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Acidic properties of *N*,*N*-naphthoquinonylamines

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Abstract—The new system in which two naphthoquinonic moieties are bridged via a NH group shows acidic properties due to its vinylogous-imide nature. In the dichloro derivative (BClNQA) strong mesomeric and inductive effects result in unusually high acidity. Its pK_a value in methanol is equal to 7.51 ± 0.02, which is several orders of magnitude lower than that of normal aliphatic or aromatic imides or even aliphatic carboxylic acids. The new system can form stable salts with various organic bases (e.g. triethylamine). The chromophoric nature of BClNQA and its anion is expressed by a dramatic bathochromic shift of its λ_3 in polar solvents from the orange (441–473 nm) to the blue region (608–624 nm). This unusual red shift is due to substantial polarization of the quinonic system and delocalization of its anionic form. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

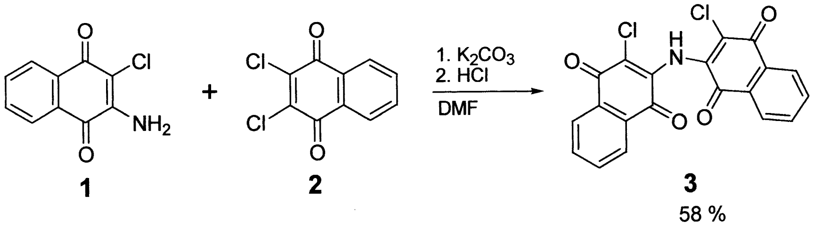
Development of dyes which are small in molecular size but produce intense colors is of interest because of their potential use in guest–host liquid-crystal displays, dye diffusion thermal transfer systems, optical recording systems, and more.[1,2] Although unsubstituted quinones emit virtually no light in the visible region[3] the introduction of a donor either with or without an additional acceptor into the quinone nucleus shifts absorption to the visible and even to the near-infrared region. 1,4-Naphthoquinones and 9,10-anthraquinones[4] are the main chromophores for the quinonic colorants. 1,4-Naphthoquinone derivatives are particularly interesting as intensely colored dyes, but find fewer applications than with 9,10-anthraquinones, because of their instability and difficult synthesis. It has been found that donor-substituted naphthoquinones, such as condensed naphthoquinone amines[5] absorb at much longer wavelengths than the corresponding anthraquinone amines.[6] It was logical to assume that connecting two naphthoquinone moieties to one amino group[7,8] will create materials exhibiting a significant bathochromic shift. Indeed, we lately reported the synthesis (Scheme 1) and spectroscopic properties of various symmetrical and non-symmetrical *N*,*N*-bisquinonyl amines and observed a strong red shift.[8]

In the present paper we would like to report on the solvent dependent acid–base equilibrium of *N*,*N*-bis-(3-chloro-1,4-naphthoquinon-2-yl)-amine 3 (BClNQA) as observed by UV–Vis spectroscopy. As this aminoquinone derivative is a vinylogous-imide, we expected it to show acidic properties. Acidity constants are of vital importance in the analysis of drugs as well as in interpretation of their mode of action.[9–10] We determined its exact pK_a by a spectrophotometric method,[11–12] compared it to ionization constants of known imides[13] and studied the properties of its ammonium salt. We also studied the nature of both BClNQA and its anion by ab initio methods.[14,15]

2. Result and discussion

2.1. UV–Vis properties of BClNQA

Absorption spectral data for *N*,*N*-bis-(3-chloro-1,4-naphthoquinon-2-yl)-amine (BClNQA) are shown in Fig. 1A and B.



Scheme 1.

Keywords: *N*,*N*-naphthoquinonylamines; acid–base equilibrium; pK_a.

