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Absolute rate constants for the reaction of peroxyl radicals with cardanol derivatives

Riccardo Amorati,[a] **Gian Franco Pedulli,***[a] **Luca Valgimigli,**[a] **Orazio A. Attanasi,***[b]
Paolino Filippone,[b] **Chiara Fiorucci**[b] **and Raffaele Saladino**[c]

[a] *Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Via S. Donato 15, I-40127 Bologna, Italy*
[b] *Istituto di Chimica Organica, Università di Urbino, Piazza Repubblica 13, I-61029 Urbino, Italy*
[c] *Unità INFM, Dipartimento di Agrobiologia e Agrochimica, Università della Tuscia, Via S. Camillo de Lellis, I-01100 Viterbo, Italy*

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Industrial grade cardanol is a yellow oil containing mostly cardanol with smaller percentages of cardol and methylcardol, obtained by thermal treatment and subsequent distillation of cashew nut shell liquid available in large amounts in some developing countries. In order to find useful applications of this widely available and renewable raw material in fine chemical processes we undertook a kinetic investigation of the antioxidant activity of some hydrogenated cardanol and cardol derivatives, compared with that of analogous commercial products.

Introduction

The shell of the cashew nut (*Anacardium occidentale* L.) contains an alkylphenolic oil internationally named "cashew nut shell liquid" (CNSL), which constitutes nearly 25% of the total weight of the nut.[1,2] This oil is composed of anacardic acid (3-*n*-pentadecylsalicylic acid), and smaller amounts of cardanol (3-*n*-pentadecylphenol), cardol (5-*n*-pentadecylresorcinol), and methylcardol (2-methyl-5-*n*-pentadecylresorcinol), the long aliphatic side-chain being saturated, mono-olefinic (8), di-olefinic (8, 11), and tri-olefinic (8, 11, 14) with an average value of two double bonds per molecule.[1,2] Since world-wide cashew nut production is nearly 500000 tons per year, CNSL is available in large amounts. It is a dark, tar-like and partially polymerized side-product, especially when derived from the most diffused roasted mechanical processing of the cashew nuts used because of the high edible value of the kernels.[3] CNSL may represent both a dangerous pollutant source, and a low-cost, widely available and renewable raw material for obtaining pure cardanol useful in fine chemical processes, particularly in the developing countries which produce the cashew nuts (India, Brazil).[3,4] In fact, thermal treatment of cashew nuts and CNSL induces the partial decarboxylation of anacardic acid, which is completed by the subsequent purifying distillation. The result is industrial grade cardanol, in the form of yellow oil containing cardanol (about 90%), with a smaller percentage of cardol and methylcardol.[2,5,6]

Considering the aforesaid, we previously dedicated our attention to the characterization, purification and stabilization of cardanol, as well as to some of its uses in the field of fine chemistry.[1,2,4–14]

In continuation of our previous investigations on this matter, we undertook the study of the antioxidant activity of some hydrogenated cardanol and cardol derivatives, compared with that of analogous commercial products.

Results and discussion

One of the more important parameters of the antioxidant power of a given phenol is the rate constant for its reaction with peroxyl radicals. In the present investigation the experimental values of this constant were obtained by studying the thermally initiated autoxidation of either styrene[15] or cumene in the presence of the antioxidant [eqns. (1)–(4)]. Measurements were

$$\text{Initiator} \xrightarrow{R_i} \text{R}^\bullet \qquad (1)$$

$$\text{R}^\bullet + \text{O}_2 \longrightarrow \text{ROO}^\bullet \qquad (2)$$

$$\text{ROO}^\bullet + \text{RH} \xrightarrow{k_p} \text{ROOH} + \text{R}^\bullet \qquad (3)$$

$$\text{ROO}^\bullet + \text{ROO}^\bullet \xrightarrow{2k_t} \text{Products} \qquad (4)$$

carried out in styrene in order to determine the rate constants of inhibition of the various antioxidants while cumene, which is characterized by a lower termination rate constant, $2k_t$, than styrene, was used for the determination of the stoichiometric factor n, *i.e.* the number of peroxyl radicals trapped by each molecule of antioxidant (*vide infra*).[16]

