Novel [2.2]paracyclophane derivatives via charge-transfer complexation

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The transannular electronic interactions in [2.2]paracyclophanes affect the selectivity of the tricyanovinylation reaction with tetracyanoethylene (TCNE). In addition to the normal *N*-tricyanovinyl product, 4-amino[2.2]paracyclophane reacts with TCNE to give oxaziridine derivatives. In the case of reaction with 4-*N*-methylamino[2.2]paracyclophane, the unusual *N*-tricyanovinylated product as well as 4-(*N*-carbonitrile-*N*-methyl)amino[2.2]paracyclophane was isolated. The reaction of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) with 4-amino[2.2]paracyclophane results in formation of 2-cyano-3-(4-[2.2]paracyclophanyl)amino-5,6-dichloro-1,4-benzoquinone.

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Les interactions électroniques transannulaires des [2.2]paracyclophanes affectent la sélectivité de la réaction de tricyanovinylation du tétracyanoéthylène (TCNE). En plus du produit *N*-tricyanovinyle normal, la réaction du 4-amino[2.2]paracyclophane avec le TCNE fournit des derivés oxaziridines. Dans le cas de la réaction avec le 4-*N*-méthylamino[2.2]paracyclophane, on a isolé le dérivé inhabituel *N*-tricyanovinylé ainsi que le 4-(*N*-carbonitrile-*N*-méthyl)amino[2.2]paracyclophane. La réaction de la 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) avec le 4-amino[2.2]paracyclophane conduit à la formation de la 2-cyano-3-(4-[2.2]paracyclophanyl)amino-5,6-dichloro-1,4-benzoquinone.

[Traduit par la rédaction]

Introduction

As part of a program designed to synthesize heterocyclics via charge-transfer (CT) complexation between heterocyclic compounds as electron donors and electron-deficient compounds as electron acceptors, we recently reported the synthesis of some interesting heterocyclic systems such as pyrazolopyrimidines (1), indanopyrazolopyrimidines (2), and pyrazoloquinazolines (3) via CT-complexation between pyrazole derivatives and tetracyanoethylene (TCNE), 2-(dicyanomethylen)indane-1,3-dione ((CNIND), as well as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), respectively.

One of the reasons for the continuing interest in the reactivity of [2.2]paracyclophane derivatives (4) is that their chemical behaviour differs considerably from that of classical aromatic systems (5–9).

In the present investigation, we turned our attention to 4-amino[2.2]paracyclophane (**1**) and its *N*-methyl derivative **5** as electron donors, aiming to shed more light on the impact of the transannular electronic interactions existing in the [2.2]paracyclophane nucleus on its behaviour towards TCNE and DDQ as π-acceptors. This aim can in principal be achieved by comparing the behaviour of the phane system with that of model compounds such as 2,5-dimethylaniline. 2,5-Dimethylaniline reacts with TCNE to give mainly the *N*-tricyanovinyl derivative (ca. 95%) (10). The attack of TCNE on the nitrogen atom of the free amino group is more favourable than on the carbon atom in the *para*-position, since the amino group is the more nucleophilic center.

Results and discussion

Interaction between 4-amino[2.2]paracyclophane (**1**) and TCNE in absolute ethyl acetate results in the formation of 4-*N*-tricyanovinyl-amino[2.2]paracyclophane (**2**), i.e., the expected product, 2-(4-[2.2]paracyclophanyl)-3,3-dicyanooxaziridine (**3**), and tetracyanoethane (**4**) (Fig. 1). It is worth noting that **3** is the first oxaziridine derivative formed by CT-complexation between TCNE and the primary aromatic amine. Figure 2 illustrates a plausible mechanism for its formation. This sequence shows initial formation of a CT-complex that absorbs at 620 nm followed by elimination of malononitrile, then addition of an H_2O molecule to the C=N bond followed by dehydrogenation by another molecule of TCNE, affording the oxaziridine derivative **3** and tetracyanoethane (**4**). The enhancement of formation of **2** and **3** may be explained as due to the transannular electronic interactions in 4-amino[2.2]paracyclophane (**1**), which tend to increase the nucleophilic character of the amino group through the donation of π-electrons from the unsubstituted half of **1** to the aminosubstituted half.