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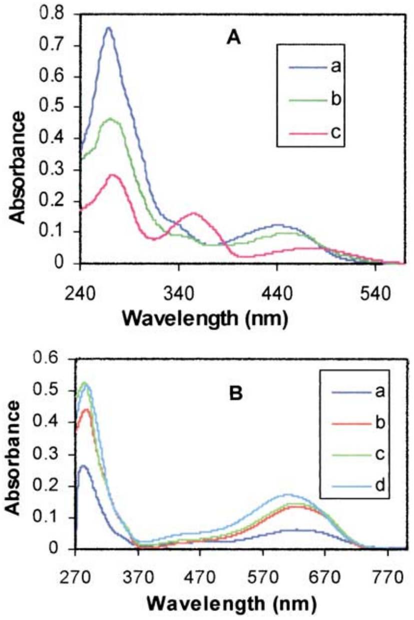


Figure 1. UV–Vis spectra of BClNQA in different solvents: (Aa—ether; Ab—MeOH+HCl_{aq}; Ac—chloroform; Ba—*n*-BuOH; Bb—DMSO; Bc—DMF; Bd—MeOH).

Table 1. UV–Vis spectrometry data of the *N*,*N*-bis-(3-chloro-1,4-naphthoquinon-2-yl)-amine in different solvents

Solvent	ε	λ_1 (nm)	log ε_1	λ_2 (nm)	log ε_2	λ_3 (nm)	log ε_3
Ether	4.2	269	4.78	338	4.00	441	3.98
MeOH+HCl		269	4.55	339	3.93	458	3.90
$CHCl_3$	4.7	272	4.35	355	4.10	473	3.59
n-BuOH	17.2	282	4.32	451	3.24	624	3.69
DMSO	45.0	288	4.55	450	3.25	623	4.03
DMF	36.7	284	4.62	450	3.27	624	4.06
MeOH	32.6	288	4.61	446	3.59	608	4.14

In non-polar aprotic solvents, e.g. diethyl ether (Fig. 1Aa) or chloroform (Fig. 1Ac), it shows three electronic transitions. A strong quinonoid π–π^* transition (λ_1) is observed at about 270 nm (Table 1). An allowed π–π^* transition (λ_2) band appears at about 350 nm. The third π–π^* quinonoid transition (λ_3) typical to amino substituted quinones[16] is observed around 441–473 nm.

A dramatic bathochromic shift of the three transitions and the development of an intense blue color is observed in polar solvents, e.g. *n*-butanol (a), DMSO (b), DMF (c), and methanol (d) (Fig. 1B). While the short UV absorption shows only a small red shift (about 16 nm), the longer UV absorption shows a much stronger shift (about 100 nm) and a very strong red shift is observed for the visible transition (about 160 nm) (Table 1). This unusual red shift of λ_3 from the orange (441–473 nm) to the blue region (608–624 nm) implies major structural and electronic changes.

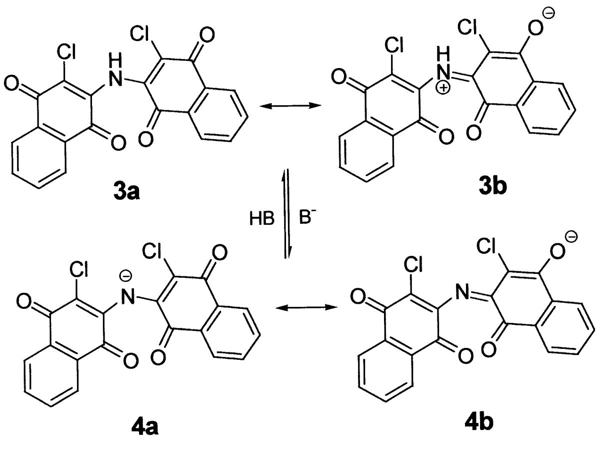
Indeed, upon acidification of the blue methanolic solution with aqueous HCl, the orange color reappears (Fig. 1Ab) and the spectrum becomes identical to the one obtained in diethyl ether. It seems that in polar solvents dissociation of BClNQA takes place to yield the stable, solvated blue anion. It is obvious that the nature of the solvent plays an important role in the acid–base equilibrium, and polar solvents grant substantial polarization to the quinonic system and stabilize the anionic form (Scheme 2).

A correlation can also be seen between the extinction coefficients of the long wavelength band (log ε_3) and the dielectric constant of the solvent (Table 1). Thus, in the nonprotic low dielectric solvents e.g. diethyl ether (ε=4.2) or chloroform (ε=4.7) the extinction coefficient are relatively small (log ε_3=3.98 and 3.59, respectively). In the nonprotic high dielectric solvents e.g. DMF (ε=36.7) or DMSO (ε=45.0) higher coefficients are obtained (log ε_3=4.06 and 4.03, respectively). A similar effect can be observed with the protic solvents. Thus, methanol (ε=32.6) shows log ε_3=4.14 while *n*-butanol (ε=17.1) gives only log ε_3=3.69. Besides supporting ionization, methanol can also stabilize the BClNQA anion via hydrogen bond formation, which explains the larger coefficient in this solvent compared to that obtained in DMSO.

