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ARTÍCULO DE REVISIÓN

Practical use of aluminium oxide in chromatographic purifications

Uso práctico del óxido de aluminio en purificaciones cromatográficas

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Recibido el 27 de noviembre de 2025; aceptado el 28 de noviembre de 2025

KEYWORDS

Silica gel
Alox chromatography
Brockmann grades
Deactivatio

ABSTRACT

The chromatographic purification on silica gel of complex mixtures can pose several issues for chemists (e.g. degradation or racemization). Switching to aluminium oxide as the stationary phase could be a strategically successful choice. Herein, some practical advice for its effective use is disclosed.

PALABRAS CLAVE

Gel de sílice
Cromatografía Alox
Grados Brockmann
Desactivación

RESUMEN

La purificación cromatográfica en gel de sílice de mezclas complejas puede plantear varios problemas para los químicos (por ejemplo, degradación o racemización). Cambiar a óxido de aluminio como fase estacionaria podría ser una elección estratégicamente exitosa. En este artículo se revelan algunos consejos prácticos para su uso efectivo.

DOI:https://doi.org/10.53519/analesranf.

The isolation of organic compounds either after chemical synthesis or extraction from natural sources constitutes a critical procedure for obtaining materials of adequate purity for subsequent studies or analysis (1). As well known, the chemical structure of substances plays a key role in selecting the method for accomplishing the purification. In this sense, chromatographic based techniques employed in academic and industrial laboratories are preferentially accomplished on silica gel (of various particle size) which – due to the intrinsic acidity of the constitutive Si-OH groups – might affect the chemical integrity of the components of the mixture to be purified (2). In some instances, not only molecular modifications can be triggered by silica gel, but also racemization phenomena on stereochemically defined entities may occur (3). Preliminary – somehow effective solutions to the problem – can be ascribed to the so-called "silica deactivation" methods consisting in pre-treating the stationary phase with an organic base (e.g. triethylamine) or a silylating agent (e.g. trimethylsilyl chloride), approximatively in 1-5% v/v (4). This is, upon adding these species to the selected eluent, the prepacked silica column is flushed once or twice with this solvent system prior to commence the column. This protocol has been successfully validated in several instances and features the objective advantage of differing from a canonical silica gel chromatographic purification for simply requiring an additional component to the selected eluent.

However, as documented in studies dealing with the obtainment of silica-sensitive substances, pre-treating this stationary phase could not suffice to the purpose. This is, the chemical environment in which the chromatography is performed may maintain some reactivity, ultimately leading to the degradation of the mixture's components. Moreover, it should be noted that including a deactivating agent in the eluent system could alter the effectiveness of the purification, thus increasing the risk of recovering contemporaneously two (or more) components: in other words, no separation is achieved!

As mentioned above, the change of the nature of the chemical interaction between the stationary phase and the mixture object of separation may constitute an effective alternative. In this sense, aluminium oxide (usually referred as Alox) represents an excellent material for accomplishing chromatographic purifications under gravimetric conditions. Because of the intrinsic characteristic of amphoteric oxide, four different types of Alox are known: basic (pH ca. 9.5), neutral (pH ca. 7.5), weakly acidic (pH ca. 6.0) and acidic (pH ca. 4.5). It appears evident that chemical groups (e.g. amines) susceptible to protonation/deprotonation events could be more or less retained depending on the specific Alox considered. A critical aspect to be highlighted for the successful use of Alox is related to the modulation of the retentive activity tuned by the content of water. The seminal work by Brockmann and Schodder in the early 1940s recognized five different scales of activity for Alox (I to V), being the grade I assigned to the anhydrous one which is also the most active form (5). This latter is almost always the only available form of Alox (basic, neutral, weakly acidic and acidic) from commercial suppliers. As a consequence, it becomes crucial for the chemist being familiar with manipulation techniques for having access to (all) the possible deactivated forms of Alox starting from the Brockmann I. Basing on the current practice, water's content (%) is measured according to the Table below.

This is, the trivial addition of water enables to transform BG-I Alox into one of the less active species to be used. For a productive utilization of Alox, our laboratory found highly versatile adding – with a pipette - the calculated amount of water to the wall of a round-bottom flask containing the previously weighted stationary phase (6). Once this operation is concluded, the flask can be

Table 1.

