,5-di-tert-butyl-4-hydroxybenzyl)-N-benzylmine **3d**: M.p. 125°C (dec) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.45 (s, 36H), 3.48 (s, 4H), 3.53 (s, 2H), 5.06 (s, 2H), 7.19 (s, 4H), 7.21 (m, 1H), 7.30 (t, J = 6.4 Hz, 2H), 7.43 (d, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 30.63, 34.52, 58.03, 58.30, 125.39, 126.85, 128.30, 128.99, 130.59, 135.67, 140.69, 152.72. HRMS: C37H53NO2 calcd: 543.4076, found: 543.4073.

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References

1 S.A. Malaika, *Plastics Additives*., Chapman & Hall, London, 1998.
2 J. Barret. P. Gijsman. J. Swagten and R.F.M. Lange. *Poly. Deg. Stab*., 2002, **76**, 441.
3 J.T. Lai, *Tetra Lett*., 2001, **42**, 557.
4 T.H. Kim and D.R. Oh. *Poly. Deg. Stab*., 2004, **84**, 499.
5 I. Rossi, A. Venturini and A. Zedda. *J. Am. Chem. Soc.*, 1999, **121**, 7914.
6 I. Bauer, W.D. Habicher, S. Korner and S.A. Malaika. *Poly. Deg. Stab*., 1997, **55**, 217.
7 P. Gijsman. *Ploymer*., 2002, **43**, 1573.
8 T. Zeng, X.G. Shu, C.M. Dong and L.G. Chen. *Acta Crystal*, 2005, **E61**, o2999.
9 M.A. Silin, V.I. Kelarev, V.A. Ammar, D.K. Putkaradze and A. Golubeva. *Petroleum Chemistry.*, 2000, **40**, 209.
10 T. Kato, T. Ozakl, K. Tamura, Y. Suzukl, M. Aklma and N. Ohl. *J. Med. Chem.*, 1998, **41**, 4309.
11 Crystallographic data for the structures of compound **3a** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 292401. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: + 44(0)-1223-336033; or http: //deposit@ccdc.cam.ac.uk.