2.2. Molecular modeling

To determine the nature of BClNQA anion, the ground state geometries of BClNQA (Fig. 2A) and its anion (Fig. 2B) were studied by McSpartan PRO ab initio program.

The orbital coefficients for the HOMO levels and the bond lengths for both acidic and basic forms were calculated. Calculated bond lengths of BClNQA (entry 3* in Table 2) were compared to data obtained by X-ray[8] (entry 3 in Table 2) to that of 2-amino-3-chloronaphthoquinone 1[17] and to that of naphthoquinone (NQ)[17] itself. It can be seen that all the C═O bond lengths in BClNQA are around 1.22 Å, which is the normal quinonic bond length. The C_2–N_1 and



Scheme 2.

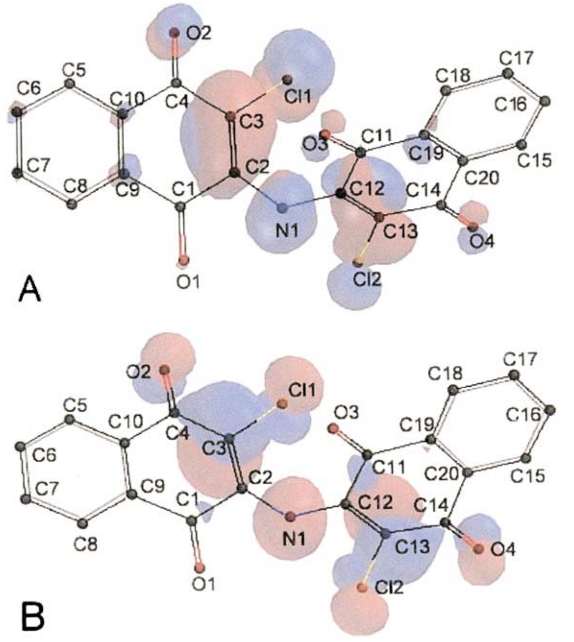


Figure 2. Highest occupied molecular orbital for BClNQA (A) and BClNQA anion (B).

C_{12}–N_1 bond lengths are 1.37 and 1.40 Å, which compares well with N–Csp_2 bonds. By comparing other bond distances of NQ, 1 and 3, it can be concluded that BClNQA is best presented as a bis-quinonic structure (Scheme 2, 3a) with very little contribution of the quinonoiminic structures (Scheme 2, 3b).

A different picture is obtained for the calculated dimension of the anionic form of BClNQA (entry 4^* in Table 2). Both C_2–N_1 and C_{12}–N_1 bonds are shorter by 0.08 Å compared to the nonionized compound. The double bonds $C_2{=}C_3$ and $C_{12}{=}C_{13}$ are longer, while C_3–C_4 and C_{13}–C_{14} bonds are shorter than in 3^*. The appropriate C=O groups are also somewhat longer. All this indicates a larger contribution of the quinonoiminic resonance structures (Scheme 2, 4b) to the real nature of the anion.

2.3. Determination of pK_a

The acidic properties of BClNQA result from its unique structure, in which an NH group is bridged from both side to a quinonic carbonyl via a double bond. Consequently, the NH group is a vinylogous imide and is expected to display imidic behavior, similar to that of phthalimide or succinimide. The acidity of this novel compound results mainly from the mesomeric effect of its anion. In addition, the two chlorine atoms might exert their strong electron withdrawing inductive power thus stabilizing further the anionic form and increasing the acidity of BClNQA. In view of the uniqueness of this novel system it was interesting to determine its exact acidity constant. The compound is poorly soluble in water, thus the determination was performed in methanol using a known spectrophotometric method. UV–Vis spectra of BClNQA at varying pH values in methanol are shown in Fig. 3. The shorter wavelength band (456 nm) that is observed at low pH values is due to the non-ionized acidic form of BClNQA, while the longer wavelength band (608 nm) represents the absorption of the anionic form. The appearance of sharp isosbestic points in the spectra indicates that only the two species (i.e. BClNQA and its anion) are in equilibrium under the experimental conditions.