The autoxidation was followed by monitoring the oxygen consumption with an automatic recording gas absorption apparatus, built in our laboratory, using a commercial differential pressure transducer. The reactions (initiated by AIBN) were carried out under controlled conditions in air-saturated solutions of the oxidizable substrate (styrene or cumene) containing various amounts of the substituted cardanols. α-Tocopherol, BHT (2,6-di-*tert*-butyl-4-methylphenol), and DBHA (2,6-di-*tert*-butyl-4-methoxyphenol), were used as reference chain-breaking antioxidants.

Fig. 1A shows the oxygen consumption observed during the 2,2′-azobis(2,4-dimethylvaleronitrile) (AMVN)-initiated autoxidation of cumene at 30 °C, in the presence of the same amount of antioxidant (either α-tocopherol, α-TOH, or one of the cardanols **2**, **3**, and **4**). With all derivatives the change in the slope of the oxygen uptake traces occurs at similar times, this providing evidence that cardanols are characterized by the same stoichiometric factor (n = 2) of α-TOH, which is known to trap two peroxyl radicals [eqns. (5) and (6)]. Fig. 1B shows the

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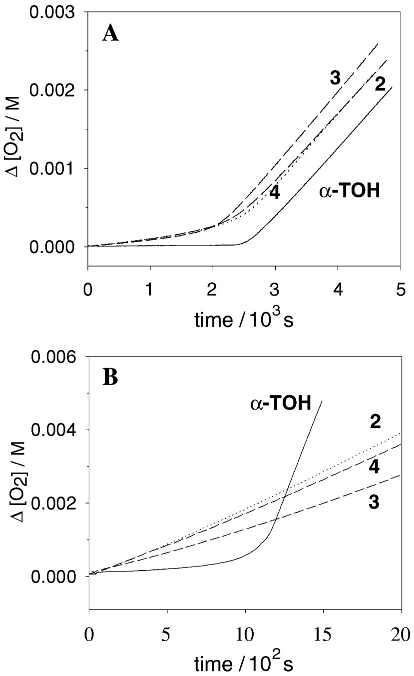

Fig. 1 Oxygen consumption observed during the autoxidation (**A**) of 7.1 M cumene initiated by 0.005 M AMVN at 30 °C in the presence of α-tocopherol (4.9×10^{-6} M) and of one of the cardanol compounds **2**, **3**, and **4** (each 4.9×10^{-6} M); and (**B**) of 8.2 M styrene initiated by 0.014 M AIBN at 50 °C in the presence of α-tocopherol (2.0×10^{-5} M) and of one of the cardanol compounds **2**, **3**, and **4** (each 2.0×10^{-4} M).

$$\text{ROO}^{\bullet} + \text{ArOH} \xrightarrow{k_{\text{inh}}} \text{ROOH} + \text{ArO}^{\bullet} \qquad (5)$$

$$\text{ROO}^{\bullet} + \text{ArO}^{\bullet} \longrightarrow \text{Products} \qquad (6)$$

oxygen consumption observed during the autoxidation of styrene in the presence of α-tocopherol and of each of the cardanols **2**, **3** and **4** at concentrations ten times larger than that of α-TOH. These plots indicate that the oxygen consumption is strongly inhibited by α-TOH during the initial reaction period, then, when the antioxidant has been completely consumed, the slope of the oxygen uptake trace increases, becoming identical to that observed in the absence of inhibitor (not shown). The length of the inhibition period τ provides the rate of chain initiation by AIBN, R_i, by means of eqn. (7).[16]

$$R_i = 2[\alpha\text{-TOH}]/\tau \qquad (7)$$

When carrying out the autoxidation reaction of styrene in the presence of each of the three cardanols **2**, **3**, and **4**, the oxygen uptake plots did not show a definite induction period but only a retardation of the autoxidation (see Fig. 1B). This indicates that not all the peroxyl radicals are quenched by the phenol, but some of them decay by self-termination. Thus, cardanols **2**, **3**, and **4** are much less effective antioxidants than α-tocopherol.