It has been reported that tertiary and secondary aromatic amines are tricyanovinylated at the *para*-position on reaction with TCNE (10). Using 4-*N*-methylamino[2.2]paracyclophane (**5**) as a secondary aromatic amine, the reaction with TCNE gave the unexpected *N*-tricyanovinylation product **6** as well as 4-(*N*-carbonitrile-*N*-methyl)amino[2.2]paracyclophane (**7**). The mechanism of formation of **7** is illustrated in Fig. 3, which indicates initial formation of a CT-complex (absorbing at 610 nm), followed by formation of *N*-tricyanovinylated intermediate **6**. Hydrolysis of **6** and elimination of one molecule of malononitrile from **14** results in formation of **7**. The formation of *N*-tricyanovinyl derivative **6** can be attributed to the effect of the transannular electronic interactions (see Fig. 4), which play an important role in increasing the electron-donating character of the nitrogen atom so that the electronic factor predominates with respect to the steric one. The structure of **6** is confirmed by the disappearance of the NH proton (IR, ^{1}H NMR spectra, cf. Experimental). (The NH proton in **5** appears as a multiplet at $\delta = 2.70–2.61$ ppm and ν(NH) ≈ 3325 cm^{-1} (11).)

The participation of moist air in formation of compounds **3** and **7** as illustrated in the proposed mechanism, in Figs. 2 and 3, was confirmed by adding both donors **1** and **5** to TCNE under nitrogen and dry conditions. Only stable CT-complexes were formed, which dissociate into their com-

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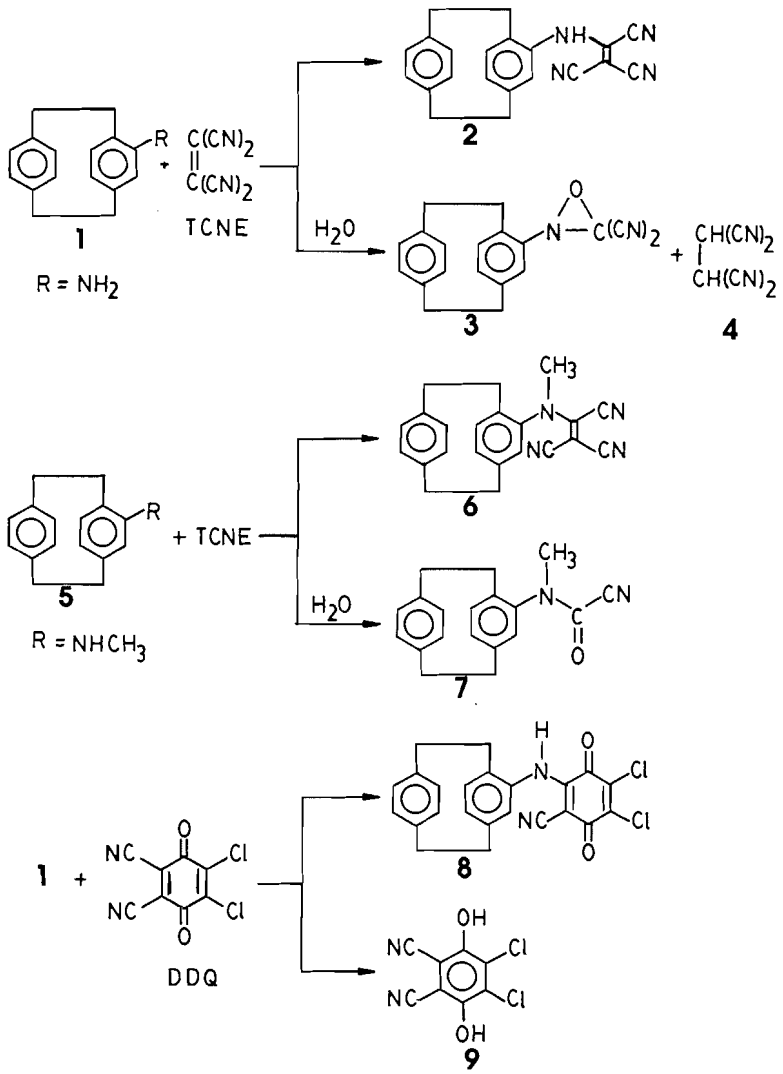

FIG. 1. Interaction of **1** and **5** with π-acceptors.

ponents after time and do not follow the given sequence of chemical reaction.