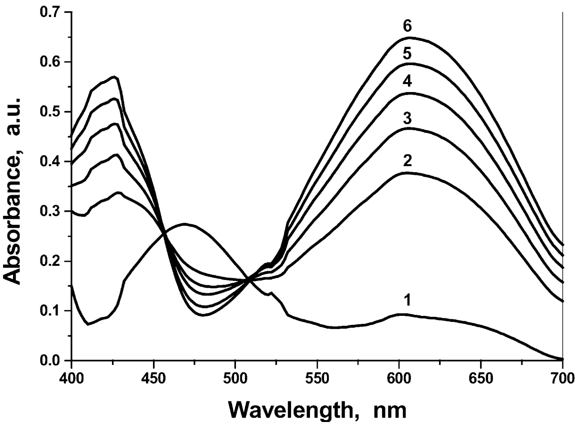


Figure 3. Absorption spectra of BClNQA in methanolic solution at different pH values: (1) acidic; (2) 7.46; (3) 7.87; (4) 8.13; (5) 8.54; (6) basic.

The pK_a value was evaluated by computer fitting of the absorbance-pH data to Eq. (1) that resulted from substituting the pH and absorbance values in the mass balances.[11,12]

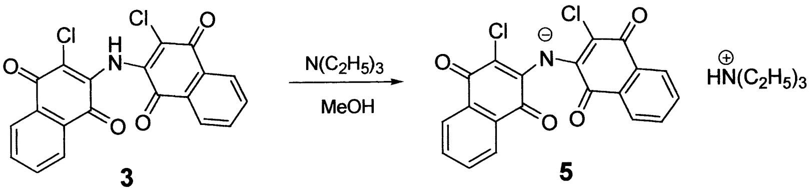
$$pK_a = \text{pH} + \log(A_i - A_1)/(A_0 - A_i) \quad (1)$$

In this equation, A_0, A_1, and A_i are integrals of the absorbance spectra ($\int A_k(\lambda)d\lambda$ k=0,1,i) observed in the range 400–700 nm at each titration point. A_0 and A_1 are the integrals of absorbance spectra of the anionic and acidic forms, respectively. By this simple calculation, it has been found that the pK_a value of BClNQA in methanol is equal to 7.51±0.02. This was a surprising finding which bestows unusualy high acidity on this compound. It is much more acidic than normal imides, thus the pK_a value (in methanol) of phthalimide is 14.5 and of succinimide is 14.1.[13] The acidity of BClNQA is even higher than that of acetic acid (9.52), phenol (14.0) or stearic acid (10.0).[18] Its acid strength is somewhat higher than that of salicylic acid (8.7) and equals to that of 2-nitrobenzoic acid (7.6).[18]

Table 2. Bond distances (Å) of 1,4-naphthoquinone, NQ; 2-amino-3-chloro-1,4-naphthoquinone, 1; BClNQA, 3; BClNQA 3^* and BClNQA anion 4^*

	N_1–C_2	C_2–C_3	C_3–C_4	C_4–O_2	C_1–C_2	C_1–O_1	N_1–C_{12}	C_{12}–C_{13}	C_{13}–C_{14}	C_{14}–O_4	C_{11}–C_{12}	C_{11}–O_3
NQ	–	1.34	1.48	1.22	1.48	1.22	–	–	–	–	–	–
1	1.36	1.35	1.49	1.24	1.49	1.23	–	–	–	–	–	–
3	1.37	1.35	1.48	1.22	1.49	1.21	1.40	1.36	1.46	1.23	1.49	1.22
3^*	1.37	1.33	1.48	1.21	1.51	1.21	1.39	1.33	1.48	1.21	1.50	1.21
4^*	1.30	1.37	1.43	1.23	1.52	1.21	1.31	1.36	1.43	1.23	1.52	1.21

NQ, 1: according to X-ray data;[17] 3: according to X-ray data;[8] 3^*, 4^*: due to ab initio computation using MacSPARTAN PRO.



Scheme 3.

This high acidity of the bisquinonyl must be attributed to its unique structure, the equivalent mesomeric forms of the anion and the strong inductive effect of the two chlorine atoms.