From the slope of the oxygen uptake traces recorded during the initial part of the autoxidation reaction, it also appears that **3** is a better inhibitor than both **2** and **4**. Since no definitive induction period was observed under these conditions with the cardanol derivatives, the values of the inhibition rate constants, k_{inh}, *i.e.* the rate constant for the reaction of peroxyl radicals with the antioxidant [eqn. (5)], could not be simply determined from the initial slopes of the oxygen uptake traces.[16] They were instead obtained either by the method proposed by Darley-Usmar *et al.*,[17] or by that developed by Denisov.[18] The former method consists of taking measurements at different antioxidant (AH) concentrations and analysing the data in order to achieve a composite rate constant k_{AH} given by eqn. (8).

$$k_{\text{AH}} = \frac{k_{\text{inh}}}{(2k_t\, R_i)^{1/2}} \qquad (8)$$

The calculation of k_{inh} from eqn. (8) requires the rate of initiation R_i, measured as described above by using α-TOH, and the rate constant of self-termination, $2k_t$, of the styrylperoxyl radicals at 50 °C, for which the value of 1.6×10^8 M^{-1} s^{-1} previously measured[19] by us was used.

The Denisov method consists of measuring the initial rates of oxidation of styrene both in the presence ($-\text{d}[\text{O}_2]/\text{d}t = R_{\text{ox}}$) and in the absence $\{(-\text{d}[\text{O}_2]/\text{d}t)_0 = R_{\text{ox},0}\}$ of antioxidant. The rate constant of inhibition, k_{inh}, could be obtained from these data by using eqn. (9), where the stoichiometric factor n was

$$\frac{R_{\text{ox},0}}{R_{\text{ox}}} - \frac{R_{\text{ox}}}{R_{\text{ox},0}} = \frac{nk_{\text{inh}}[\text{AH}]_0}{(R_i 2k_t)^{1/2}} \qquad (9)$$

assumed in all cases to be equal to 2 for similarity with **2**, **3**, and **4**.

The values of k_{inh} determined for a number of cardanol derivatives and for some related reference compounds are reported in Fig. 2. These constants are believed to be accurate to within 15%.

An examination of the data reported in Fig. 2 shows that the inhibition rate constants are very similar for the alkylated cardanol derivatives **2**–**4** and slightly greater than those measured for cardanol **1** and the commercial antioxidant BHT. The presence of phenyl substituents in the cardanol derivatives **5**–**7** seems to have no influence on the inhibition rate constant of the parent cardanol **1**. Cardanols brominated at the positions *para* and/or *ortho* to the hydroxy group show the lowest k_{inh} values in agreement with the reported effect of electro-negative substituents, which are known to depress the antioxidant activity of phenols.[20–22]

p-Hydroxylated cardanols (3-*n*-pentadecyl-1,4-hydroquinones) **12** and **13**, behaved instead as much better antioxidants, being characterized by inhibition rate constants which are about an order of magnitude larger than those of alkylated cardanols and quite similar to that of commercial specimen **11**. This is clearly due to the simultaneous presence of two OH groups in the ring, since it is well known that an oxygen substituent (hydroxy or alkoxy) in a *para* position to the phenolic hydroxy group strongly increases the reactivity of phenolic antioxidants towards peroxyl radicals.[20–22] A drawback of **11**–**13** is that, similarly to other hydroquinone derivatives,[23] they easily undergo autoxidation of the quinol moiety leading to the corresponding quinone. Indeed, unlike the other phenol derivatives of Fig. 2, which, in all cases where it was measured, showed stoichiometric factors [*i.e.* the number of peroxyl radicals trapped by one molecule of antioxidant, see eqns. (5) and (6)] of approximately two, compounds **11**–**13** showed stoichiometric factors lower than one. This means that the amount of hydroquinone available for antioxidant activity is considerably less than that originally introduced into the system, thus reducing the overall efficiency of hydroquinones as antioxidants.