Addition of DDQ to **1** results in formation of a CT-complex (absorbing at 580 nm), accompanied by elimination of HCN, giving rise to the reaction product **8** in addition to DDQ-H_2 (**9**), as shown in Fig. 1. The proposed mechanism of formation of **8** and **9** is given in Fig.5.

In conclusion, the transannular electronic interaction existing in [2.2]paracyclophanylamines tends to change the mode of reaction with π-acceptors significantly as compared to normal aromatic amines; consequently, interesting and unexpected reaction products were obtained that cannot be easily prepared by conventional synthetic methods.

Experimental

Melting points are uncorrected. UV/vis: Perkin–Elmer Lambda 2 spectrophotometer. IR: Nicolet 320 FT-IR(KBr). ^{1}H and ^{13}C NMR: Bruker WM 400 (400.1 MHz). MS: Finigan 8430 at 70 eV. Elemental analyses: microanalytical unit at Cairo University.

Electron acceptors

Tetracyanoëthylene (Aldrich) was recrystallized from chlorobenzene and sublimed. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (Aldrich) was recrystallized from benzene–chloroform (2:3).

Electron donors

4-Amino[2.2]paracyclophane (**1**) and 4-*N*-methylamino[2.2]-paracyclophane (**5**) were prepared according to refs. 12 and 11, respectively.

Reaction of 4-amino[2.2]paracyclophane (1) with TCNE

A solution of **1** (0.223 g, 0.001 mol) in 10 mL of absolute ethyl acetate was added to a solution of TCNE (0.256 g, 0.002 mol) in 10 mL of absolute ethyl acetate and the reaction mixture was stirred for 48 h at room temperature. On concentration and chromatography on thin-layer plates (Merck Silica Gel 60 PF 254) using toluene – ethyl acetate (1:1), two zones were well separated. The first zone contained compound **2** and the second zone contained compound **3**. The base line of the tlc rechromatographed using toluene – ethyl acetate (1:2) contained the tetracyanoethane (**4**).

2: Yellow crystals, yield 41%, mp 204–206°C (toluene). IR (KBr), $\bar{\nu}$: 3445 (NH); 3100 (Ar-CH); 2900–2800 (Ali-CH); 2235, 2212 (CN); 1645 (Ar-C=C) cm^{-1}. ^{1}H NMR ($CDCl_3$), δ: 7.80 (s, br, 1H, NH), 6.75–6.48 (m, 6H, Ar-H), 6.18 (d, 1H, Ar-H), 3.45–2.70 (m, 8H, CH_2). ^{13}C NMR, δ: 142.60, 139.56, 138.78, 136.67, 134.62, 134.48, 134.22, 133.84, 132.13 (Ar-C=C, Ali C=C); 111.62, 111.36, 109.33 (CN); 35.08, 34.65, 34.43, 32.36 (CH_2). MS (70 eV), *m/z* (%): 324 [M^+] (16), 297 (6), 193 (10), 104 (100), 103 (16). Anal. calcd. for $C_{21}H_{16}N_4$ (324.38): C 77.76, H 4.97, N 17.27; found: C 77.60, H 4.95, N 17.30.