2.4. Spectroscopic properties of BClNQA triethylamine salt

Being a strong acid, BClNQA is able to form crystalline salts with inorganic bases as well as with organic amines. Thus, it reacts spontaneously with triethylamine to yield blue crystals of the triethylammonium salt (Scheme 3).

This triethylammonium salt is unusual in the sense that it is formed from a nitrogenous cation and a nitrogenous quinonic anion. As expected, its UV–Vis spectrum shows a pattern similar to that of anionic BClNQA with λ_2 at 426 nm and λ_3 at 608 nm. In the FT-IR spectrum the carbonyl absorption frequencies (1648 and 1667 cm^{-1}) are lower by about 10 cm^{-1} compared with BClNQA itself (1657 and 1677 cm^{-1}). This shift is attributed to the strong conjugation with the iminic group. The ^{1}H NMR spectrum shows two four-spin systems characteristic of two different *ortho*-disubstituted naphthalenic groups. The four hydrogens H(C5), H(C15) and H(C8), H(C18) (Fig. 2B) show chemical shifts at 8.18 and 8.02 ppm, respectively and appear as two double doublets. The four protons H(C6), H(C16) and H(C7), H(C17) show chemical shifts at 7.78 and 7.70 ppm, respectively, which appear as two double triplets resulting from two overlapping *ortho* as well as *meta* splittings. While these chemical shifts and splittings of the eight naphthalenic protons of the salt are similar to those of BClNQA itself, the NH signal is significantly shifted upfield from 7.08 to 5.99 ppm. In addition, a quartet at 2.66 ppm and a triplet at 1.10 ppm represent the three ethyl groups. The aromatic carbon patterns in the ^{13}C NMR resembles those of the parent molecule, but a profound difference is observed in the shifts of the quinonic carbons. Thus the signals of the carbons attached to nitrogen C2 and C12 shifts from 142.5 ppm for BClNQA to 152.8 ppm for its salt. This shift results from the change in bond nature (C=C to C=N) (Scheme 2). The signal of the carbons C3 and C13 attached to the chlorines, shifts from 124.9 to 116.2 ppm. This upfield shift is due to delocalization of the negative charge, which increases the electron density on chlorine substitued carbon atoms. The same effect results in a small upfield shift of the carbonyl carbons C4 and C14 from 176.9 to 175.0 ppm. However, there are no changes in the chemical shifts of C1 and C11 carbonyl carbons (178.9 ppm in both molecules) which proves non-participation of these carbonyls in the delocalization of the negative charge. All these spectroscopic results are in good correlation with the molecular modeling calculations and proves delocalization of the charge as described in Fig. 2.

3. Conclusions

The attachment of two naphthoquinonic moieties to ammonia leads to the formation of a new system, which shows unique and unusual properties. In the dichloro derivative (BClNQA) both the mesomeric effects of this vinylogous imide and the strong inductive effects of the chlorine atoms contribute to the high acidity of the compound. Its pK_a value in methanol is several orders of magnitude lower than that of normal aliphatic or aromatic imides and it is even a stronger acid than aliphatic carboxylic acids. Its acidity can be expressed by facile formation of stable salts with various organic bases e.g. triethylamine. The unusual chromophoric nature of BClNQA is expressed by a dramatic bathochromic shift (more than 160 nm) in polar solvents. Substantial polarization of the quinonic system and delocalization of the anionic form produces a system having pronounced *o*-quinone–imine character. We are currently preparing new dyes, derivatives of *bis*-quinonylamines, which will absorb in the near-infrared region for electro-optical applications.

4. Experimental

4.1. Materials and methods

All chemicals and reagents are commercially available. The synthesis of *N*,*N*-Bis-(3-chloro-1,4-naphthoquinon-2-yl)-amine was described by us previously.[7]

Spectrophotometric grade methanol, analytical grade butanol, chloroform, DMSO, DMF, diethyl ether, and triethylamine (Aldrich) were used as received. Tetrabutylammonium perchlorate (TBAP) (Fluka), succinic acid, oxalic acid and lithium hydroxide (Aldrich) were dried for 72 h. The electronic spectra were recorded on a UV–Vis Spectrophotometer Jasco V-560. Measurements of pH were carried out with Accumet Model 20 of Fisher Scientific pH/conductivity meter using a combined electrode. FT-IR spectrum (KBr) was recorded on a Nicolet 5 ZDX FT-spectrophotometer. ^{1}H and ^{13}C NMR spectra were performed on Bruker DMX 200 instrument, with tetramethylsilane as internal standard. Coupling constant (*J*) are given in Hz. Mass spectra (CI in isobutane) were obtained using a Finnigan 4020 quadropole mass spectrometer. Elemental analysis was obtained from the microanalytical laboratory of the Hebrew University, Jerusalem.