Brockmann Grade	Alox (g)	Water (g)
I	100	-
II	97	3
III	94	6
IV	90	10
V	85	15

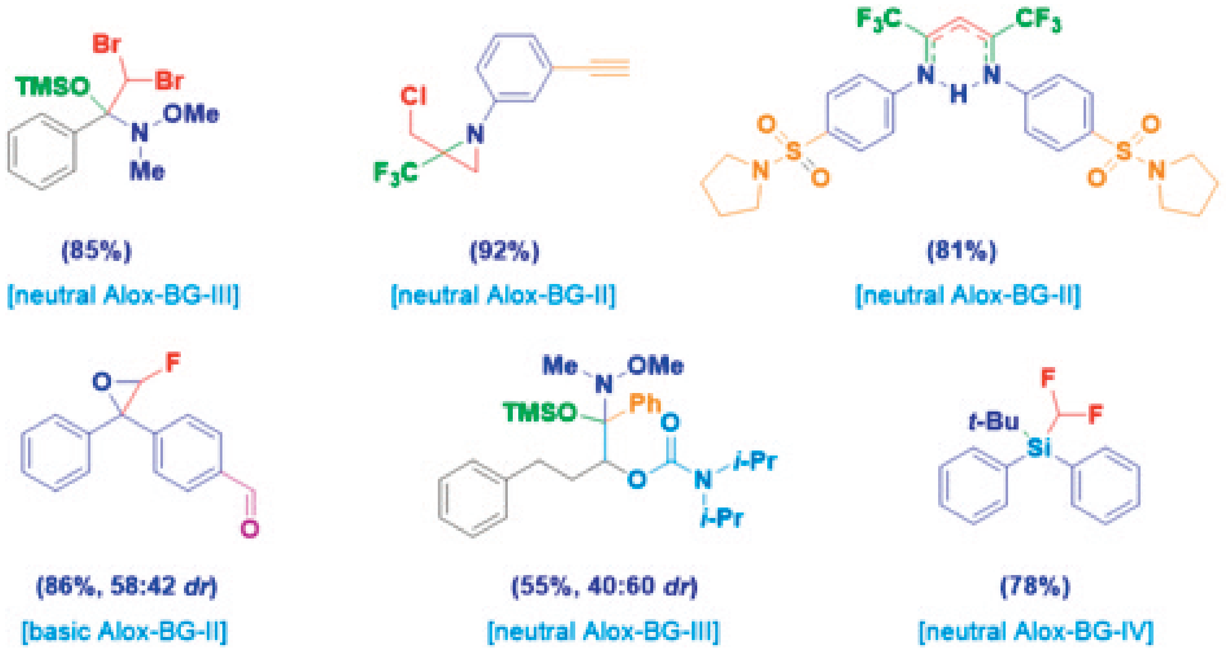
connected to a rotary evaporation apparatus (at 20 °C) without the application of any reduced pressure. As such, the rotational movement serves exclusively for homogenizing the water content on the Alox surface and, thus for deactivating the Brockmann grade I form. After approximately 2 hours of rotation (at medium speed), Alox is ready to be used for preparing the usual slurry – with the selected eluent - for chromatography. Several suppliers offer pre-coated Brockmann grade I Alox TLCs which can be advantageously used for determining the most suitable mobile phase. Because of the inherent high activity of these TLCs, it is recommended for users considering the increasing of Rf values upon the progressive deactivation of Alox (I →→ V) in order to perform an efficient purification. Based on our experience, neutral Alox provides excellent results for separating complex mixtures con-taining densely functionalized amines (7) or activated halomethyl functionalities,(8) in-cluding highly sensitive reaction intermedi-ates. Finally, a note of attention for avoiding degradative effects after the (successful) chromatographic purification with Alox: unsta-ble compounds could undergo decomposition even in deuterated NMR solvents exhibiting some (very minor) acidity as CDCl3. Replacing it with an inert one, as benzene-d6, could be extremely valuable to hamper this undesired event and thus, to secure satisfactory NMR analyses.

Conflict of Interest statement

The Authors report no conflict of interest.

Declaration of Funding

The Authors gratefully acknowledge project PRIN 2022 (ref. 20228W9TBL) and generous support from All4Labels (Hamburg, Germany).



Scheme 1. Representative structures purified with deactivated Alox.

Data Availability Statement

Data sharing is not applicable as no new data were generated or analysed during this study.

2. REFERENCES

1. Constable, D. J. C.; Jimenez-Gonzalez, C.; Henderson, R. K. Org. Proc. Res. Dev. 2007, 11, 133-137.
2. Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923-2925.
3. Lelo, L.; Pillari, V.; Miele, M.; Castiglione, D.; Pace, V. Synlett 2021, 32, 551-560.
4. Castoldi, L.; Ielo, L.; Hoyos, P.; Hernáiz, M. J.; De Luca, L.; Alcántara, A. R.; Holzer, W.; Pace, V. Tetrahedron 2018, 74, 2211-2217.
5. Brockmann, H.; Schodder, H. Ber. Deut. Chem. Ges. 1941, 74, 73-78.
6. Castoldi, L.; Holzer, W.; Langer, T.; Pace, V. Chem. Commun. 2017, 53, 9498-9501.
7. (a) Lelo, L.; Castoldi, L.; Touqeer, S.; Lombino, J.; Roller, A.; Prandi, C.; Holzer, W.; Pace, V. Angew. Chem. Int. Ed. 2020, 59, 20852-20857. (b) Ielo, L.; Touqeer, S.; Roller, A.; Langer, T.; Holzer, W.; Pace, V. Angew. Chem. Int. Ed. 2019, 58, 2479-2484.
8. Miele, M.; Castoldi, L.; Simeone, X.; Holzer, W.; Pace, V. Chem. Commun. 2022, 58, 5761-5764.

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Practical use of aluminium oxide in chromato
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Laura Castoldi and Vittorio Pace
An Real Acad Farm (Internet).
An. Real Acad. Farm.Vol. 91. nº 4 (2025) · pp. 393-396
DOI:http://dx.doi.org/10.53519/analesranf.2025.91.04.06