Fig. 3 reports the data collected for several bis-phenols obtained from cardanol derivatives and for structurally similar commercial compounds. An examination of the data shows that compounds having both positions *ortho* to the OH group free of substituents are characterized by a modest antioxidant activity, while bis-phenols containing at least one bulky alkyl substituent in an *ortho* position have inhibition rate constants, k_{inh}, larger than 10^5 M^{-1} s^{-1}, and thus behave as good antioxidants. In the bis-phenol **18**, where the environment of the OH groups is only slightly crowded, a rate constant of 4.5×10^4

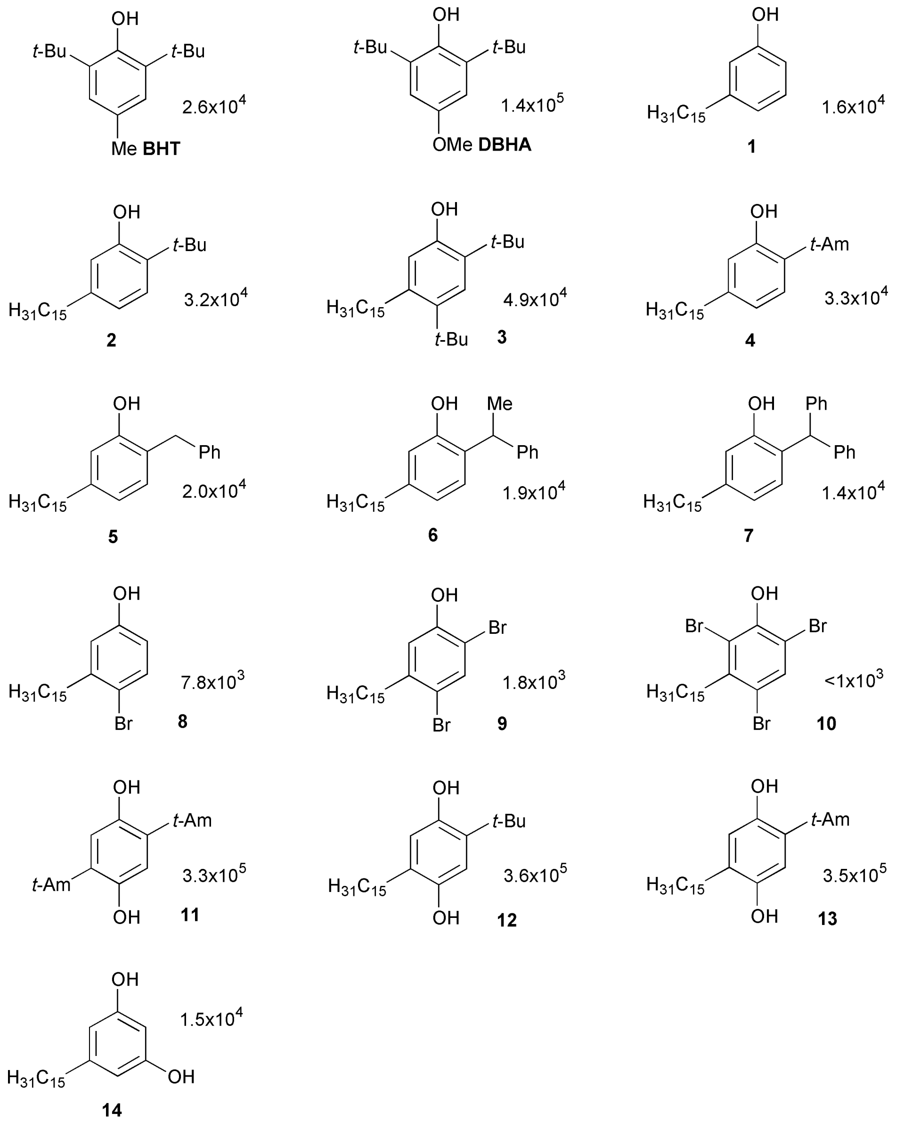

Fig. 2 Inhibition rate constants (M^{-1} s^{-1}) in styrene at 50 °C.