The melting point was determined using a Thomas–Hoover capillary apparatus and is uncorrected.

4.2. Acid–base equilibrium and spectrophotometric method for acidity constant determination

UV–Vis spectra of BClNQA (1.25×10^{-5} M) in butanol, chloroform, DMSO, DMF, diethyl ether and methanol were recorded. For the measurements in MeOH/HCl, 10 μl of concentrated HCl_{aq} were added to the methanolic solution of BClNQA (10 ml). The modified form of the procedure, introduced by Albert et al.[11] was used to determine the acidity constant. The absorbance of a solution with fixed concentration of BClNQA in methanol (8×10^{-5} M) was measured in highly acidic and highly basic solutions. Acidic conditions were achieved by adding glacial acetic acid (10 μl) to BClNQA (10 ml) in methanol. Basic conditions were achieved by adding triethylamine (10 μl) to methanolic BClNQA (10 ml). The absorbency of protonated and anionic forms of BClNQA in the range 400–700 nm was measured vs pH, while the solution was titrated with triethylamine using a precalibrated micropipet. All the pH values are expressed in terms of activity. The ionic strength of the solutions was kept constant using 0.1 M TBAP. To calibrate the pH meter, methanolic solution of oxalate and succinate (0.01 M) buffers were employed.[19]

4.3. Computational details

Density functional calculations were carried out with the MacSPARTAN PRO ab initio Program, and a standard RHF/3-21G basis set was chosen. During geometry optimization, no symmetry constraints were applied. Calculations of open shell systems, were performed using separate orbitals for α and β electrons as in the unrestricted Hartree–Fock formalism (UHF).

4.4. Synthesis of triethylammonium salt of *N*,*N*-bis-(3-chloro-1,4-naphthoquinon-2-yl) amine

1.985 g (50 mmol) of BClNQA was suspended in methanol (50 ml) and an excess of triethylamine (4 ml) was added. A spontaneous reaction took place and the solution turned dark-blue. The solvent and excess of triethylamine were evaporated in vacuo and the product was dried over KOH for 48 h. The salt was recrystallized from chloroform to yield 2.17 g (87%) of dark-blue needles decomposing at 262–264°C. (Found: C, 62.73; H, 4.89; Cl, 14.58, N, 5.88 $C_{26}H_{24}Cl_2N_2O_4$ requires C, 62.66; H, 4.65; Cl, 14.23; N, 5.62%). IR ν (KBr) (cm^{-1}): 2979, 1667, 1648; ^{1}H NMR δ (200 MHz): 1.10 (t, 9H, J=7.2 Hz), 2.66 (q, 6H, J=7.2 Hz), 5.99 (br s, NH), 7.70 (dt, 2H, J=7.4, 1.5 Hz), 7.78 (dt, 2H, J=7.4, 1.6 Hz), 8.02 (dd, 2H, J=7.0, 1.6 Hz), 8.18 (dd, 2H, J=7.6, 1.8 Hz). ^{13}C NMR δ (50 MHz) (numbering of the carbons according to Fig. 2b) 11.2 (CH_3), 45.7 (–CH_2–N), 116.2 (C-3 and C-13), 125.8 (C-6 and C-16), 127.2 (C-7 and C-17), 130.8 (C-9 and C-19, C10 and C20), 131.5 (C-5 and C-15), 134.0 (C-8 and C-18), 152.8 (C-2 and C-12), 175.0 (C-4 and C-14), 178.9 (C-1 and C-11). UV–Vis λ_{max} (nm, log ε): 290 (4.17), 426 (3.89), 608 (3.93). MS (*m/z*): 398 (25), 362 (100), 99 (13).

Acknowledgements

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