3: Yellow crystals, yield 31%, mp 289–291°C (toluene). IR

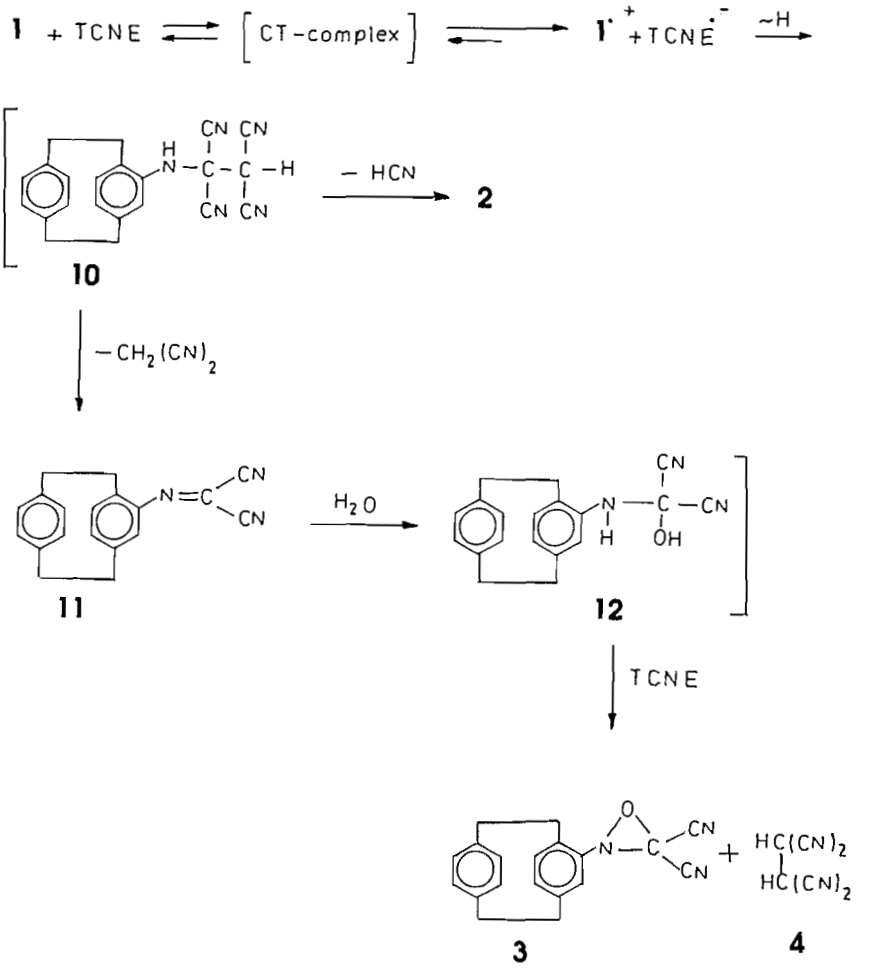

FIG. 2. Proposed mechanism for formation of **2** and **3**.

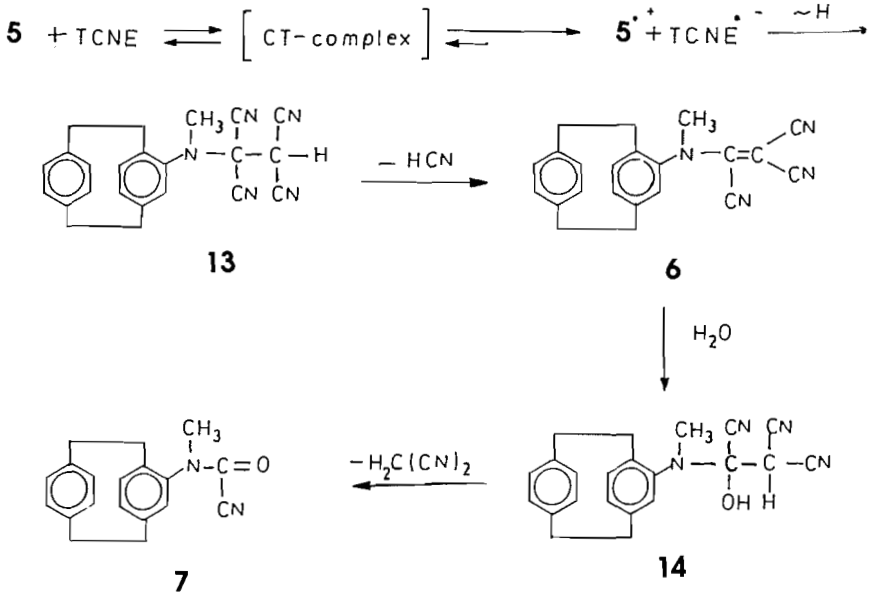

FIG. 3. Proposed mechanism for formation of **6** and **7**.

(KBr), $\tilde{\nu}$: 3162, 3138 (Ar-CH); 2961, 2935 (Ali-CH); 2241, 2225 (CN) cm^{-1}. ^1H NMR ($CDCl_3$), δ: 7.00–6.30 (m, 7H, Ar-H), 3.30–2.85 (m, 8H, CH_2). MS (70 eV), *m/z* (%): 301 (8) [M^+], 265 (68), 197 (10), 195 (22), 161 (100), 119 (82), 104 (72). Anal. calcd. for $C_{19}H_{15}N_3O$ (301.35): C 75.73, H 5.02, N 13.94; found: C 75.53, H 4.90, N 13.90.