M^{-1} s^{-1}, *i.e.* intermediate between the above two extremes, was measured.

The *tert*-butylated thiobis-cardanol derivative **22** exhibits an inhibition rate constant considerably higher than that of the related cardanol derivative **21**, and quite similar to that of the commercial products **17** and **20**. An inhibition rate constant similar to those of the last two compounds is also exhibited by the *tert*-butylated dithiobis-cardanol derivative **24**, which in turn is a better antioxidant than cardanol **23**. An advantage of the *tert*-butylated thio- and dithio-bis-cardanol is the lower volatility with respect to the corresponding commercial materials, due to the long alkyl side-chain. Such a characteristic is very important in the antioxidative stabilization of some polymers because of the high temperatures at which the reticulation process is carried out (*ca.* 300 °C).[24,25]

On the average, bis-phenols are better antioxidants than structurally related mono-phenols and this larger activity cannot be explained solely on the basis of the more favourable statistical factor due to the presence of two OH groups in the same molecule. Presumably, cooperative effects between the hydroxy groups engaged in intramolecular hydrogen bonding both in the bis-phenols and in the corresponding aroxyl radicals are responsible for this behaviour. Further studies are in progress on some selected compounds in order to clarify this point.

Conclusions

The experimental results reported in this paper demonstrate that cardanol **1** represents a renewable, low-cost, and convenient alternative source of a number of products having good antioxidant properties. Therefore, this raw material may be of particular importance for the developing countries producing cashew nuts.

In principle, even better antioxidant properties could be obtained by substituting both positions *ortho* to the hydroxy group with bulky alkyl groups. Unfortunately, position 2 of the benzo ring of cardanol **1** is not easily accessible to bulky groups.

Experimental

Hydrogenated cardanol (3-*n*-pentadecylphenol) **1** and cardol (5-*n*-pentadecylresorcinol) **14** were kindly supplied by Oltremare SpA (Bologna, Italy). Compounds **11**, **15**–**17**, **19** and **20** were kindly supplied by Great Lakes Chemical Italia srl (Milano, Italy). Compounds **2**–**7** were synthesized by alkylation of hydrogenated cardanol with MTBE (*tert*-butyl methyl ether), MTAE (*tert*-amyl methyl ether), *tert*-butyl chloride or *tert*-amyl chloride in the presence of Lewis acid as previously reported.[9] Compounds **8**–**10** were synthesized by successive bromination with Br_2 of hydrogenated cardanol under different reaction conditions.[11] Compounds **12** and **13** were synthesized by catalytic oxidation of the hydrogenated cardanol derivatives with the system methylrhenium trioxide–hydrogen peroxide (MTO–H_2O_2) followed by quantitative reduction with sodium borohydride.[13] Compound **18** was synthesized according to the procedure described in a previous paper.[26] Compounds **21**–**24**