4: The structure of TCNE-H_2 was established from comparison of its IR spectrum (which shows characteristic strong C—H ab-

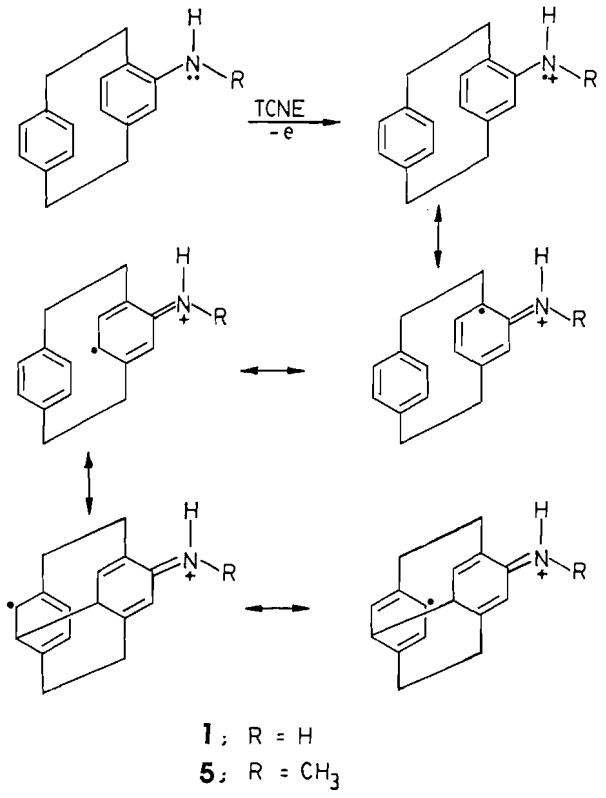

FIG. 4. Transannular electronic interactions in compounds **1** and **5**.

sorption at 2900 cm^{-1} and weak cyano absorption at 2260 cm^{-1}) and melting point with those of an authentic sample prepared according to ref. 13.

The reaction of 4-N-methylamino[2.2]paracyclophane (5) with TCNE

A solution of **5** (0.337 g, 0.001 mol) in absolute ethyl acetate (10 mL) was added to a solution of TCNE (0.256 g, 0.002 mol) in 10 mL of absolute ethyl acetate and the reaction mixture was stirred for 3 days at room temperature. The colour of the reaction mixture changed from blue to red after 48 h. Concentration of the mixture under reduced pressure and chromatography on thin-layer plates of Silica Gel 60 PF 254 using toluene – ethyl acetate (10:1) as eluent afforded two zones containing compounds **6** and **7** that were rechromatographed by successive elution with toluene.

6: Pink crystals, yield 28%, mp >360°C (ether – pet. ether). IR (KBr), $\bar{\nu}$: 2964–2926 (Ali-CH); 2213 (CN); 1597 (Ar-C=C) cm^{-1}. ^1H NMR ($CDCl_3$), δ: 6.90–6.50 (m, 7H, Ar-H), 3.80–2.80 (m, 8H, CH_2), 2.40 (s, 3H, $\geq$ N (CH_3)). MS (70 eV), *m/z* (%): 339 (10) [M^+], 338 (38), 324 (8), 234 (100), 208 (38), 104 (50). Anal. calcd. for $C_{22}H_{18}N_4$ (338.41): C 78.08, H 5.36, N 16.56; found: C 77.90, H 5.30, N 16.40.

7: Colourless crystals, yield 34%, mp 201–203°C (ethanol). IR (KBr), $\bar{\nu}$: 2958–2853 (Ali-CH); 2240 (CN); 1695 (CO) cm^{-1}. ^1H NMR ($CDCl_3$), δ: 6.80–6.36 (m, 7H, Ar-H), 3.20–2.90 (m, 8H, CH_2), 2.43 (s, 3H, $\geq$N (CH_3)). ^{13}C NMR, δ: 191.57 (CO), 139.53, 139.26, 136.48, 135.19, 133.35, 132.65, 130.92 (Ar-CH), 126.78 (C=N). MS (70 eV), *m/z* (%): 290 (90) [M^+], 263 (4), 186 (30), 185 (78), 104 (100). Anal. calcd. for $C_{19}H_{18}N_2O$ (290.36): C 78.60, H 6.25, N 9.65; found: C 78.45, H 6.20, N 9.60.

Reaction of 4-amino[2.2]paracyclophane (1) with DDQ

To a solution of DDQ (0.454 g, 0.002 mol) in 10 mL of absolute ethyl acetate, a solution of **1** (0.223 g, 0.001 mol) in 10 mL

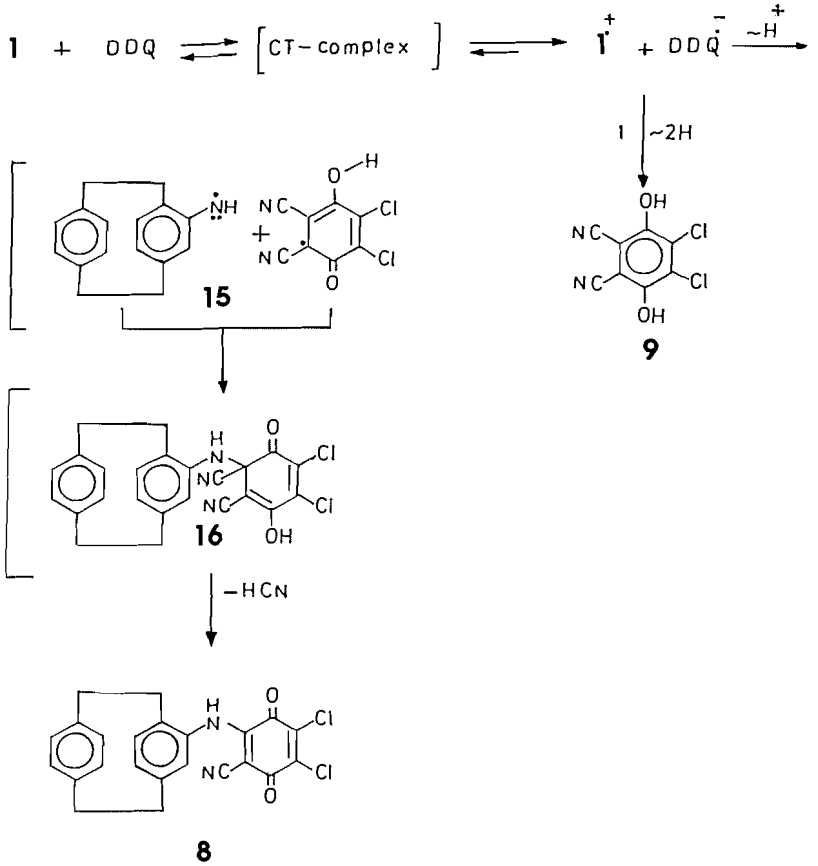

FIG. 5. Proposed mechanism for formation of **8** and **9**.

of absolute ethyl acetate was added. The reaction mixture was stirred for 72 h at room temperature. The colour of the reaction mixture changed spontaneously from blue to reddish brown. The solution was concentrated under reduced pressure and applied on chromatographic plates using toluene – ethyl acetate (1:1) as eluent. Two zones were well separated; the fastest migrating zone contained compound **8**, the slowest migrating zone (which is always characterized by quenching all indicator fluorescence upon exposure to 254-nm UV light) contained compound **9**.

8: Orange crystals, yield 47%, mp >360°C (ethanol). IR(KBr), $\bar{\nu}$: 3423 cm^{-1} (NH); 3009 (Ar-CH); 2931–2858 (Ali-CH); 2230 (CN); 1632 (Ar-C=C). ^1H NMR ($CDCl_3$), δ: 7.73 (s, br, 1H, NH), 7.10–6.20 (m, 8H, Ar-H), 3.80–2.60 (m, 8H, CH_2). MS (70 eV), *m/z*(%): 424 (100) [M^+], 423 (26), 422 (68), 396 (48), 364 (84), 337 (58), 104 (12). Anal. calcd. for $C_{23}H_{16}N_2O_2Cl_2$ (423.30): C 65.26, H 3.81, N 6.62; found: C 65.35, H 3.80, N 6.60.

9: Was identified by comparing its physical properties with that of an authentic sample.

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