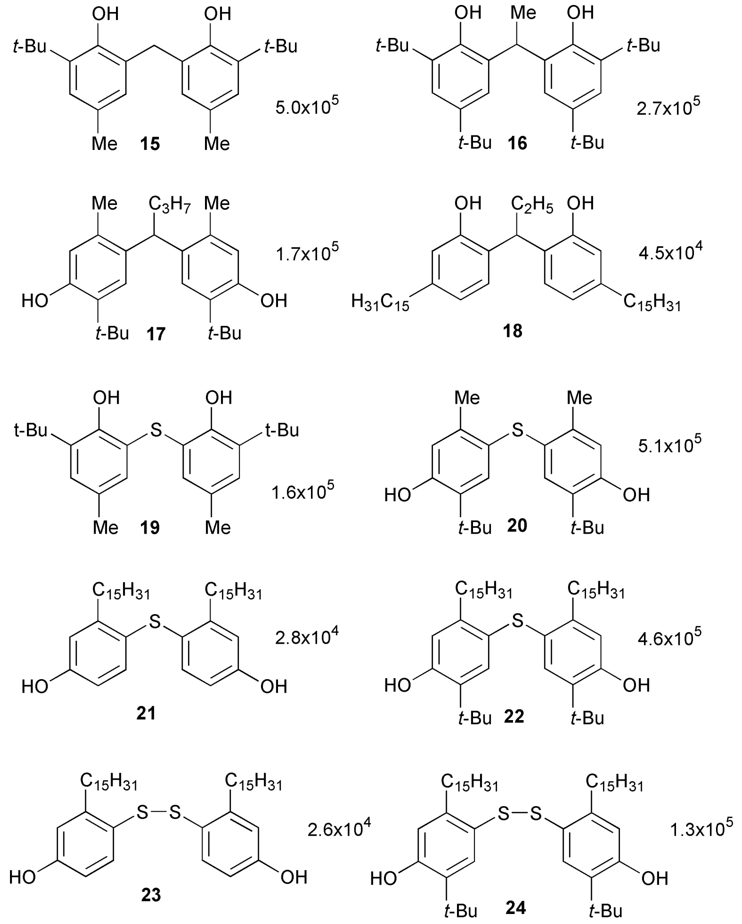

Fig. 3 Inhibition rate constants (M^{-1} s^{-1}) in styrene at 50 °C.

were synthesized by reaction of hydrogenated cardanol derivatives with SCl_2 or S_2Cl_2 as previously reported.[10]

Kinetic measurements

Autoxidation experiments were performed in a two-channel oxygen uptake apparatus, built in our laboratories, similar to that developed by Burton and Ingold[27] but optimized for low volume samples. The apparatus is based on a Validyne DP 15 differential pressure transducer interfaced to a Pentium II 200 MHz Personal Computer through a fast response (50 kHz) 14 bit A/D converter card (Validyne UPC card). Each channel of the transducer (sample and reference channels) was connected to a hand-made calibrated 1–5 ml round-bottomed flask, equipped with a three-way glass connector, through HPLC stainless steel low dead-volume junctions and 1/16 inch HPLC peek tubing (Varian). Equilibration between the two channels and between each channel and the outer atmosphere was regulated by a Varian HPLC three-way valve. Direct access to the sample and reference flasks was possible by means of a Hamilton syringe through the three-way glass connectors. The entire apparatus was set to have a total dead volume of *ca.* 5–8 ml (depending on the flasks employed) for each channel, under operative conditions. Sample and reference flasks were equipped with 2 magnetic micro-stirrers (H+P, Variomag®) whose speeds were synchronized by a digital control unit. The entire apparatus was immersed in a thermostatted bath (Haake DC1-W18), which ensured a constant temperature to within ±0.02 °C.

In a typical experiment an air saturated benzene solution of cumene (or styrene) containing the phenolic antioxidant (5×10^{-6} M to 1×10^{-4} M) was equilibrated with the reference solution containing an excess of α-tocopherol (1×10^{-3}–1×10^{-2} M) in the same solvent at 50 °C. After equilibration a concentrated benzene solution of AIBN (final concentration $1\text{–}10 \times 10^{-2}$ M) was injected into both the reference and sample flasks and the oxygen consumption in the sample was measured, after calibration of the apparatus, from the differential pressure recorded with time between the two channels. Initiation rates, R_i, were determined for each set of conditions in preliminary experiments by the inhibitor method using α-tocopherol as reference antioxidant: $R_i = 2[\alpha\text{-tocopherol}]/\tau$.[16]

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